### UNITED STATES SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

### **FORM 20-F**

(Mark One)

□ REGISTRATION STATEMENT PURSUANT TO SECTION 12(b) OR (g) OF THE SECURITIES EXCHANGE ACT OF 1934

OR

ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the fiscal year ended December 31, 2017

OR

□ TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the transition period from \_\_\_\_\_\_ to \_\_\_\_\_

OR

□ SHELL COMPANY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

Date of event requiring this shell company report Commission File Number 001-38281

### **ERYTECH Pharma S.A.**

(Exact name of registrant as specified in its charter and translation of registrant's name into English)

France (Jurisdiction of incorporation or organization) Bâtiment Adénine, 60 Avenue Rockefeller 69008 Lyon France (Address of principal executive offices) Gil Beyen

**Chairman and Chief Executive Officer** 

ERYTECH Pharma S.A.

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Tel: +33 4 78 74 44 38 Fax: +33 4 78 75 56 29

(Name, Telephone, E-mail and/or Facsimile number and Address of Company Contact Person)

Securities registered or to be registered pursuant to Section 12(b) of the Act.

Title of each class

American Depositary Shares, each representing one ordinary share, nominal value €0.10 per share Ordinary shares, nominal value €0.10 per share\* Name of each exchange on which registered The Nasdaq Global Select Market

The Nasdaq Global Select Market\*

\* Not for trading, but only in connection with the registration of the American Depositary Shares.

Securities registered or to be registered pursuant to Section 12(g) of the Act. None

Securities for which there is a reporting obligation pursuant to Section 15(d) of the Act. None

Indicate the number of outstanding shares of each of the issuer's classes of capital or common stock as of the close of the period covered by the annual report.

Ordinary shares, nominal value €0.10 per share: 17,937,559 as of December 31, 2017

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. 🗆 Yes 🛛 No

If this report is an annual or transition report, indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934.  $\Box$  Yes  $\boxtimes$  No

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days.  $\boxtimes$  Yes  $\Box$  No

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files).  $\Box$  Yes  $\boxtimes$  No

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or an emerging growth company. See definition of "large accelerated filer," "accelerated filer," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer		Accelerated filer		
Non-accelerated filer	$\boxtimes$	Emerging growth company	X	

Non-accelerated filer  $\times$ 

U.S. GAAP  $\Box$ 

Emerging growth company

If an emerging growth company that prepares its financial statements in accordance with U.S. GAAP, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards† provided pursuant to Section 13(a) of the Exchange Act.  $\Box$ 

Indicate by check mark which basis of accounting the registrant has used to prepare the financial statements included in this filing:

Other  $\Box$ International Financial Reporting Standards as issued by the International Accounting Standards Board

If "Other" has been checked in response to the previous question, indicate by check mark which financial statement item the registrant has elected to follow. 

Item 17 
Item 18

If this is an annual report, indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act).  $\Box$  Yes 🗵 No

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Item 19. **Exhibits** 

### INTRODUCTION

Unless otherwise indicated in this Annual Report on Form 20-F, "ERYTECH," "the company," "our company," "we," "us" and "our" refer to ERYTECH Pharma S.A. and its consolidated subsidiary.

"ERYTECH Pharma," "ERYCAPS," "GRASPA," the ERYTECH logo and other trademarks or service marks of ERYTECH Pharma S.A. appearing in this Annual Report on Form 20-F are the property of ERYTECH Pharma S.A. or its subsidiary, ERYTECH Pharma, Inc. Solely for convenience, the trademarks, service marks and trade names referred to in this Annual Report on Form 20-F are listed without the <sup>®</sup> and <sup>TM</sup> symbols, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their right thereto. All other trademarks, trade names and service marks appearing in this Annual Report on Form 20-F are the property of their respective owners. We do not intend to use or display other companies' trademarks and trade names to imply any relationship with, or endorsement or sponsorship of us by, any other companies.

Our audited consolidated financial statements have been prepared in accordance with International Financial Reporting Standards, or IFRS, as issued by the International Accounting Standards Board, or IASB. Our consolidated financial statements are presented in euros, and unless otherwise specified, all monetary amounts are in euros. All references in this Annual Report on Form 20-F to "\$," "US\$," "U.S.\$," "U.S. dollars," "dollars," and "USD" mean U.S. dollars and all references to "€" and "euros" mean euros, unless otherwise noted. Throughout this Annual Report on Form 20-F, references to ADSs mean American Depositary Shares or ordinary shares represented by such ADSs, as the case may be.

### SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 20-F contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, that are based on our management's beliefs and assumptions and on information currently available to our management. All statements other than present and historical facts and conditions contained in this Annual Report on Form 20-F, including statements regarding our future results of operations and financial positions, business strategy, plans and our objectives for future operations, are forward-looking statements. When used in this Annual Report on Form 20-F, the words "anticipate," "believe," "can," "could," "estimate," "expect," "intend," "is designed to," "may," "might," "plan," "potential," "predict," "objective," "should," or the negative of these and similar expressions identify forward-looking statements. Forward-looking statements include, but are not limited to, statements about:

- our ability to attain, maintain and expand marketing approval for eryaspase, which is known under the trade name GRASPA in Europe and Israel;
- the initiation, timing, progress and results of our pre-clinical studies and clinical trials;
- our ability to successfully develop our ERYCAPS platform and advance our pipeline of product candidates;
- our ability to maintain our collaborations with Orphan Europe or Teva Pharmaceutical, or Teva, or to enter into and successfully complete other collaborations, licensing arrangements or in-license or acquire rights to other products, product candidates or technologies;
- our reliance on third parties to manufacture and conduct the clinical trials of our lead product candidate, which we refer to as eryaspase or GRASPA, and our other ERYCAPS product candidates, which could limit our commercialization efforts or delay or limit their future development or regulatory approval;
- our ability to develop sales, commercialization, marketing and manufacturing capabilities and strategy, including future hiring plans;
- our ability to produce adequate supplies of our product candidates for preclinical and clinical testing and to fulfill our contractual obligations to thirdparty distributors;
- the effects of increased competition as well as innovations by new and existing competitors in our industry;
- our ability to obtain funding for our operations;
- our ability to maintain, protect and enhance our intellectual property rights and propriety technologies and to operate our business without infringing the
  intellectual property rights and proprietary technology of third parties;
- regulatory developments in the United States, Europe and other foreign countries;
- our estimates regarding expenses, future revenues, capital requirements and needs for additional financing;
- our planned level of capital expenditures and our belief that our existing cash, cash equivalents and short-term investments will be sufficient to fund our
  operating expenses and capital expenditure requirements for at least the next 24 months;
- the uncertainty of economic conditions in certain countries in Europe and Asia such as related to the United Kingdom's referendum in June 2016 in which voters approved an exit from the European Union, commonly referred to as "Brexit," and general economic conditions; and
- other risks and uncertainties, including those listed in the section of this Annual Report on Form 20-F titled "Item 3.D—Risk Factors."

You should refer to the section of this Annual Report on Form 20-F titled "Item 3.D—Risk Factors" for a discussion of important factors that may cause our actual results to differ materially from those expressed or implied by our forward-looking statements. As a result of these factors, we cannot assure you that the forward-looking statements in this Annual Report on Form 20-F will prove to be accurate. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified time frame or at all. We undertake no obligation to publicly update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

You should read this Annual Report on Form 20-F and the documents that we reference in this Annual Report on Form 20-F and have filed as exhibits to this Annual Report on Form 20-F completely and with the understanding that our actual future results, levels of activity, performance and events and circumstances may be materially different from what we expect. We qualify all of our forward-looking statements by these cautionary statements.

Unless otherwise indicated, information contained in this Annual Report on Form 20-F concerning our industry and the markets in which we operate, including our general expectations and market position, market opportunity and market size estimates, is based on information from independent industry analysts, third-party sources and management estimates. Management estimates are derived from publicly available information released by independent industry analysts and third-party sources, as well as data from our internal research, and are based on assumptions made by us based on such data and our knowledge of such industry and market, which we believe to be reasonable. In addition, while we believe the market opportunity information included in this Annual Report on Form 20-F is generally reliable and is based on reasonable assumptions, such data involve risks and uncertainties and are subject to change based on various factors, including those discussed under the section of this Annual Report on Form 20-F titled "Item 3.D—Risk Factors."

### PART I

Item 1. Identity of Directors, Senior Management and Advisers.

Not applicable.

### Item 2. Offer Statistics and Expected Timetable.

Not applicable.

### Item 3. Key Information.

### A. Selected Financial Data

Our consolidated audited financial statements have been prepared in accordance with IFRS, as issued by the IASB. We derived the selected consolidated statement of income (loss) data for the years ended December 31, 2015, 2016 and 2017 and selected consolidated statement of financial position data as of December 31, 2015, 2016 and 2017 from our consolidated audited financial statements included elsewhere in this Annual Report on Form 20-F. This data should be read together with, and is qualified in its entirety by reference to, "Item 5. Operating and Financial Review and Prospects" as well as our financial statements and notes thereto appearing elsewhere in this Annual Report on Form 20-F. Our historical results are not necessarily indicative of the results to be expected in the future.

### Selected Consolidated Statement of Income (Loss) Data (in thousands, except share and per share data):

	December 31,			
	2015	2016	201	
	Euros	Euros	Euros	US\$(1)
Revenues	€ —	€ —	€ —	\$ —
Other income	2,929	4,138	3,364	4,045
Total operating income	2,929	4,138	3,364	4,045
Operating expenses:				
Research and development	(10,776)	(19,720)	(25,463)	(30,611
General and administrative	(7,736)	(6,808)	(8,791)	(10,569
Total operating expenses	(18,512)	(26,528)	(34,254)	(41,180
Operating loss	(15,583)	(22,390)	(30,889)	(37,135
Financial income	567	488	(2,644)	(3,178
Income tax	3	(10)	3	3
Net loss	€ (15,013)	€ (21,913)	€ (33,530)	\$ (40,310
Basic and diluted loss per share <sup>(2)</sup>	€ (2.16)	€ (2.74)	€ (2.95)	\$ (3.54
Weighted number of shares used for computing basic and diluted				
loss per share	6,957,654	7,983,642	11,370,557	11,370,557

Translated solely for convenience into dollars at the noon buying rate of the Federal Reserve Bank of New York of €1.00 = \$1.2022 at December 29, 2017 (the last business day of 2017).

(2) See Note 4.19 to our financial statements for further details on the calculation of basic and diluted loss per ordinary share.

### Selected Consolidated Statement of Financial Position Data (in thousands, except share and per share data):

As of December 31,					
2015 2016		20			
Euros	Euros	Euros	US\$(1)		
45,634	37,646	185,525	223,038		
53,004	44,967	195,261	234,743		
47,132	35,638	181,419	218,102		
251	2,982	2,236	2,688		
5,621	6,347	11,606	13,953		
5,872	9,329	13,842	16,641		
53,004	44,967	195,261	234,743		
792,461.1	873,264.8	1,793,755.9	2,156,453.3		
7,924,611	8,732,648	17,937,559			
	Euros 45,634 53,004 47,132 251 5,621 5,872 53,004 792,461.1	Euros         Euros           45,634         37,646           53,004         44,967           47,132         35,638           251         2,982           5,621         6,347           5,872         9,329           53,004         44,967           792,461.1         873,264.8	EurosEurosEuros45,63437,646185,52553,00444,967195,26147,13235,638181,4192512,9822,2365,6216,34711,6065,8729,32913,84253,00444,967195,261792,461.1873,264.81,793,755.9		

Translated solely for convenience into dollars at the noon buying rate of the Federal Reserve Bank of New York of €1.00 = \$1.2022 at December 29, 2017 (the last business day of 2017). Note that the European Central Bank exchange rate of €1.00 = \$1.1993 at December 29, 2017 was used to convert the accounts of our U.S. subsidiary, ERYTECH Pharma, Inc., into euros.

#### **Exchange Rate Information**

In this Annual Report on Form 20-F, for convenience only, we have translated certain euro amounts reflected in our financial statements as of and for the year ended December 31, 2017 into U.S. dollars at the rate of  $\leq 1.00 = \$1.2022$ , the noon buying rate of the Federal Reserve Bank of New York for euros at December 29, 2017 (the last business day of 2017). You should not assume that, on that or on any other date, one could have converted these amounts of euros into U.S. dollars at that or any other exchange rate.

The following table sets forth, for each period indicated, the low and high exchange rates for euros expressed in U.S. dollars, the exchange rate at the end of such period and the average of such exchange rates on the last day of each month during such period, based on the noon buying rate of the Federal Reserve Bank of New York for euros into dollars. As used in this Annual Report, the term "noon buying rate" refers to the rate of exchange for the euro, expressed in U.S. dollars per euro, as certified by the Federal Reserve Bank of New York for customs purposes.

		Year Ended December 31,			
	2013	2014	2015	2016	2017
High	1.3816	1.3927	1.2015	1.1516	1.2041
Low	1.2774	1.2101	1.0524	1.0375	1.0416
Rate at end of period	1.3779	1.2101	1.0859	1.0552	1.2022
Average rate per period	1.3281	1.3297	1.1096	1.1072	1.1301

The following table sets forth, for each of the last six months, the low and high exchange rates for euros expressed in U.S. dollars and the exchange rate at the end of such period, based on the noon buying rate of the Federal Reserve Bank of New York for the euro.

	October 2017	November 2017	December 2017	January 2018	February 2018	March 2018
High	1.1847	1.1936	1.2022	1.2488	1.2482	1.2440
Low	1.1580	1.1577	1.1725	1.1922	1.2211	1.2216
Rate at end of period	1.1648	1.1898	1.2022	1.2428	1.2211	1.2320

On December 29, 2017 (the last business day of 2017), the noon buying rate of the Federal Reserve Bank of New York for the euro was  $\leq 1.00 =$  \$1.2022. Unless otherwise indicated, currency translations in this Annual Report on Form 20-F reflect the December 29, 2017 exchange rate.

On March 30, 2018, the noon buying rate of the Federal Reserve Bank of New York for the euro was €1.00 = \$1.2320.

#### **B.** Capitalization and Indebtedness

Not applicable.

### C. Reasons for the Offer and Use of Proceeds

Not applicable.

#### **D. Risk Factors**

Our business faces significant risks. You should carefully consider all of the information set forth in this Annual Report on Form 20-F and in our other filings with the United States Securities and Exchange Commission, or the SEC, including the following risk factors which we face and which are faced by our industry. Our business, financial condition or results of operations could be materially adversely affected by any of these risks. This report also contains forward-looking statements that involve risks and uncertainties. Our results could materially differ from those anticipated in these forward-looking statements, as a result of certain factors including the risks described below and elsewhere in this Annual Report on Form 20-F and our other SEC filings. See "Special Note Regarding Forward-Looking Statements" above.

### **Risks Related to Our Business**

### We have no approved products, which makes it difficult to assess our future prospects.

A key element of our strategy is to use and expand our proprietary ERYCAPS platform to build a pipeline of innovative product candidates and to progress these drug candidates through clinical development for the treatment of severe forms of cancer and orphan diseases. The discovery of therapeutic drugs based on encapsulating molecules inside red blood cells is an emerging field, and the scientific discoveries that form the basis for our efforts to discover and develop drug candidates are relatively new. The scientific evidence to support the feasibility of developing drug candidates based on these discoveries is both preliminary and limited. Although our research and development efforts to date have resulted in a pipeline of product candidates, we have not yet obtained approval for any products, we have not yet generated any revenues from the sale of approved products and we may not be able to develop product candidates that are considered to be safe and effective. Our operations to date have been limited to developing our ERYCAPS platform technology and undertaking preclinical studies and clinical trials of our product candidates, including our lead product candidate, eryaspase, also known as GRASPA, the approved trade name for eryaspase in Europe and in Israel. However, we have not yet demonstrated an ability to overcome many of the risks and uncertainties frequently encountered by companies in new and rapidly evolving fields, particularly in the pharmaceutical industry. Consequently, the ability to predict our future operating results or business prospects is more limited than if we had a longer operating history or approved products on the market.

#### We are heavily dependent on the success of our most advanced product candidate, eryaspase.

Our business and future success depends on our ability to obtain regulatory approval for and, together with third-party collaborators, to successfully commercialize our lead product candidate, eryaspase, which is under clinical development for oncology indications. Eryaspase is our only product candidate in late-stage clinical development, and our business currently depends heavily on its successful development. Eryaspase will require additional clinical and non-clinical development, regulatory review and approval in multiple jurisdictions, substantial investment, access to sufficient commercial manufacturing capacity and significant marketing efforts before we can generate any revenue from product sales. We cannot be certain eryaspase will receive regulatory approval or be successfully commercialized even if we receive regulatory approval. In addition, because eryaspase is our most advanced product candidate, and because our other product candidates are based on the same ERYCAPS platform technology, if eryaspase encounters safety or efficacy problems, developmental delays or regulatory issues or other problems, our development plans and business would be significantly harmed.

### The data we provided to the EMA in connection with our MAA may not be sufficient to support regulatory approval of GRASPA for the treatment of relapsed or refractory ALL on the timeline we expect, or at all.

We submitted an MAA to the EMA for GRASPA for the treatment of relapsed or refractory ALL in September 2015. The Committee for Medicinal Products for Human Use, or CHMP, is the EMA committee responsible for reviewing the MAA. In September 2016, we received from CHMP a Day 180 List of Outstanding Issues. Following discussions with the EMA, we determined that the collection of the additional information requested by CHMP would take more time than allowed in the regulatory approval procedures. Accordingly, we decided to withdraw the MAA in November 2016. We completed activities that are designed to provide data regarding immunogenicity and pharmacodynamics of eryaspase, as well as comparability of eryaspase produced with native versus recombinant asparaginase, and we resubmitted the MAA using this data in October 2017. The EMA is currently reviewing our MAA. The data from these activities may not be sufficient to support regulatory approval, and we may need to conduct additional preclinical studies or clinical trials to support our MAA. The process of conducting preclinical studies and clinical trials necessary to obtain regulatory approval is costly and time consuming, and we may never succeed in achieving marketing approval for GRASPA.

#### We may not be successful in our efforts to use and expand our ERYCAPS platform to develop marketable products.

We believe that our ERYCAPS platform has broad potential application and can be used to encapsulate a wide range of therapeutic agents within red blood cells for which long-circulating therapeutic activity and rapid and specific targeting is desired. However, we are at an early stage of development and our platform has not yet, and may never, lead to approved or marketable products. Even if we are successful in continuing to build our product pipeline, the potential product candidates that we identify may not be suitable for clinical development, including for reasons related to their harmful side effects, limited efficacy or other characteristics that indicate that they are unlikely to be products that will receive marketing approval and achieve market acceptance. Use of red blood cells as the basis for our ERYCAPS platform may result in similar risks that affect the ability of our products to receive marketing approval and achieve market acceptance. If we do not successfully develop and commercialize product candidates based upon our technological approach, we may not be able to obtain product or collaboration revenues in future periods, which would harm our business and our prospects.

### We face substantial competition from companies with considerably more resources and experience than we have, which may result in others discovering, developing, receiving approval for, or commercializing products before or more successfully than us.

The biopharmaceuticals industry is highly competitive. Numerous biopharmaceutical laboratories, biotechnology companies, institutions, universities and other research entities are actively involved in the discovery, research, development and marketing of therapeutics to treat severe forms of cancer and orphan diseases, making it a highly competitive field. We have competitors in a number of jurisdictions, many of which have substantially greater name recognition, commercial infrastructures and financial, technical and personnel resources than we have.

L-asparaginase is currently available in four forms, and the current market primarily includes several products marketed by large pharmaceutical companies, including Jazz Pharmaceuticals PLC and Shire plc. In addition to currently available forms of L-asparaginase and new forms in development, our product candidates also compete with other products that could be used in the treatment of ALL or AML. These potential treatments include monoclonal antibodies, bispecific monoclonal antibodies and chimeric antigen receptor T-cells approaches. Several large pharmaceutical and biotechnology companies, including Amgen Inc., Pfizer Inc., Cellectis S.A., Kite Pharma, Inc. and Novartis AG, are developing these types of therapies for the treatment of AML and ALL. To our knowledge, there is no potential treatment being developed using L-asparaginase for the treatment of pancreatic cancer or other solid tumor indications, but this may change and current marketed asparaginase products may attempt to broaden their indications. Our products and product candidates may also have to compete with other products and product candidates in development by established pharmaceutical companies and biotechnology companies.

Established competitors may invest heavily to quickly discover and develop novel compounds that could make our product candidates obsolete or uneconomical. Any new product that competes with an approved product may need to demonstrate compelling advantages in efficacy, convenience, tolerability and safety to be commercially successful. Any of our product candidates that are approved in the future will also face other competitive factors, including generic competition, which could force us to lower prices or could result in reduced sales. In addition, new products developed by others could emerge as competitors to our product candidates. If we are not able to compete effectively against our current and future competitors, our business will not grow and our financial condition and operations will suffer.

#### Administration of our product candidates could present risks that exist in relation to blood transfusions.

Our product candidates must be intravenously injected and are therefore subject to risks associated with blood transfusions and the blood type compatibility of the donor. We currently acquire red blood cells from blood donations prepared and tested by blood banks, notably the Établissement Français du Sang and the American Red Cross. However, using donor-derived red blood cells presents risks associated with the potential transmission of infectious agents, such as viruses, bacteria, prions and parasites, as well as risks associated with the development of allergies or other complications, such as allo-immunization, post-transfusion graft-versus-host disease, anaphylactic shock or death. Risks associated with the encapsulation of molecules inside red blood cells may vary and will depend on their toxicity. Although the blood banks that supply our red blood cells follow a strict preparation process, approved by health authorities, to detect and reduce possible risks for contamination by infectious agents, we cannot guarantee that our product candidates will not be contaminated, which could be detrimental to our product development and commercialization efforts.

#### **Risks Related to our Financial Position and Capital Needs**

### We have incurred significant losses since our inception and anticipate that we will continue to incur significant losses for the foreseeable future.

We have not yet generated significant revenues and have incurred significant operating losses since our inception. We incurred net losses of  $\in$ 15.0 million,  $\notin$ 21.9 million and  $\notin$ 33.5 million for the years ended December 31, 2015, 2016 and 2017, respectively; and these losses have adversely impacted, and will continue to adversely impact, our equity attributable to shareholders and net assets. These losses are principally the result of our research expenditures and development costs for conducting preclinical studies and clinical trials, as well as general and administrative expenses associated with our operations. We anticipate that our operating losses will continue for at least the next several years as we continue our research and development activities and until we generate substantial revenues from approved product candidates. As of December 31, 2017, we had an accumulated deficit of  $\notin$ 113.5 million.

We have devoted most of our financial resources to research and development, including our clinical and preclinical development activities. To date, we have financed our operations primarily through the sale of equity securities and by obtaining public assistance in support of innovation, such as conditional advances and subsidies from the Banque Publique d'Investissement, or BPI France, and research tax credits. The amount of our future net losses will depend, in part, on the pace and amount of our future expenditures and our ability to obtain funding through equity or debt financings, strategic collaborations or additional grants or tax credits until such time, if ever, as we can generate substantial product revenue. We have not yet received marketing approval for any of our product candidates. Even if we obtain regulatory approval to market a product candidate, our future revenues will depend upon the size of any markets in which our product candidates have received approval, and our ability to achieve sufficient market acceptance, reimbursement from third-party payors and adequate market share for our product candidates in those markets.

We anticipate that our expenses will increase substantially as we:

- continue the preclinical and clinical development of our product candidates;
- expand the scope of our current clinical trials for our product candidates;
- expand our clinical and commercial manufacturing capabilities for our product candidates;
- seek regulatory and marketing approvals for our product candidates that successfully complete clinical trials;
- establish a sales, marketing and distribution infrastructure to commercialize any products for which we may obtain marketing approval and for which we have not entered into a third-party collaboration;
- seek to identify and validate additional product candidates;
- acquire or in-license other product candidates and technologies;
- make milestone, royalty or other payments under in-license or collaboration agreements;
- maintain, protect and expand our intellectual property portfolio;
- attract new and retain existing skilled personnel; and
- create additional infrastructure to support our operations in the United States.

Our operating results may fluctuate significantly from year to year, such that a period-to-period comparison of our results of operations may not be a good indication of our future performance. In any particular period or periods, our operating results could be below the expectations of securities analysts or investors, which could cause the price of the ordinary shares and ADSs to decline.

# We may need to raise additional funding, which may not be available on acceptable terms, or at all, and failure to obtain this necessary capital when needed may force us to delay, limit or terminate our product development efforts or other operations.

We are currently advancing our product candidates through preclinical and clinical development. Developing product candidates is expensive, lengthy and risky, and we expect our research and development expenses to increase substantially in connection with our ongoing activities, particularly as we advance our product candidates toward commercialization.

As of December 31, 2017, our cash and cash equivalents were &185.5 million (\$223 million). The net proceeds from our November 2017 global offering were approximately &112.1 million (\$130.4 million), after deducting underwriting commissions and offering expenses which amounted to &11.5 million (\$13.4 million). We expect that our existing cash and cash equivalents (of which the net proceeds from the global offering are a part) will be sufficient to fund our current operations for at least the next 24 months. However, our operating plan may change as a result of many factors currently unknown to us, and we may need to seek additional funds sooner than planned, through public or private equity or debt financings, government or other third-party funding, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements or a combination of these approaches. In any event, we will require additional capital to pursue preclinical and clinical activities, obtain regulatory approval for and commercialize our product candidates. Even if we believe we have sufficient funds for our current or future operating plans, we may seek additional capital if market conditions are favorable or if we have specific strategic considerations.

Any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize our product candidates. In addition, we cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. Moreover, the terms of any financing may adversely affect the holdings or the rights of our shareholders and the issuance of additional securities, whether equity or debt, by us, or the possibility of such issuance, may cause the market price of the ADSs or ordinary shares to decline. The sale of additional equity or convertible securities would be dilutive to our shareholders. The incurrence of indebtedness would result in increased fixed payment obligations and we may be required to agree to certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. We could also be required to seek funds through arrangements with collaborative partners or otherwise at an earlier stage than otherwise would be desirable and we may be required to relinquish rights to some of our technologies or product candidates or otherwise agree to terms

unfavorable to us. If we are unable to obtain funding on a timely basis, we may be required to significantly curtail, delay or discontinue one or more of our research or development programs or the commercialization of any product candidate or be unable to expand our operations or otherwise capitalize on our business opportunities, as desired, which could impair our growth prospects.

# We may be forced to repay conditional advances prematurely if we fail to comply with our contractual obligations under certain innovation grant agreements.

Since inception through December 31, 2017, we have received &2.7 million in non-refundable grants and &2.0 million in conditional advances from BPI France. If we fail to comply with our contractual obligations under the applicable innovation grant agreements, including if we lose our exclusive right to commercially develop our product candidates, we could be forced to repay the conditional advances (amounting to &1.2 million at December 31, 2017) ahead of schedule. Such premature repayment could adversely affect our ability to finance our research and development projects, in which case we would need to locate alternative sources of capital, which may not be available on commercially reasonable terms or at all.

#### Risks Related to the Discovery and Development of and Obtaining Regulatory Approval for our Product Candidates

### If our product candidates are not approved for marketing by applicable government authorities, we will be unable to commercialize them.

The European Commission (following review by the EMA) in Europe, the FDA in the United States and comparable regulatory authorities in other jurisdictions must approve new drug or biologic candidates before they can be commercialized, marketed, promoted or sold in those territories. We must provide these regulatory authorities with data from preclinical studies and clinical trials that demonstrate that our product candidates are safe and effective for a defined indication before they can be approved for commercial distribution. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is inherently uncertain as to outcome. We must provide data to ensure the identity, strength, quality and purity of the drug substance and drug product. Also, we must assure the regulatory authorities that the characteristics and performance of the clinical batches will be replicated consistently in the commercial batches. We have focused our development and planned commercialization efforts on Europe and the United States. In September 2015, we submitted an MAA to the EMA for the approval of GRASPA as a treatment for ALL. However, we announced our withdrawal of the MAA for GRASPA in November 2016. In October 2017, we resubmitted to the EMA our MAA for GRASPA for relapsed or refractory ALL and the EMA is currently reviewing our MAA. The processes by which regulatory approvals are obtained from the EMA and FDA to market and sell a new product are complex, require a number of years and involve the expenditure of substantial resources. We cannot assure you that GRASPA, eryaspase or any of our future product candidates will receive EMA or FDA approval. Even if we obtain marketing approval of any of our product candidates in a major pharmaceutical market such as the United States or Europe, we may never obtain approval or commercialize our products in other major markets, due to varying approval procedures or otherwise, which would limit our ability to realize their full market potential.

### Our product candidates will need to undergo clinical trials that are time-consuming and expensive, the outcomes of which are unpredictable, and for which there is a high risk of failure. If clinical trials of our product candidates fail to satisfactorily demonstrate safety and efficacy to the EMA, FDA and other regulators, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of these product candidates.

Preclinical testing and clinical trials are long, expensive and unpredictable processes that can be subject to extensive delays. We cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, if at all. It may take several years to complete the preclinical testing and clinical development necessary to commercialize a product candidate, and delays or failure can occur at any stage. Interim results of clinical trials do not necessarily predict final results, and success in preclinical testing and early clinical trials does not ensure that later clinical trials will be successful. A number of companies in the pharmaceutical, biopharmaceutical and biotechnology industries have suffered significant setbacks in advanced clinical trials even after promising results in earlier trials, and we cannot be certain that we will not face similar setbacks. The design of a clinical trial can determine whether its results will support approval of a product, and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced. An unfavorable outcome in one or more trials may require us to delay, reduce the scope of, or eliminate one or more product development programs, which could have a material adverse effect on our business and financial condition and on the value of our securities.

In connection with clinical testing and trials, we face a number of risks, including risks that:

a product candidate is ineffective, inferior to existing approved medicines, unacceptably toxic, or has unacceptable side effects;

- patients may die or suffer other adverse effects for reasons that may or may not be related to the product candidate being tested;
- extension studies on long-term tolerance could invalidate the use of our product;
- the results may not confirm the positive results of earlier testing or trials; and
- the results may not meet the level of statistical significance required by the EMA, FDA or other regulatory agencies to establish the safety and efficacy of our product candidates.

The results of preclinical studies do not necessarily predict clinical success, and larger and later-stage clinical trials may not produce the same results as earlier-stage clinical trials. Our clinical trials of eryaspase conducted to date have generated favorable safety and efficacy data other than the results obtained in our Phase 2b clinical trial in AML noted below; however, we may have different results in other indications. Differences in enrollment criteria and different combinations with other treatment modalities may also lead to different outcomes in our future clinical trials. As a result, we may not observe a similarly favorable safety or efficacy profile as in our prior clinical trials. In addition, we cannot assure you that in the course of potential widespread use in the future, we will not suffer setbacks in maintaining production quality or stability. Frequently, product candidates developed by pharmaceutical, biopharmaceutical and biotechnology companies have shown promising results in early preclinical studies or clinical trials, but have subsequently suffered significant setbacks or failed in later clinical trials. In addition, clinical trials of product candidates often reveal that it is not possible or practical to continue development efforts for these product candidates. For example, in December 2017, we announced that our ENFORCE 1 trial, a multinational, randomized Phase 2b clinical trial in Europe in AML patients over the age of 65 who are unfit for treatment with intensive chemotherapy, did not meet its primary endpoint of overall survival.

If we do not successfully complete preclinical and clinical development, we will be unable to market and sell our product candidates and generate revenues. Even if we do successfully complete clinical trials, those results are not necessarily predictive of results of additional trials that may be needed before marketing applications may be submitted to the EMA or FDA, as applicable. Although there are a large number of drugs and biologics in development in Europe, the United States and other countries, only a small percentage result in the submission of a marketing application, even fewer are approved for commercialization, and only a small number achieve widespread physician and consumer acceptance following regulatory approval. If our clinical trials are substantially delayed or fail to prove the safety and effectiveness of our product candidates in development, we may not receive regulatory approval of any of these product candidates and our business and financial condition will be materially harmed.

### Delays, suspensions and terminations in our clinical trials could result in increased costs to us and delay or prevent our ability to generate revenues.

Human clinical trials are very expensive, time-consuming, and difficult to design, implement and complete. The completion of trials for eryaspase or our other product candidates may be delayed for a variety of reasons, including delays in:

- demonstrating sufficient safety and efficacy to obtain regulatory approval to commence a clinical trial;
- reaching agreement on acceptable terms with prospective contract research organizations, or CROs, and clinical trial sites;
- validating test methods to support quality testing of the drug substance and drug product;
- obtaining sufficient quantities of the drug substance or other materials necessary to conduct clinical trials;
- manufacturing sufficient quantities of a product candidate;
- obtaining approval of applications from regulatory authorities for the commencement of a clinical trial;
- obtaining institutional review board, or IRB, approval to conduct a clinical trial at a prospective clinical trial site;
- determining dosing and clinical trial design; and
- patient enrollment, which is a function of many factors, including the size of the patient population, the nature of the protocol, the proximity of patients to clinical trial sites, the availability of effective treatments for the relevant disease and the eligibility criteria for the clinical trial.

For example, in our Phase 1 clinical trial in the United States in adult ALL patients, patient enrollment took longer than expected.

The commencement and completion of clinical trials for our product candidates may be delayed, suspended or terminated due to a number of factors, including:

- lack of effectiveness of product candidates during clinical trials;
- adverse events, safety issues or side effects relating to the product candidates or their formulation;
- inability to raise additional capital in sufficient amounts to continue clinical trials or development programs, which are very expensive;
- the need to sequence clinical trials as opposed to conducting them concomitantly in order to conserve resources;
- our inability to enter into collaborations relating to the development and commercialization of our product candidates;
- our failure to conduct clinical trials in accordance with regulatory requirements;
- our inability to manufacture or obtain from third parties materials sufficient for use in preclinical studies and clinical trials;
- governmental or regulatory delays and changes in regulatory requirements, policy and guidelines, including mandated changes in the scope or design of clinical trials or requests for supplemental information with respect to clinical trial results;
- delays in patient enrollment, variability in the number and types of patients available for clinical trials, and lower-than anticipated retention rates for patients in clinical trials;
- difficulty in patient monitoring and data collection due to failure of patients to maintain contact after treatment; and
- varying interpretations of our data, and regulatory commitments and requirements by the EMA, FDA and similar regulatory agencies.

For example, our Investigational New Drug application, or IND, submitted to the FDA for eryaspase was on clinical hold from its original submission in July 2011 until March 21, 2013, and we cannot assure you that our current IND for eryaspase or any future IND will not be subject to clinical holds.

Many of these factors may also ultimately lead to denial of our marketing application for eryaspase or our other product candidates. If we experience delay, suspensions or terminations in a clinical trial, the commercial prospects for the related product candidate will be harmed, and our ability to generate product revenues will be delayed or such revenues could be reduced or fail to materialize.

### We may find it difficult to enroll patients in our clinical trials, which could delay or prevent us from proceeding with clinical trials of our product candidates.

Identifying and qualifying patients to participate in clinical trials of our product candidates is critical to our success. The timing of our clinical trials depends on our ability to recruit patients to participate, as well as completion of required follow-up periods. If patients are unwilling to enroll in our clinical trials because of competitive clinical trials for similar patient populations or for other reasons, the timeline for recruiting patients, conducting studies and obtaining regulatory approval of our product candidates may be delayed. These delays could result in increased costs, delays in advancing our product candidates, delays in testing the effectiveness of our product candidates or termination of clinical trials altogether.

Some of our current product candidates are being developed to treat severe forms of cancer and other orphan diseases, which are generally defined as having a patient population of fewer than 200,000 individuals in the United States. For example, 150,000 new cases of pancreatic cancer diagnosed each year in the United States and Europe. We may not be able to initiate or continue clinical trials if we cannot enroll a sufficient number of eligible patients to participate in the clinical trials required by the FDA, EMA or other regulatory authorities. Also, we may not be able to identify, recruit and enroll a sufficient number of patients, or those with required or desired characteristics, to complete our clinical trials in a timely manner. Patient enrollment can be affected by many factors, including:

- size of the patient population and process for identifying patients;
- eligibility and exclusion criteria for our clinical trials;
- perceived risks and benefits of our product candidates;
- severity of the disease under investigation;
- proximity and availability of clinical trial sites for prospective patients;
- ability to obtain and maintain patient consent;
- patient drop-outs prior to completion of clinical trials;
- patient referral practices of physicians; and
- ability to monitor patients adequately during and after treatment.

Our ability to successfully initiate, enroll and complete clinical trials in any foreign country is subject to numerous risks unique to conducting business in foreign countries, including:

- difficulty in establishing or managing relationships with CROs and physicians;
- different standards for the conduct of clinical trials;
- inability to locate qualified local consultants, physicians and partners; and
- the potential burden of complying with a variety of foreign laws, medical standards and regulatory requirements, including the regulation of pharmaceutical and biotechnology products and treatment.

If we have difficulty enrolling a sufficient number of patients or finding additional clinical trial sites to conduct our clinical trials as planned, we may need to delay, limit or terminate ongoing or planned clinical trials, any of which could have an adverse effect on our business, financial condition, results of operations and prospects.

# Changes in regulatory requirements, guidance from regulatory authorities or unanticipated events during our clinical trials of our product candidates could necessitate changes to clinical trial protocols or additional clinical trial requirements, which would result in increased costs to us and could delay our development timeline.

Changes in regulatory requirements, FDA guidance or guidance from the EMA or other European regulatory authorities, or unanticipated events during our clinical trials, may force us to amend clinical trial protocols. The regulatory authorities could also impose additional clinical trial requirements. Amendments to our clinical trial protocols would require resubmission to the FDA, EMA, national clinical trial regulators and IRBs for review and approval, which may adversely impact the cost, timing or successful completion of a clinical trial. If we experience delays completing, or if we terminate, any of our clinical trials, or if we are required to conduct additional clinical trials, the commercial prospects for our product candidates may be harmed and our ability to generate product revenue will be delayed.

The United States and European formulations of eryaspase differ, and regulatory authorities in each jurisdiction may not accept data from alternative eryaspase formulations in other jurisdiction(s), which may result in delays and additional costs in order to conduct additional comparability studies or the need to repeat nonclinical and clinical studies in order to obtain approval in each jurisdiction in which we intend to commercialize eryaspase.

We use different formulations of eryaspase in our United States and European manufacturing processes, including the use of different preservative solutions for the storage and transportation of red blood cells and L-asparaginase encapsulated in red blood cells, an additional washing step that is used in our United States formulation in order to meet lower free hemoglobin

standards in the United States, and separate sourcing of the active substance starting material of L-asparaginase. Although we have conducted in vitro comparability studies designed to demonstrate the equivalence of both formulations, additional comparability studies may be required by regulatory authorities. Even with additional comparability studies, regulatory authorities may not accept nonclinical or clinical data generated using an alternative formulation of ervaspase which may result in delays and costly requirements to repeat nonclinical and clinical studies in order to obtain marketing approval.

### In the United States, our product candidates will be regulated as biological products, or biologics, which may subject them to competition sooner than we currently anticipate.

The Biologics Price Competition and Innovation Act of 2009, or BPCIA, was enacted as part of the 2010 enactments of the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively, the ACA, to establish an abbreviated licensure pathway for biological products shown to be biosimilar to, or interchangeable with, an FDA-licensed biological reference product. "Biosimilarity" means that the biological product is highly similar to the reference product notwithstanding minor differences in clinically inactive components and there are no clinically meaningful differences between the biological product and the reference product in terms of safety, purity, and potency of the product. To meet the higher standard of "interchangeability," an applicant must provide sufficient information to show biosimilarity and demonstrate that the biological product can be expected to produce the same clinical result as the reference product in any given patient and, if the biological product is administrated more than once to an individual, the risk in terms of safety or diminished efficacy of alternating or switching between the use of the biological product and the reference product is not greater than the risk of using the reference product without such alternation or switch.

Under the BPCIA, an application for a biosimilar or interchangeable product cannot be approved by the FDA until 12 years after the reference product was first licensed, and the FDA will not even accept an application for review until four years after the date of first licensure. The law is evolving, complex and is still being interpreted and implemented by the FDA. As a result, its ultimate impact, implementation, and meaning are subject to uncertainty. While it is uncertain when such processes intended to implement BPCIA may be fully adopted by the FDA, any such processes could have a material adverse effect on the future commercial prospects for our biological products.

We believe that any of our product candidates approved as a biological product under a Biologics License Application, or BLA, should qualify for the 12-year period of exclusivity. However, there is a risk that this exclusivity could be shortened due to congressional action or otherwise, potentially creating the opportunity for biosimilar or interchangeable competition sooner than we currently anticipate. Moreover, the process by which an interchangeable product, once approved, will be substituted for any one of our reference products in a way that is similar to traditional generic substitution for non-biological products, such as drugs, is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing and subject to interpretation.

### In the European Union, GRASPA contains a known active substance, which would undermine its data and marketing exclusivities; however, this will not affect GRASPA's orphan product exclusivity.

Data exclusivity refers to the period of time during which another company cannot refer to our data held in the authority's files in support of its marketing authorization. The subsequent market exclusivity refers to the period of time during which another company may use our data in support of its marketing authorization for a generic, hybrid or biosimilar product, but the product in question may not be placed on the market. For products containing new active substances, this effectively prevents certain products, such as generics and similar biological products, from being placed on the market during the combined data and marketing exclusivity period. This combined period usually lasts for 10 years from the date of approval of the product containing the new active substance.

Because the active ingredient in GRASPA is not a new active substance, the 10-year period of protection against generics and similar biological products is undermined. Competitors developing such products could receive European Union marketing authorizations and place their products on the European Union market within 10 years of GRASPA's own marketing authorization, if obtained.

However, if we still have orphan drug designation for GRASPA at the time we receive marketing approval from the EMA, we would still benefit from the independent period of market exclusivity afforded to orphan products. In the European Union, this is usually a period of 10 years from the date of marketing approval. The exclusivity period can be reduced to six years if a drug no longer meets the criteria for orphan drug designation or if the drug is sufficiently profitable so that market exclusivity is no longer justified. The exclusivity period may increase to 12 years if, among other things, the MAA includes the results of studies from an agreed pediatric investigation plan. During the orphan exclusivity period, regulators should not accept or approve applications for the approval of a similar medicine for the same therapeutic indication, unless the second product is demonstrably safer, more effective or otherwise clinically superior. Regulators may approve different products for the same condition as GRASPA.

# We rely on third parties to assist in our discovery and development activities, and the loss of any of our relationships with research institutions could hinder our product development prospects.

We currently have and expect to continue to depend on collaborations with public and private research institutions to conduct some of our early-stage drug discovery activities. If we are unable to enter into research collaborations with these institutions, or if any one of these institutions fails to work efficiently with us, the research, development or marketing of our product candidates planned as part of the research collaboration could be delayed or canceled. In the event a research agreement is terminated or we become no longer in a position to renew the arrangement under acceptable conditions, our drug discovery and development activities may also be delayed.

### We rely on third parties to conduct our clinical trials and perform data collection and analysis, which may result in costs and delays that prevent us from successfully commercializing our product candidates.

We rely, and will rely in the future, on medical institutions, clinical investigators, CROs, contract laboratories and collaborators to perform data collection and analysis and to carry out our clinical trials. Our development activities or clinical trials conducted in reliance on third parties may be delayed, suspended, or terminated if:

- the third parties do not devote a sufficient amount of time or effort to our activities or otherwise fail to successfully carry out their contractual duties or to meet regulatory obligations or expected deadlines;
- we replace a third party; or
- the quality or accuracy of the data obtained by third parties is compromised due to their failure to adhere to clinical protocols, regulatory requirements, or for other reasons.

We generally would not have the ability to control the performance of third parties in their conduct of development activities. In the event of a default, bankruptcy or shutdown of, or a dispute with, a third party, we may be unable to enter into a new agreement with another third party on commercially acceptable terms. Further, third-party performance failures may increase our development costs, delay our ability to obtain regulatory approval, and delay or prevent the commercialization of our product candidates. In addition, our third-party agreements usually contain a clause limiting such third party's liability, such that we may not be able to obtain full compensation for any losses we may incur in connection with the third party's performance failures. While we believe that there are numerous alternative sources to provide these services, in the event that we seek such alternative sources, we may not be able to enter into replacement arrangements without incurring delays or additional costs.

# We have entered, and may in the future enter into, collaboration agreements with third parties for the development and commercialization of our product candidates, which may affect our ability to generate revenues.

We have limited capabilities for product development and may seek to enter into collaborations with third parties for the development and potential commercialization of our product candidates. Should we seek to collaborate with a third party with respect to a prospective development program, we may not be able to locate a suitable collaborator and may not be able to enter into an agreement on commercially reasonable terms or at all. Even if we succeed in securing collaborators for the development and commercialization of our product candidates, such as the arrangements we have entered into related to the commercialization of GRASPA for the treatment of ALL and AML in Europe and Israel, we have limited control over the amount and timing that our collaborators may dedicate to the development or commercialization of our product candidates. These collaborations pose a number of risks, including the following:

- collaborators may not have sufficient resources or decide not to devote the necessary resources due to internal constraints such as budget limitations, lack of human resources, or a change in strategic focus;
- collaborators may believe our intellectual property is not valid or is unenforceable or the product candidate infringes on the intellectual property rights of others;
- collaborators may dispute their responsibility to conduct development and commercialization activities pursuant to the applicable collaboration, including the payment of related costs or the division of any revenues;
- collaborators may decide to pursue a competitive product developed outside of the collaboration arrangement;
- collaborators may not be able to obtain, or believe they cannot obtain, the necessary regulatory approvals; or
- collaborators may delay the development or commercialization of our product candidates in favor of developing or commercializing another party's product candidate.

Thus, collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all.

Some collaboration agreements are terminable without cause on short notice. Once a collaboration agreement is signed, it may not lead to commercialization of a product candidate. We also face competition in seeking out collaborators. If we are unable to secure new collaborations that achieve the collaborator's objectives and meet our expectations, we may be unable to advance our product candidates and may not generate meaningful revenues.

# Due to our limited resources and access to capital, our decisions to prioritize development of certain product candidates may adversely affect our business prospects.

Because we have limited resources and access to capital to fund our operations, we must decide which product candidates to pursue and the amount of resources to allocate to each. As such, we are currently primarily focused on the development of eryaspase for the treatment of pancreatic cancer, solid tumors and ALL. Our decisions concerning the allocation of research, collaboration, management and financial resources toward particular compounds, product candidates or therapeutic areas may not lead to the development of viable commercial products and may divert resources away from more promising opportunities. Similarly, our potential decisions to delay, terminate or collaborate with third parties with respect to some of our product development programs may also prove not to be optimal and could cause us to miss valuable opportunities. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights. If we make incorrect determinations regarding the market potential of our product candidates or misread trends in the pharmaceutical industry, our business prospects could be harmed.

### **Risks Related to the Commercialization of Our Product Candidates**

# We will be largely dependent on Orphan Europe and Teva for the marketing of GRASPA for the treatment of ALL and AML in Europe and ALL in Israel, respectively.

We have entered into exclusive distribution agreements with Orphan Europe and Teva with respect to the commercialization of GRASPA for the treatment of ALL and AML in Europe and in Israel, respectively. If approved, the marketing and commercial success of GRASPA in these countries will be largely driven by the efforts of Orphan Europe and Teva and will depend on marketing and commercial efforts deployed by these third parties.

Our exclusive license and distribution agreement with Orphan Europe requires Orphan Europe to commercialize GRASPA for the treatment of ALL and AML in 38 countries in Europe, including every country in the European Union, if we are granted regulatory approval. In addition, Orphan Europe is responsible for seeking regulatory approval for GRASPA in the treatment of ALL and AML in the 10 countries that are not part of the European Union. Although our agreement requires Orphan Europe to submit periodic marketing plans to estimate the future sales of GRASPA, Orphan Europe is not subject to any minimum sales requirements, and we cannot assure you that they will be successful in commercializing GRASPA, if it is approved. In addition, if Orphan Europe's sales of GRASPA fail to meet our expectations, we have limited recourse and may be subject to a substantial penalty should we choose not to renew our agreement at the end of its term. If Orphan Europe fails to successfully perform or deliver on its obligations under our agreement, we may incur additional, potentially significant costs or delays in connection with our commercialization, distribution and sales efforts.

Our exclusive distribution agreement with Teva requires Teva to seek regulatory approval for GRASPA in Israel for the treatment of ALL and, if approved, to market and distribute GRASPA within Israel. Although our agreement requires Teva to meet minimum sales objectives each year after GRASPA's launch, our only remedy for Teva's failure to meet those objectives is termination of the agreement, which would require us to spend considerable time and resources either developing our own marketing capabilities in Israel or identifying a suitable alternative distributor, if one exists. We cannot guarantee that Teva will be successful in obtaining regulatory approval for or commercializing GRASPA, and any failure of Teva to do so would negatively impact our business and our future revenues.

In addition to our dependence on the marketing efforts of Orphan Europe and Teva, we also face the risk of noncompliance by these and other future distributors with local anti-corruption laws, the U.S. Foreign Corrupt Practices Act, and other local and international regulations, and we have limited ability to control their actions to ensure they are in compliance. Noncompliance by these or future distributors could expose us to civil or criminal liability, fines and/or prohibitions on selling our products in certain countries.

We expect that our product revenues would be adversely impacted with the loss or transition of these or any future distributors of our products. If we or any of our current or future commercialization partners choose to terminate any of our distribution agreements, we would either need to reach agreement with, qualify, train and supply a replacement distributor or supply and service customer accounts in those territories ourselves. Although our existing distribution agreements generally provide that the distributor will promptly and efficiently transfer its existing customer agreements to us, there can be no

assurance that this will happen in a timely manner or at all. These factors may be disruptive for our customers, and our reputation may be damaged as a result. Our distributors may have more established relationships with potential customers than a new distributor or we may have in particular territories, which could adversely impact our ability to successfully commercialize GRASPA in these territories. In addition, it may take longer for us to be paid if payment timing and terms in these new arrangements are less favorable to us than those in our existing distribution arrangements. If we service customers directly rather than through distributors, we will incur additional expense and our working capital may be negatively impacted due to longer periods from cash collection from direct sales customers when compared to the timing of cash collection from distributors. Current or transitioning distributors may irreparably harm relationships with local existing and prospective customers and our standing with the biopharmaceutical community in general. In the event that we are unable to find alternative distributors or mobilize our own sales efforts in the territories in which a particular distributor operates, customer supply, our reputation and our operating results may be negatively impacted.

#### Even if we successfully complete clinical trials of our product candidates, those candidates may not be commercialized successfully for other reasons.

Even if we successfully complete clinical trials for one or more of our product candidates and obtain relevant regulatory approvals, those candidates may not be commercialized for other reasons, including:

- failing to receive regulatory clearances required to market them as drugs;
- being subject to proprietary rights held by others;
- failing to obtain clearance from regulatory authorities on the manufacturing of our products;
- being difficult or expensive to manufacture on a commercial scale;
- having adverse side effects that make their use less desirable;
- failing to compete effectively with products or treatments commercialized by competitors; or
- failing to show that the long-term benefits of our products exceed their risks.

### Even if any of our product candidates are commercialized, they may fail to achieve the degree of market acceptance by physicians, patients, third-party payors or the medical community in general necessary for commercial success.

Even if the medical community accepts a product as safe and efficacious for its indicated use, physicians may choose to restrict the use of the product if we are unable to demonstrate that, based on experience, clinical data, side-effect profiles and other factors, our product is preferable to any existing drugs or treatments. We cannot predict the degree of market acceptance of any product candidate that receives marketing approval, which will depend on a number of factors, including, but not limited to:

- the demonstration of the clinical efficacy and safety of the product;
- the approved labeling for the product and any required warnings;
- the advantages and disadvantages of the product compared to alternative treatments;
- our ability to educate the medical community about the safety and effectiveness of the product;
- the experience of clinicians with other potential treatments that use red blood cells to deliver therapeutics;
- · the coverage and reimbursement policies of government and commercial third-party payors pertaining to the product; and
- the market price of our product relative to competing treatments.

If we are unable to establish sales, marketing and distribution capabilities for our product candidates, whether it be an internal infrastructure or an arrangement with a commercial partner such as the ones that we have entered into for commercialization of GRASPA for the treatment of ALL and AML in Europe and in Israel, we may not be successful in commercializing those product candidates if and when they are approved.

We do not have a sales or marketing infrastructure and have no experience in the sale, marketing or distribution of pharmaceutical drugs. Under our arrangements with Orphan Europe and Teva, these third parties are responsible for the commercialization of eryaspase under the brand name GRASPA for the treatment of ALL and AML in Europe and in Israel, respectively, if GRASPA receives regulatory approval in such territory. To achieve commercial success for eryaspase outside of those countries, including in the United States, for the treatment of pancreatic cancer, ALL and AML, as well as eryaspase for the treatment of other indications and any other product candidates for which we may obtain marketing approval, we will need to establish a sales and marketing organization to market or co-promote those products. There are risks involved with establishing our own sales, marketing and distribution capabilities. For example, recruiting and training a sales force is expensive and time-consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

Factors that may inhibit our efforts to commercialize products on our own include:

- our inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to physicians and educate an adequate number of physicians on the benefits of any future products;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more products; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

If we are unable to establish our own sales, marketing and distribution capabilities and enter into arrangements with third parties to perform these services, our revenue and our profitability, if any, are likely to be lower than if we were to sell, market and distribute any products that we develop ourselves.

# Even though we have obtained orphan drug designation from the EMA for eryaspase for the treatment of pancreatic cancer, ALL and AML and from the FDA for eryaspase for the same indications, we may not be able to obtain orphan drug marketing exclusivity for eryaspase or any of our other product candidates for other indications.

Regulatory authorities in some jurisdictions, including the United States and the European Union, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a drug as an orphan drug if it is intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals annually in the United States. Similarly, in Europe, a medicinal product may receive orphan designation under Article 3 of Regulation (EC) 141/2000. This applies to products that are intended for a life-threatening or chronically debilitating condition and either the condition affects no more than five in 10,000 persons in the European Union when the application is made or the product, without the benefits derived from orphan status, would unlikely generate sufficient return in the European Union to justify the necessary investment. Moreover, in order to obtain orphan designation in the European Union, it is necessary to demonstrate that there exists no satisfactory method of diagnosis, prevention or treatment of the condition. The EMA will reassess whether GRASPA continues to meet the criteria for orphan drug designation in the European Union at the time it reviews a marketing authorization application for the product. If the EMA considers that GRASPA no longer meets these criteria, for example, because it does not offer a significant benefit over existing therapies, it may revoke GRASPA's orphan drug designation prior to approval.

The EMA has granted orphan drug designation for GRASPA for the treatment of pancreatic cancer, ALL and AML, and the FDA has granted orphan drug designation for eryaspase for the same indications. We may seek orphan drug designation for our other product candidates, and with respect to other indications. Generally, if a drug with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the drug is entitled to a period of marketing exclusivity, which precludes the FDA from approving another marketing application for the same drug for that time period or the EMA or any other medicines regulator in the European Union from approving a similar medicinal product. The applicable period is seven years in the United States and usually 10 years in the European Union. The European Union exclusivity period can be reduced to six years if a drug no longer meets the criteria for orphan drug designation or if the drug is sufficiently profitable so that market exclusivity is no longer justified. Orphan drug exclusivity may be lost if the FDA or EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition.

Even if we obtain orphan drug exclusivity for a product candidate, that exclusivity may not effectively protect the candidate from competition because different drugs can be approved for the same condition. Even after an orphan drug is approved, the applicable regulatory authority can subsequently approve another drug for the same condition if it concludes that the later



drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care. Similarly, if our competitors are able to obtain orphan product exclusivity for their products in the same indications for which we are developing our product candidates, we may not be able to have our products approved by the applicable regulatory authority for a significant period of time.

### Even if we obtain marketing approvals for our product candidates, the terms of approvals and ongoing regulation of our products may limit how we or they market our products, which could materially impair our ability to generate revenues.

Even if we receive regulatory approval for a product candidate, this approval may carry conditions that limit the market for the product or put the product at a competitive disadvantage relative to alternative therapies. For instance, a regulatory approval may limit the indicated uses for which we can market a product or the patient population that may utilize the product, or may be required to carry a warning in its labeling and on its packaging. Products with boxed warnings are subject to more restrictive advertising regulations than products without such warnings. These restrictions could make it more difficult to market any product candidate effectively. Accordingly, assuming we receive marketing approval for one or more of our product candidates, we will continue to expend time, money and effort in all areas of regulatory compliance.

# Government restrictions on pricing and reimbursement, as well as other healthcare payor cost-containment initiatives, may negatively impact our ability to generate revenues even if we obtain regulatory approval to market a product.

Our ability to commercialize any products successfully also will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. Government authorities and other third-party payors, such as private health insurers and health maintenance organizations, determine which medications they will cover and establish reimbursement levels. Assuming we obtain coverage for a given product by a third-party payor, the resulting reimbursement payment rates may not be adequate or may require co-payments that patients find unacceptably high. Patients who are prescribed medications for the treatment of their conditions, and their prescribing physicians, generally rely on third-party payors to reimburse all or part of the costs associated with their prescription drugs. Patients are unlikely to use our products unless coverage is provided and reimbursement is adequate to cover all or a significant portion of the cost of our products. Therefore, coverage and adequate reimbursement is critical to new product acceptance. Coverage decisions may depend upon clinical and economic standards that disfavor new drug products when more established or lower cost therapeutic alternatives are already available or subsequently become available.

Government authorities and other third-party payors are developing increasingly sophisticated methods of controlling healthcare costs, such as by limiting coverage and the amount of reimbursement for particular medications. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices as a condition of coverage, are using restrictive formularies and preferred drug lists to leverage greater discounts in competitive classes, and are challenging the prices charged for medical products. In addition, in the United States, federal programs impose penalties on drug manufacturers in the form of mandatory additional rebates and/or discounts if commercial prices increase at a rate greater than the Consumer Price Index-Urban, and these rebates and/or discounts, which can be substantial, may impact our ability to raise commercial prices. Further, no uniform policy requirement for drug products exists among third-party payors in the United States. Therefore, coverage and reimbursement for drug products exists among third-party payors in the United States. Therefore, coverage and reimbursement for drug products exists among third-party payors is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance.

The continuing efforts of governments, insurance companies, managed care organizations and other payors of healthcare costs to contain or reduce costs of healthcare may negatively affect our commercialization prospects, including:

- our ability to set a price we believe is fair for our products, if approved;
- our ability to obtain and maintain market acceptance by the medical community and patients;
- our ability to generate revenues and achieve profitability; and
- the availability of capital.

We cannot be sure that coverage and reimbursement will be available for any potential product candidate that we may commercialize and, if reimbursement is available, what the level of reimbursement will be. Coverage and reimbursement may impact the demand for, or the price of, any product candidate for which we obtain marketing approval. If coverage and reimbursement are not available or reimbursement is available only to limited levels, we may not successfully commercialize any product candidate for which we obtain marketing approval.

In the United States, the ACA is significantly impacting the provision of, and payment for, healthcare. Various provisions of the ACA are designed to expand Medicaid eligibility, subsidize insurance premiums, provide incentives for businesses to provide healthcare benefits, prohibit denials of coverage due to pre-existing conditions, establish health insurance exchanges, and provide additional support for medical research. With regard to pharmaceutical products specifically, the ACA, among other things, expanded and increased industry rebates for drugs covered under Medicaid programs and made changes to the coverage requirements under the Medicare prescription drug benefit.

Some of the provisions of the ACA have yet to be implemented, and there have been judicial and Congressional challenges to certain aspects of the ACA, as well as recent efforts by the Trump administration to repeal or replace certain aspects of the ACA. Since January 2017, President Trump has signed two Executive Orders and other directives designed to delay the implementation of certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. Concurrently, the U.S. Congress has considered legislation that would repeal or repeal and replace all or part of the ACA. While Congress has not passed comprehensive repeal legislation, two bills affecting the implementation of certain taxes under the ACA have been signed into law. The Tax Cuts and Jobs Act of 2017 includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate". Additionally, on January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain health insurance providers based on market share, and the medical device excise tax on non-exempt medical devices. Further, the Bipartisan Budget Act of 2018, or the BBA, among other things, amends the ACA, effective January 1, 2019, to increase from 50 percent to 70 percent the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole". We continue to evaluate the effect that the ACA and its possible repeal and replacement has on our business.

In addition, both the Budget Control Act of 2011 and the American Taxpayer Relief Act of 2012 have instituted, among other things, mandatory reductions in Medicare payments to certain providers. Additional legislative proposals to reform healthcare and government insurance programs, along with the trend toward managed healthcare in the United States, could influence the purchase of medicines and reduce reimbursement and/or coverage of our product candidates, if approved.

Recently, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products. Such scrutiny has resulted in several recent U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. At the federal level, the Trump administration's budget proposal for fiscal year 2019 contains further drug price control measures that could be enacted during the 2019 budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. While any proposed measures will require authorization through additional legislation to become effective, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, legislatures are increasingly passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

We expect that the ACA, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and lower reimbursement, and in additional downward pressure on the price that we receive for any approved product candidate. Any reduction in reimbursement from Medicare or other government-funded programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our drugs. Moreover, we cannot predict what healthcare reform initiatives may be adopted in the future.

In some foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. In addition, in some foreign markets, the pricing of prescription drugs is subject to government control and reimbursement may in some cases be unavailable. The requirements governing drug pricing vary widely from country to country. For example, the European Union provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product, may refuse to reimburse a product at the price set by the manufacturer or may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. There can be no assurance that any country that has price controls or reimbursement

limitations for biopharmaceutical products will allow favorable reimbursement and pricing arrangements for eryaspase or any of our other product candidates that may be approved. Historically, biopharmaceutical products launched in the European Union do not follow price structures of the United States and generally tend to have significantly lower prices.

We believe that pricing pressures at the federal and state levels in the United States, as well as internationally, will continue and may increase, which may make it difficult for us to sell our potential product candidates that may be approved in the future at a price acceptable to us or any third parties with whom we may choose to collaborate.

# Any of our product candidates for which we obtain marketing approval could be subject to post-marketing restrictions or withdrawal from the market, and we may be subject to substantial penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our products following approval.

Any of our product candidates for which we obtain marketing approval, as well as the manufacturing processes, post-approval studies and measures, labeling, advertising and promotional activities for such products, among other things, will be subject to continual requirements of and review by the EMA, FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping. Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to the conditions of approval, including the FDA requirement to implement a REMS to ensure that the benefits of a drug or biological product outweigh its risks.

The EMA and FDA may also impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of a product, such as long term observational studies on natural exposure. The FDA and other agencies, including the Department of Justice, closely regulate and monitor the post-approval marketing and promotion of products to ensure that they are manufactured, marketed and distributed only for the approved indications and in accordance with the provisions of the approved labeling. The EMA and FDA impose stringent restrictions on manufacturers' communications regarding off-label use and if we do not market any of our product candidates for which we receive marketing approval for only their approved indications, we may be subject to warnings or enforcement action for off-label marketing. Violation of the Federal Food, Drug and Cosmetic Act, or FDCA, and other statutes, including the civil False Claims Act, relating to the promotion and advertising of prescription drugs may lead to investigations or allegations of violations of federal and state health care fraud and abuse laws and state consumer protection laws.

# The EMA, FDA and other regulatory agencies actively enforce the laws and regulations prohibiting the promotion of drugs for off-label uses. If we are found to have improperly promoted off-label use, we may become subject to significant liability.

The EMA, FDA and other regulatory agencies strictly regulate the promotional claims that may be made about prescription drug products, such as our product candidates, if approved. In particular, a product may not be promoted for uses that are not approved by the EMA, FDA or such other regulatory agencies as reflected in the product's approved labeling. For example, if we receive marketing approval for eryaspase for ALL, physicians, in their professional medical judgment, may nevertheless prescribe eryaspase to their patients in a manner that is inconsistent with the approved label. If we are found to have promoted such off-label use, we may become subject to significant liability under the FDCA and other statutory authorities, such as laws prohibiting false claims for reimbursement. The federal government has levied large civil and criminal fines against companies for alleged improper promotion and has enjoined several companies from engaging in off-label promotion. The FDA has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed. If we cannot successfully manage the promotion of our products, if approved, we could become subject to significant liability, which would harm our reputation and negatively impact our financial condition.

# Our future growth depends, in part, on our ability to penetrate foreign markets, where we would be subject to additional regulatory burdens and other risks and uncertainties.

Our future profitability will depend, in part, on our ability to commercialize our product candidates in markets within and without the United States and Europe. If we commercialize our product candidates in foreign markets, we would be subject to additional risks and uncertainties, including:

- economic weakness, including inflation, or political instability in particular economies and markets;
- the burden of complying with complex and changing foreign regulatory, tax, accounting and legal requirements, many of which vary between countries;
- different medical practices and customs in foreign countries affecting acceptance in the marketplace;

- tariffs and trade barriers;
- other trade protection measures, import or export licensing requirements or other restrictive actions by U.S. or foreign governments;
- longer accounts receivable collection times;
- longer lead times for shipping;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- workforce uncertainty in countries where labor unrest is common;
- language barriers for technical training;
- reduced protection of intellectual property rights in some foreign countries, and related prevalence of generic alternatives to therapeutics;
- foreign currency exchange rate fluctuations and currency controls;
- differing foreign reimbursement landscapes;
- · uncertain and potentially inadequate reimbursement of our products; and
- the interpretation of contractual provisions governed by foreign laws in the event of a contract dispute.

Foreign sales of our products could also be adversely affected by the imposition of governmental controls, political and economic instability, trade restrictions and changes in tariffs.

#### Adverse market and economic conditions may exacerbate certain risks associated with commercializing our product candidates.

Future sales of our product candidates, it they are approved, will be dependent on purchasing decisions of and reimbursement from government health administration authorities, distributors and other organizations. As a result of adverse conditions affecting the global economy and credit and financial markets, including disruptions due to political instability or otherwise, these organizations may defer purchases, may be unable to satisfy their purchasing or reimbursement obligations, or may delay payment for eryaspase or any of our product candidates that are approved for commercialization in the future. In addition, there have been concerns for the overall stability and suitability of the euro as a single currency given the economic and political challenges facing individual Eurozone countries. Continuing deterioration in the creditworthiness of Eurozone countries, the withdrawal of one or more member countries from the European Union, or the failure of the euro as a common European currency or an otherwise diminished value of the euro could materially and adversely affect our future product revenue from European sales of our products.

#### Risks Related to the Production and Manufacturing of our Product Candidates

# Our production capacity could prove insufficient for our needs. In particular, our inability to produce and supply adequate amounts of GRASPA to Orphan Europe and Teva under our distribution agreements would give rise to potential financial liability and termination of our agreements, which would harm our business and financial condition.

Our production capacity may prove insufficient in the future to meet the growth of our business, including producing sufficient quantities of product candidates for preclinical studies, clinical trials and, ultimately, our customers and distributors. For instance, we plan to initiate a Phase 3 clinical trial in the United States and Europe in patients with second-line metastatic pancreatic cancer during the third quarter of 2018, and our production capacity may be insufficient to timely commence and conduct that trial. Although we are in the process of adding additional manufacturing capacity in the United States and are evaluating our production capacity needed in Europe, there is no guarantee that we will properly estimate our required manufacturing capacities in or outside of the United States or that the third parties we rely on to provide required machinery and materials for the manufacturing process will be able to perform on our proposed timelines or meet our manufacturing demands, if at all. Also, if we must increase production capacity for any reason, we may need to make considerable investments that could lead to significant financing needs or require us to enter into subcontracting agreements in order to outsource part of the production. Our distribution agreement with Teva provides that if we are unable to supply Teva with sufficient quantities of GRASPA for specified lengths of time, after notice and cure periods, Teva will be able to terminate our agreement and we could be required to reimburse Teva for all milestone payments we received prior to

termination. Our distribution agreement with Orphan Europe requires us to use commercially reasonable efforts to supply them with their requested quantities of GRASPA, and our failure to do so could result in Orphan Europe's ability to terminate our agreement. Termination of either agreement, including any financial penalties associated with termination, would negatively impact our financial condition.

### We may not have access to the raw materials and other components necessary for the manufacturing of our product candidates.

We are dependent on third parties for the supply of various materials that are necessary to produce our product candidates for clinical trials. With respect to eryaspase, we rely on medac GmbH, or Medac, for the supply of asparaginase and on the American Red Cross in the United States and the Établissement Français du Sang in Europe for the supply of red blood cells. The Établissement Français du Sang is the sole operator in its territory for blood transfusions and is in charge of satisfying national needs for blood products. Although we have entered into agreements with the American Red Cross and the Établissement Français du Sang related to the supply of those materials, the supply could be reduced or interrupted at any time. In such case, we may not be able to find other suppliers of acceptable materials in appropriate quantities at an acceptable cost. If we lose key suppliers or the supply of materials is diminished or discontinued, or in the event of a major or international crisis impacting blood banks and the practice of blood donation, we may not be able to continue to develop, manufacture and market our product candidates or products in a timely and competitive manner. In addition, these materials are subject to stringent manufacturing processes and rigorous testing. Delays in the completion and validation of facilities and manufacturing processes of these materials could adversely affect our ability to complete trials and commercialize our products in a cost-effective and timely manner. If we encounter difficulties in the supply of these materials, chemicals or biological products, or if we were not able to maintain our supply agreements or establish new supply agreements in the future, our product development and our business prospects could be significantly compromised.

### Our manufacturing facilities are subject to significant government regulations and approvals. If we or our third-party manufacturers fail to comply with these regulations or maintain these approvals, our business will be materially harmed.

We currently manufacture our product candidates for use in Europe in our facility in Lyon, France. In addition, we have entered into an agreement with the American Red Cross to produce eryaspase for use in our clinical trials in the United States, and we have an agreement with Medac to provide us with L-asparaginase for use in our production of eryaspase. We and our third-party manufacturers are subject to ongoing regulation and periodic inspection by the EMA, FDA and other regulatory bodies to ensure compliance with current Good Manufacturing Practices, or cGMP. Any failure to follow and document our or their adherence to such cGMP regulations or other regulatory requirements may lead to significant delays in the availability of products for commercial sale or clinical trials, may result in the termination of or a hold on a clinical trial, or may delay or prevent filing or approval of marketing applications for our products.

Failure to comply with applicable regulations could also result in the EMA, FDA or other applicable regulatory authorities taking various actions, including:

- levying fines and other civil penalties;
- imposing consent decrees or injunctions;
- requiring us to suspend or put on hold one or more of our clinical trials;
- suspending or withdrawing regulatory approvals;
- delaying or refusing to approve pending applications or supplements to approved applications;
- requiring us to suspend manufacturing activities or product sales, imports or exports;
- requiring us to communicate with physicians and other customers about concerns related to actual or potential safety, efficacy, and other issues involving our products;
- mandating product recalls or seizing products;
- imposing operating restrictions; and
- seeking criminal prosecutions.



Any of the foregoing actions could be detrimental to our reputation, business, financial condition or operating results. Furthermore, our key suppliers may not continue to be in compliance with all applicable regulatory requirements, which could result in our failure to produce our products on a timely basis and in the required quantities, if at all. In addition, before any additional products would be considered for marketing approval in the United States, Europe or elsewhere, our suppliers will have to pass an audit by the applicable regulatory agencies. We are dependent on our suppliers' cooperation and ability to pass such audits, and the audits and any audit remediation may be costly. Failure to pass such audits by us or any of our suppliers would affect our ability to commercialize our product candidates in the United States, Europe or elsewhere.

#### Our production costs may be higher than we currently estimate.

We manufacture our product candidates according to manufacturing best practices applicable to drugs for clinical trials and to specifications approved by the applicable regulatory authorities. If any of our products are found to be non-compliant, we would be required to manufacture the product again, which would entail additional costs and may prevent delivery of the product to patients on time.

Other risks inherent in the production process may have the same effect, such as:

- contamination of the controlled atmosphere area;
- unusable premises and equipment;
- new regulatory requirements requiring a partial and/or extended stop to the production unit to meet the requirements;
- unavailable qualified personnel;
- power failure of extended duration;
- logistical error; and
- rupture in the cold chain, which is a system for storing and transporting blood and blood products within the correct temperature range and conditions.

In addition, a rise in direct or indirect energy rates may increase product manufacturing and logistical costs. Any of these risks, should they occur, could disrupt our activities and compromise our financial position, results, reputation or growth.

#### **Risks Related to Our Operations**

### We may encounter difficulties in managing our growth, which could disrupt our operations.

As of December 31, 2017, we had 114 full-time equivalent employees, and we expect to increase our number of employees and the scope of our operations. To manage our anticipated development and expansion, including the potential commercialization of our product candidates in Europe and the United States, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Also, our management may need to divert a disproportionate amount of its attention away from its day-to-day activities and devote a substantial amount of time to managing these development activities. Due to our limited resources, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. This may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. The physical expansion of our operations may lead to significant costs and may divert financial resources from other projects, such as the development of our product candidates. If our management is unable to effectively manage our expected development and expansion, our expenses may increase more than expected, our ability to generate or increase our revenue could be reduced and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize our product candidates, if approved, and compete effectively will depend, in part, on our ability to effectively manage the future development and expansion of our company.

### We depend on qualified management personnel and our business could be harmed if we lose key personnel and cannot attract new personnel.

Our success depends to a significant degree upon the technical and management skills of our senior management team, including, in particular, Gil Beyen, our Chairman and Chief Executive Officer; Iman El-Hariry, our Chief Medical Officer; Jean-Sébastien Cleiftie, our Chief Business Officer; Eric Soyer, our Chief Financial Officer and Chief Operating Officer; Alexander Scheer, our Chief Scientific Officer and Jérôme Bailly, our Vice President and Director of Pharmaceutical Operations and Qualified Person. The loss of the services of any of these individuals would likely have a material adverse effect on us. Our success also will depend upon our ability to attract and retain additional qualified management, marketing, technical, and

sales executives and personnel. We compete for key personnel against numerous companies, including larger, more established companies with significantly greater financial resources than we possess. There can be no assurance that we will be successful in attracting or retaining such personnel, and the failure to do so, could harm our operations and our growth prospects.

#### Our failure to maintain certain tax benefits applicable to French biopharmaceutical companies may adversely affect our results of operations.

As a French biopharmaceutical company, we have benefited from certain tax advantages, including, for example, the CIR, which is a French tax credit aimed at stimulating research and development. The CIR can be offset against French corporate income tax due and the portion in excess, if any, may be refunded. The CIR is calculated based on our claimed amount of eligible research and development expenditures in France and represented €3.3 million and €3.2 million as of December 31, 2016 and 2017, respectively. The French tax authorities, with the assistance of the Research and Higher Education Ministry, may audit each research and development program in respect of which a CIR benefit has been claimed and assess whether such program qualifies in its view for the CIR benefit. The French tax authorities may challenge our eligibility for, or our calculation of, certain tax reductions or deductions in respect of our research and development activities and, should the French tax authorities be successful, our credits may be reduced, which would have a negative impact on our results of operations and future cash flows. We believe, due to the nature of our business operations, that we will continue to be eligible to receive the CIR tax credit. In 2017, our CIR authorization from the Research and Higher Education Ministry was renewed. However, if the French Parliament decides to eliminate, or to reduce the scope or the rate of, the CIR benefit, either of which it could decide to do at any time, our results of operations could be adversely affected.

#### Our business may be exposed to foreign exchange risks.

We incur some of our expenses, and may in the future derive revenues, in currencies other than the euro. In particular, as we expand our operations and conduct clinical trials in the United States, we will incur expenses in U.S. dollars. We also received and currently hold a portion of the net proceeds from our 2017 global public offering in U.S. dollars. As a result, we are exposed to foreign currency exchange risk as our results of operations and cash flows are subject to fluctuations in foreign currency exchange rates. We currently do not engage in hedging transactions to protect against uncertainty in future exchange rates between particular foreign currencies and the euro. Therefore, for example, an increase in the value of the euro against the U.S. dollar could have a negative impact on our revenue and earnings growth as U.S. dollar revenue and earnings, if any, are translated into euros at a reduced value. We cannot predict the impact of foreign currency fluctuations, and foreign currency fluctuations in the future may adversely affect our financial condition, results of operations and cash flows. The ADSs sold in the U.S. offering were quoted in U.S. dollars on the Nasdaq Global Select Market, while our ordinary shares (including those sold in the European private placement and the underlying ordinary shares of the ADSs sold in the U.S. offering) trade in euros on the Euronext Paris exchange. Our financial statements are prepared in euros. Therefore, fluctuations in the exchange rate between the euro and the U.S. dollar will also affect, among other matters, the value of our ordinary shares and ADSs.

### We may use hazardous chemicals and biological materials in our business. Any claims relating to improper handling, storage or disposal of these materials could be time-consuming and costly.

Our research and development processes involve the controlled use of hazardous materials, including chemicals and biological materials. We cannot eliminate the risk of accidental contamination or discharge and any resultant injury from these materials. We may be sued for any injury or contamination that results from our use or the use by third parties of these materials, and our liability may exceed any insurance coverage and our total assets. French and U.S. federal, state, local or foreign laws and regulations govern the use, manufacture, storage, handling and disposal of these hazardous materials and specified waste products, as well as the discharge of pollutants into the environment and human health and safety matters. Compliance with environmental laws and regulations may be expensive and may impair our research and development efforts. If we fail to comply with these requirements, we could incur substantial costs, including civil or criminal fines and penalties, clean-up costs or capital expenditures for control equipment or operational changes necessary to achieve and maintain compliance. In addition, we cannot predict the impact on our business of new or amended environmental laws or regulations or any changes in the way existing and future laws and regulations are interpreted and enforced.

### Product liability and other lawsuits could divert our resources, result in substantial liabilities and reduce the commercial potential of our product candidates.

The risk that we may be sued on product liability claims is inherent in the development and commercialization of biopharmaceutical products. Side effects of, or manufacturing defects in, products that we develop could result in the deterioration of a patient's condition, injury or even death. For example, our liability could be sought after by patients participating in the clinical trials in the context of the development of the therapeutic products tested and unexpected side effects resulting from the administration of these products. Once a product is approved for sale and commercialized, the likelihood of product liability lawsuits increases. Criminal or civil proceedings might be filed against us by patients, regulatory authorities, biopharmaceutical companies and any other third party using or marketing our products. These actions could include claims resulting from acts by our partners, licensees and subcontractors, over which we have little or no

control. These lawsuits may divert our management from pursuing our business strategy and may be costly to defend. In addition, if we are held liable in any of these lawsuits, we may incur substantial liabilities and may be forced to limit or forgo further commercialization of the affected products.

We maintain product liability insurance coverage for our clinical trials at levels which we believe are appropriate for our clinical trials. Nevertheless, our insurance coverage may be insufficient to reimburse us for any expenses or losses we may suffer. In addition, in the future, we may not be able to obtain or maintain sufficient insurance coverage at an acceptable cost or to otherwise protect against potential product or other legal or administrative liability claims by us or our collaborators, licensees or subcontractors, which could prevent or inhibit the commercial production and sale of any of our product candidates that receive regulatory approval. Product liability claims could also harm our reputation, which may adversely affect our ability to commercialize our products successfully.

### Our internal computer systems, or those of our third-party contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our product development programs.

Despite the implementation of security measures, our internal computer systems and those of our third-party contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. If such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our programs. For example, the loss of clinical trial data for our product candidates could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the lost data. To the extent that any disruption or security breach results in a loss of or damage to our data or applications or other data or applications relating to our technology or product candidates, or inappropriate disclosure of confidential or proprietary information, we could incur liabilities and the further development of our product candidates could be delayed.

### We may acquire businesses or products, or form strategic alliances, in the future, and we may not realize the benefits of such acquisitions.

Our current growth strategy does not involve plans to acquire companies or technologies facilitating or enabling us to access to new medicines, new research projects, or new geographical areas, or enabling us to express synergies with our existing operations. However, if such acquisitions were to become necessary in the future, we may not be able to identify appropriate targets or make acquisitions under satisfactory conditions, in particular, satisfactory price conditions. In addition, we may be unable to obtain the financing for these acquisitions on favorable terms, which could require us to finance these acquisitions using our existing cash resources that could have been allocated to other purposes. If we acquire businesses with promising markets or technologies, we may not be able to realize the benefit of acquiring such businesses if we are unable to successfully integrate them with our existing operations and company culture. We may encounter numerous difficulties in developing, manufacturing and marketing any new products resulting from a strategic alliance or acquisition that delay or prevent us from realizing their expected benefits or enhancing our business. We cannot assure you that, following any such acquisition, we will achieve the expected synergies to justify the transaction.

### **Risks Related to Other Legal Compliance Matters**

### We are subject to healthcare laws and regulations which may require substantial compliance efforts and could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings, among other penalties.

Healthcare providers, physicians and others will play a primary role in the recommendation and prescription of our products, if approved. Our business operations in the United States and our arrangements with clinical investigators, healthcare providers, consultants, third party payors and patients may expose us to broadly applicable federal and state fraud and abuse and other healthcare laws. These laws may impact, among other things, our research, proposed sales, marketing and education programs of our product candidates that obtain marketing approval. Restrictions under applicable U.S. federal, state and foreign healthcare laws and regulations include, but are not limited to, the following:

- the U.S. federal Anti-Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving or providing remuneration, including any kickback, bribe or rebate, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase or lease, order or recommendation of, any item, good, facility or service, for which payment may be made under federal healthcare programs such as Medicare and Medicaid;
- the U.S. federal civil and criminal false claims laws and civil monetary penalties laws, including the civil False Claims Act, which impose criminal and civil penalties, including those from civil whistleblower or qui tam actions, against individuals or entities for, among other things, knowingly presenting, or causing to be presented, claims for payment that are false or fraudulent or making a false statement to avoid, decrease, or conceal an obligation to pay money to the federal government;



- the U.S. federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created additional federal criminal statutes that impose criminal and civil liability for, among other things, executing or attempting to execute a scheme to defraud any healthcare benefit program or knowingly and willingly falsifying, concealing or covering up a material fact or making false statements relating to healthcare matters;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and its implementing regulations, which impose requirements on certain healthcare providers, health plans and healthcare clearinghouses, known as "covered entities" and persons or entities that perform functions or activities that involve individually identifiable health information on behalf of a covered entity, known as "business associates," including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- U.S. federal transparency requirements under the Physician Payments Sunshine Act, enacted as part of the ACA, that require applicable
  manufacturers of covered drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid, or the
  Children's Health Insurance Program, with specific exceptions, to track and annually report to the Centers for Medicare & Medicaid Services, or
  CMS, payments and other transfers of value provided to physicians and teaching hospitals, and certain ownership and investment interests held
  by physicians or their immediate family members; and
- analogous state or foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to items or services
  reimbursed by any third-party payor, including commercial insurers, state marketing and/or transparency laws applicable to manufacturers that
  may be broader in scope than the federal requirements, state laws that require biopharmaceutical companies to comply with the
  biopharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government,
  state and local laws that require the registration of pharmaceutical sales representatives and state laws governing the privacy and security of
  health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect as
  HIPAA, thus complicating compliance efforts.

Ensuring that our business arrangements with third parties comply with applicable healthcare laws and regulations will likely be costly. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations were found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, disgorgement, individual imprisonment, possible exclusion from government funded healthcare programs, such as Medicare and Medicaid, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations, any of which could substantially disrupt our operations. If the physicians or other providers or entities with whom we expect to do business are found not to be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

### Our employees may engage in misconduct or other improper activities, including violating applicable regulatory standards and requirements or engaging in insider trading, which could significantly harm our business.

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include intentional failures to comply with legal requirements or the requirements of CMS, EMA, FDA and other government regulators, provide accurate information to applicable government authorities, comply with fraud and abuse and other healthcare laws and regulations in the United States and abroad, report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Employee misconduct also involve the improper use of, including trading on, information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. We have adopted a Code of Business Conduct and Ethics, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may be ineffective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant civil, criminal and administrative penalties, damages, fines, disgorgement, individual imprisonment, possible exclusion from government funded healthcare programs, such as Medicare and Medicaid, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance,

#### Comprehensive tax reform bills could adversely affect our business and financial condition.

In December 2017, the U.S. government enacted the Tax Cuts and Jobs Act, a comprehensive piece of tax legislation that includes significant changes to the taxation of business entities. These changes include, among others, a permanent reduction to the corporate income tax rate. Notwithstanding the reduction in the corporate income tax rate, the overall impact of this tax reform is uncertain, and our business and financial condition could be adversely affected. This Annual Report does not discuss any such tax legislation or the manner in which it might affect holders or purchasers of our ordinary shares or ADSs. We urge our shareholders to consult with their legal and tax advisors with respect to any such legislation and the potential tax consequences of investing in our ordinary shares or ADSs.

### **Risks Related to Intellectual Property**

#### Our ability to compete may decline if we do not adequately protect our proprietary rights.

Our commercial success depends on obtaining and maintaining proprietary rights to our product candidates and defending these rights against third-party challenges. We will only be able to protect our product candidates and their uses from unauthorized use by third parties to the extent that valid and enforceable patents, or effectively protected trade secrets, cover them. Our ability to obtain patent protection for our product candidates is uncertain due to a number of factors, including:

- we or our licensors may not have been the first to make the inventions covered by pending patent applications or issued patents;
- we or our licensors may not have been the first to file patent applications for our product candidates or the compositions we developed or for their uses;
- others may independently develop identical, similar or alternative products or compositions and uses thereof;
- our or our licensors' disclosures in patent applications may not be sufficient to meet the statutory requirements for patentability;
- any or all of our or our licensors' pending patent applications may not result in issued patents;
- we or our licensors may not seek or obtain patent protection in countries that may eventually provide us a significant business opportunity;
- any patents issued to us or our licensors may not provide a basis for commercially viable products, may not provide any competitive advantages, or may be successfully challenged by third parties;
- our or our licensors' compositions and methods may not be patentable;
- others may design around our patent claims to produce competitive products which fall outside of the scope of our patents; or
- others may identify prior art or other bases which could invalidate our or our licensors' patents.

Even if we have or obtain patents covering our product candidates or compositions, we may still be barred from making, using and selling our product candidates or technologies because of the patent rights of others. Others may have filed, and in the future, may file, patent applications covering compositions or products that are similar or identical to ours. There are many issued U.S. and foreign patents relating to chemical compounds and therapeutic products, and some of these relate to compounds we intend to commercialize. Numerous U.S. and foreign issued patents and pending patent applications owned by others exist in the cancer treatment field in which we are developing products. These could materially affect our ability to develop our product candidates or sell our products if approved. Because patent applications can take many years to issue, there may be currently pending applications unknown to us that may later result in issued patents that our product candidates or compositions may infringe. These patent applications may have priority over patent applications filed by us.

Obtaining and maintaining a patent portfolio entails significant expense and resources. Part of the expense includes periodic maintenance fees, renewal fees, annuity fees, various other governmental fees on patents and/or applications due in several stages over the lifetime of patents and/or applications, as well as the cost associated with complying with numerous procedural provisions during the patent application process. We may not choose to pursue or maintain protection for

particular inventions. In addition, there are situations in which failure to make certain payments or noncompliance with certain requirements in the patent process can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. If we choose to forgo patent protection or allow a patent application or patent to lapse purposefully or inadvertently, our competitive position could suffer.

Legal actions to enforce our patent rights can be expensive and may involve the diversion of significant management time. In addition, these legal actions could be unsuccessful and could also result in the invalidation of our patents or a finding that they are unenforceable. We may or may not choose to pursue litigation or other actions against those that have infringed on our patents, or used them without authorization, due to the associated expense and time commitment of monitoring these activities. If we fail to protect or to enforce our intellectual property rights successfully, our competitive position could suffer, which could harm our results of operations.

#### Issued patents covering our product candidates could be found invalid or unenforceable if challenged in court.

If we initiate legal proceedings against a third party to enforce a patent covering our product candidate or technology, the defendant could counterclaim that the patent covering our product candidate or technology is invalid or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and unenforceability are commonplace. Grounds for a validity challenge include alleged failures to meet any of several statutory requirements, including lack of novelty, obviousness or non-enablement. Grounds for unenforceability assertions include allegations that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. Third parties may also raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include re-examination, post-grant review and/or inter partes review and equivalent proceedings in foreign jurisdictions, and opposition proceedings. Such proceedings could result in revocation or amendment of our patents in such a way that they no longer cover our product candidates or competitive products. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to validity, for example, we cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our product candidates.

### Biopharmaceutical patents and patent applications involve highly complex legal and factual questions, which, if determined adversely to us, could negatively impact our patent position.

The patent positions of biopharmaceutical companies can be highly uncertain and involve complex legal and factual questions. The interpretation and breadth of claims allowed in some patents covering biopharmaceutical compositions may be uncertain and difficult to determine, and are often affected materially by the facts and circumstances that pertain to the patented compositions and the related patent claims. The standards of the U.S. Patent and Trademark Office, or USPTO, are evolving and could change in the future. Consequently, we cannot predict the issuance and scope of patents with certainty. Patents, if issued, may be challenged, invalidated or circumvented. U.S. patents and patent applications may also be subject to interference proceedings, and U.S. patents may be subject to reexamination proceedings, post-grant review and/or inter partes review in the USPTO. Foreign patents may be subject also to opposition or comparable proceedings in the corresponding foreign patent office, which could result in either loss of the patent or denial of the patent application or loss or reduction in the scope of one or more of the claims of the patent or patent application. In addition, such interference, reexamination, post-grant review, inter partes review and opposition proceedings may be costly. Accordingly, rights under any issued patents may not provide us with sufficient protection against competitive products or processes.

In addition, changes in or different interpretations of patent laws in the United States and foreign countries may permit others to use our or our licensors' discoveries or to develop and commercialize our technology and products without providing any compensation to us, or may limit the number of patents or claims we can obtain. The laws of some countries do not protect intellectual property rights to the same extent as U.S. laws and those countries may lack adequate rules and procedures for defending our intellectual property rights.

If we fail to obtain and maintain patent protection and trade secret protection for our product candidates, we could lose our competitive advantage and competition we face would increase, reducing any potential revenues and adversely affecting our ability to attain or maintain profitability.

#### Developments in patent law could have a negative impact on our business.

From time to time, the U.S. Supreme Court, other federal courts, the U.S. Congress, the USPTO or similar foreign authorities may change the standards of patentability and any such changes could have a negative impact on our business. In addition, the Leahy-Smith America Invents Act, or the America Invents Act, which was signed into law in 2011, includes a number of significant changes to U.S. patent law. These changes include a transition from a "first-to-invent" system to a "first-to-file" system, changes to the way issued patents are challenged, and changes to the way patent applications are disputed during the examination process. These changes may favor larger and more established companies that have greater resources to devote to patent application filing and prosecution. The USPTO has developed new regulations and procedures to govern the full

implementation of the America Invents Act, and many of the substantive changes to patent law associated with the America Invents Act, and, in particular, the first-to-file provisions, became effective on March 16, 2013. Substantive changes to patent law associated with the America Invents Act, or any subsequent U.S. legislation regarding patents, may affect our ability to obtain patents, and if obtained, to enforce or defend them. Accordingly, it is not clear what, if any, impact the America Invents Act will have on the cost of prosecuting our U.S. patent applications, our ability to obtain U.S. patents based on our discoveries and our ability to enforce or defend any patents that may issue from our patent applications, all of which could have a material adverse effect on our business.

### If we do not obtain protection under the Hatch-Waxman Amendments and similar non-U.S. legislation for extending the term of patents covering each of our product candidates, our business may be materially harmed.

Depending upon the timing, duration and conditions of FDA marketing approval of our product candidates, one or more of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Amendments, and similar legislation in the European Union. The Hatch-Waxman Amendments permit a patent term extension of up to five years for a patent covering an approved product as compensation for effective patent term lost during product development and the FDA regulatory review process. However, we may not receive an extension if we fail to apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. Moreover, the length of the extension could be less than we request. If we are unable to obtain patent term extension or the term of any such extension is less than we request, the period during which we can enforce our patent rights for that product will be shortened and our competitors may obtain approval to market competing products sooner. As a result, our revenue from applicable products could be reduced, possibly materially.

#### If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition to patent protection, because we operate in the highly technical field of development of therapies, we rely in part on trade secret protection in order to protect our proprietary technology and processes. However, trade secrets are difficult to protect. We have entered into confidentiality and intellectual property assignment agreements with our employees, consultants, outside scientific collaborators, sponsored researchers, and other advisors. These agreements generally require that the other party keep confidential and not disclose to third parties all confidential information developed by the party or made known to the party by us during the course of the party's relationship with us. These agreements also generally provide that inventions conceived by the party in the course of rendering services to us will be our exclusive property. However, these agreements may not be honored and may not effectively assign intellectual property rights to us.

In addition to contractual measures, we try to protect the confidential nature of our proprietary information using physical and technological security measures. Such measures may not, for example, in the case of misappropriation of a trade secret by an employee or third party with authorized access, provide adequate protection for our proprietary information. Our security measures may not prevent an employee or consultant from misappropriating our trade secrets and providing them to a competitor, and recourse we take against such misconduct may not provide an adequate remedy to protect our interests fully. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret can be difficult, expensive, and time-consuming, and the outcome is unpredictable. In addition, courts outside the United States may be less willing to protect trade secrets. Trade secrets may be independently developed by others in a manner that could prevent legal recourse by us. If any of our confidential or proprietary information, such as our trade secrets, were to be disclosed or misappropriated, or if any such information was independently developed by a competitor, our competitive position could be harmed.

### We will not seek to protect our intellectual property rights in all jurisdictions throughout the world and we may not be able to adequately enforce our intellectual property rights even in the jurisdictions where we seek protection.

Filing, prosecuting and defending patents on our product candidates in all countries and jurisdictions throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States could be less extensive than those in the United States, assuming that rights are obtained in the United States. Competitors may use our technologies in jurisdictions where we do not pursue and obtain patent protection to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our products and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing. Even if we pursue and obtain issued patents in particular jurisdictions, our patent claims or other intellectual property rights may not be effective or sufficient to prevent third parties from so competing.

In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as the federal and state laws in the United States. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. The legal systems of some countries, particularly developing countries, do not favor the enforcement of patents and other intellectual property protection, especially those relating to biopharmaceuticals or biotechnologies. This could make it difficult for us to stop the infringement of our patents, if obtained, or the misappropriation of our other intellectual property rights. For example, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. In addition, many countries limit the



enforceability of patents against third parties, including government agencies or government contractors. In these countries, patents may provide limited or no benefit. Patent protection must ultimately be sought on a country-by-country basis, which is an expensive and time-consuming process with uncertain outcomes. Accordingly, we may choose not to seek patent protection in certain countries, and we will not have the benefit of patent protection in such countries.

Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly, could put our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. In addition, changes in the law and legal decisions by courts in the United States and foreign countries may affect our ability to obtain adequate protection for our technology and the enforcement of intellectual property. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

#### Third parties may assert ownership or commercial rights to inventions we develop.

Third parties may in the future make claims challenging the inventorship or ownership of our intellectual property. We have written agreements with collaborators that provide for the ownership of intellectual property arising from our collaborations. These agreements provide that we must negotiate certain commercial rights with collaborators with respect to joint inventions or inventions made by our collaborators that arise from the results of the collaboration. In some instances, there may not be adequate written provisions to address clearly the resolution of intellectual property rights that may arise from a collaborator's materials where required, or if disputes otherwise arise with respect to the intellectual property developed with the use of a collaborator's samples, we may be limited in our ability to capitalize on the market potential of these inventions. In addition, we may face claims by third parties that our agreements with employees, contractors, or consultants obligating them to assign intellectual property to us are ineffective, or in conflict with prior or competing contractual obligations of assignment, which could result in ownership disputes regarding intellectual property we have developed or will develop and interfere with our ability to capture the commercial value of such inventions. Litigation may be necessary to resolve an ownership dispute, and if we are not successful, we may be precluded from using certain intellectual property, or may lose our exclusive rights in that intellectual property. Either outcome could have an adverse impact on our business.

# If we fail to comply with our obligations under license or technology agreements with third parties, we could lose license rights that are critical to our business.

We license intellectual property that is critical to our business, including licenses underlying the technology in our diagnostic tests, and in the future, we may enter into additional agreements that provide us with licenses to valuable intellectual property or technology. These licenses impose various royalty payments, milestones, and other obligations on us. If we fail to comply with any of these obligations, the licensor may have the right to terminate the license. Termination by the licensor would cause us to lose valuable rights, and could prevent us from distributing our current tests, or inhibit our ability to commercialize future test candidates. Our business would suffer if any current or future licenses terminate, if the licensors fail to abide by the terms of the license, if the licensors fail to prevent infringement by third parties, if the licensed patents or other rights are found to be invalid or unenforceable, or if we are unable to enter into necessary licenses on acceptable terms.

#### Third parties may assert that our employees or consultants have wrongfully used or disclosed confidential information or misappropriated trade secrets.

We employ individuals who were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees and consultants do not use the proprietary information or know-how of others in their work for us, and no such claims against us are currently pending, we may be subject to claims that we or our employees, consultants or independent contractors have used or disclosed intellectual property, including trade secrets or other proprietary information, of a former employer or other third parties. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

### A dispute concerning the infringement or misappropriation of our proprietary rights or the proprietary rights of others could be time-consuming and costly, and an unfavorable outcome could harm our business.

There is significant litigation in the biopharmaceutical industry regarding patent and other intellectual property rights. While we are not currently subject to any pending intellectual property litigation, and are not aware of any such threatened litigation, we may be exposed to future litigation by third parties based on claims that our product candidates, technologies or activities infringe the intellectual property rights of others. If our development activities are found to infringe any such patents, we may have to pay significant damages or seek licenses to such patents. A patentee could prevent us from using the patented drugs or compositions. We may need to resort to litigation to enforce a patent issued to us, to protect our trade

secrets, or to determine the scope and validity of third-party proprietary rights. From time to time, we may hire scientific personnel or consultants formerly employed by other companies involved in one or more areas similar to the activities conducted by us. Either we or these individuals may be subject to allegations of trade secret misappropriation or other similar claims as a result of prior affiliations. If we become involved in litigation, it could consume a substantial portion of our managerial and financial resources, regardless of whether we win or lose. We may not be able to afford the costs of litigation. Any adverse ruling or perception of an adverse ruling in defending ourselves against these claims could have a negative impact on our cash position. Any legal action against us or our collaborators could lead to:

- payment of damages, potentially treble damages, if we are found to have willfully infringed a party's patent rights;
- injunctive or other equitable relief that may effectively block our ability to further develop, commercialize, and sell products; or
- us or our collaborators having to enter into license arrangements that may not be available on commercially acceptable terms, if at all.

Any of these outcomes could hurt our cash position and financial condition and our ability to develop and commercialize our product candidates.

### If our trademarks and trade names are not adequately protected, we may not be able to build name recognition in our markets of interest.

Our registered or unregistered trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names, which we will need to build name recognition by potential partners or customers in our markets of interest. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, we may not be able to compete effectively.

#### Risks Related to Ownership of our Securities and our Status as a Non-U.S. Company with Foreign Private Issuer Status

#### The market price of our equity securities may be volatile or may decline regardless of our operating performance.

The market price for our ADSs and ordinary shares has fluctuated and is likely to continue to fluctuate, substantially. The stock market in general and the market for biopharmaceutical companies in particular have experienced extreme volatility that in some instances is unrelated to the operating performance of particular companies. As a result of this volatility, holders of our equity securities may not be able to sell their ADSs or ordinary shares at or above the price originally paid for the security. The market price for our ADSs and ordinary shares may be influenced by numerous factors, some of which are beyond our control, including:

- actual or anticipated fluctuations in our financial condition and operating results;
- actual or anticipated changes in our growth rate relative to our competitors;
- competition from existing products or new products that may emerge;
- · announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures, collaborations, or capital commitments;
- · failure to meet or exceed financial estimates and projections of the investment community or that we provide to the public;
- issuance of new or updated research or reports by securities analysts;
- fluctuations in the valuation of companies perceived by investors to be comparable to us;
- share and ADS price and volume fluctuations attributable to inconsistent trading volume levels of our shares and ADSs;
- additions or departures of key management or scientific personnel;
- lawsuits threatened or filed against us, disputes or other developments related to proprietary rights, including patents, litigation matters, and our ability to obtain patent protection for our technologies;



- changes to coverage policies or reimbursement levels by commercial third-party payors and government payors and any announcements relating to coverage policies or reimbursement levels;
- announcement or expectation of additional debt or equity financing efforts;
- adverse regulatory decisions, including failure to receive regulatory approval for any of our product candidates;
- the termination of a strategic alliance or the inability to establish additional strategic alliances;
- sales of our ordinary shares or ADSs by us, our insiders or our other shareholders; and
- general economic and market conditions.

These and other market and industry factors may cause the market price and demand for our ordinary shares and ADSs to fluctuate substantially, regardless of our actual operating performance, which may limit or prevent holders of our equity securities from readily selling their ordinary shares or ADSs and may otherwise negatively affect the liquidity of the trading market for the ordinary shares and ADSs.

In addition, in the past, stockholders have initiated class action lawsuits against pharmaceutical and biotechnology companies following periods of volatility in the market prices of these companies' stock. Such litigation, if instituted against us, could cause us to incur substantial costs and divert management's attention and resources from our business.

#### The dual listing of our ordinary shares and our ADSs may adversely affect the liquidity and value of our ordinary shares and ADSs.

Our ADSs are listed on Nasdaq, and our ordinary shares are admitted to trading on Euronext Paris. We cannot predict the effect of this dual listing on the value of our ADSs and ordinary shares. However, the dual listing of our ADSs and ordinary shares may dilute the liquidity of these securities in one or both markets and may adversely affect the trading market or price for our ADSs or ordinary shares.

### If we do not achieve our projected development and commercialization goals in the timeframes we announce and expect, our business will be harmed and the price of our securities could decline as a result.

We sometimes estimate for planning purposes the timing of the accomplishment of various scientific, clinical, regulatory and other product development objectives. These milestones may include our expectations regarding the commencement or completion of scientific studies, clinical trials, the submission of regulatory filings, or commercialization objectives. From time to time, we may publicly announce the expected timing of some of these milestones, such as the completion of an ongoing clinical trial, the initiation of other clinical programs, receipt of marketing approval, or a commercial launch of a product. The achievement of many of these milestones may be outside of our control. All of these milestones are based on a variety of assumptions which may cause the timing of achievement of the milestones to vary considerably from our estimates, including:

- our available capital resources or capital constraints we experience;
- the rate of progress, costs and results of our clinical trials and research and development activities, including the extent of scheduling conflicts with participating clinicians and collaborators, and our ability to identify and enroll patients who meet clinical trial eligibility criteria;
- our receipt of approvals by the EMA, FDA and other regulatory agencies and the timing thereof;
- other actions, decisions or rules issued by regulators;
- our ability to access sufficient, reliable and affordable supplies of compounds and raw materials used in the manufacture of our product candidates;
- · the efforts of our collaborators with respect to the commercialization of our products; and
- the securing of, costs related to, and timing issues associated with, product manufacturing as well as sales and marketing activities.

If we fail to achieve announced milestones in the timeframes we expect, the commercialization of our product candidates may be delayed, our business and results of operations may be harmed, and the trading price of the ordinary shares and ADSs may decline as a result.

### Our ownership is concentrated in the hands of our principal shareholders and ADS holders and management, who continue to be able to exercise a direct or indirect controlling influence on us.

As of December 31, 2017, our executive officers, directors, current 5% or greater shareholders and their respective affiliated entities, including Auriga Ventures III FCPR, Baker Bros. Advisors LP and BVF Inc., together beneficially owned approximately 40% of our ordinary shares (including ordinary shares in the form of ADSs). As a result, these shareholders, acting together, will have significant influence over all matters that require approval by our shareholders, including the election of directors and approval of significant corporate transactions. Corporate action might be taken even if other shareholders oppose them. This concentration of ownership might also have the effect of delaying or preventing a change of control of our company that other shareholders may view as beneficial.

### If securities or industry analysts do not publish research or publish inaccurate or unfavorable research about our business, the price of the ordinary shares and ADSs and their trading volume could decline.

The trading market for the ADSs and ordinary shares depends in part on the research and reports that securities or industry analysts publish about us or our business. If no or few securities or industry analysts cover our company, the trading price for the ADSs and ordinary shares would be negatively impacted. If one or more of the analysts who covers us downgrades our equity securities or publishes incorrect or unfavorable research about our business, the price of the ordinary shares and ADSs would likely decline. If one or more of these analysts ceases coverage of our company or fails to publish reports on us regularly, or downgrades our securities, demand for the ordinary shares and ADSs could decrease, which could cause the price of the ordinary shares and ADSs or their trading volume to decline.

## We do not currently intend to pay dividends on our securities and, consequently, the ability of our shareholders and ADS holders to achieve a return on investment will depend on appreciation in the price of the ordinary shares and ADSs. In addition, French law may limit the amount of dividends we are able to distribute.

We have never declared or paid any cash dividends on our share capital and do not currently intend to do so for the foreseeable future. We currently intend to invest our future earnings, if any, to fund our growth. Therefore, our shareholders and ADS holders are not likely to receive any dividends for the foreseeable future and any increase in value will depend solely upon future appreciation. Consequently, holders of our equity securities may need to sell all or part of their holdings of ordinary shares or ADSs after price appreciation, which may never occur, as the only way to realize any future gains.

Further, under French law, the determination of whether we have been sufficiently profitable to pay dividends is made on the basis of our statutory financial statements prepared and presented in accordance with accounting standards applicable in France. In addition, payment of dividends may subject us to additional taxes under French law. Please see the section of this Annual Report on Form 20-F titled "Item 10.B—Memorandum and Articles of Association" for further details on the limitations on our ability to declare and pay dividends and the taxes that may become payable by us if we elect to pay a dividend. Therefore, we may be more restricted in our ability to declare dividends than companies not based in France.

In addition, exchange rate fluctuations may affect the amount of euros that we are able to distribute, and the amount in U.S. dollars that our shareholders receive upon the payment of cash dividends or other distributions we declare and pay in euros, if any. These factors could harm the value of our equity securities, and, in turn, the U.S. dollar proceeds that holders receive from the sale of ADSs.

### Future sales, or the possibility of future sales, of a substantial number of our ADSs or ordinary shares could adversely affect the market price of our ADSs and ordinary shares.

Future sales of a substantial number of our ADSs or ordinary shares, or the perception that such sales will occur, could cause a decline in the market price of our ADSs and/or ordinary shares. Sales in the United States of our ADSs and ordinary shares held by our directors, officers and affiliated shareholders or ADS holders are subject to restrictions. If these shareholders or ADS holders sell substantial amounts of ordinary shares or ADSs in the public market, or the market perceives that such sales may occur, the market price of our ADSs or ordinary shares and our ability to raise capital through an issue of equity securities in the future could be adversely affected.

### The rights of shareholders in companies subject to French corporate law differ in material respects from the rights of shareholders of corporations incorporated in the United States.

We are a French company with limited liability. Our corporate affairs are governed by our bylaws and by the laws governing companies incorporated in France. The rights of shareholders and the responsibilities of members of our board of directors are in many ways different from the rights and obligations of shareholders in companies governed by the laws of U.S. jurisdictions. For example, in the performance of its duties, our board of directors is required by French law to consider the interests of our company, its shareholders, its employees and other stakeholders, rather than solely our shareholders and/or creditors. It is possible that some of these parties will have interests that are different from, or in addition to, the interests of our shareholders or holders of our ADSs. See the sections of this Annual Report on Form 20-F titled "Item 10. B—Memorandum and Articles of Association" and "Item 16.G—Corporate Governance."

### U.S. holders of our equity securities may have difficulty enforcing civil liabilities against our company and directors and senior management and experts named herein.

Certain members of our board of directors and senior management and certain experts named herein are non-residents of the United States, and all or a substantial portion of our assets and the assets of such persons are located outside the United States. As a result, it may not be possible to serve process on such persons or us in the United States or to enforce judgments obtained in U.S. courts against them or us based on civil liability provisions of the securities laws of the United States. Additionally, it may be difficult to assert U.S. securities law claims in actions originally instituted outside of the United States. Foreign courts may refuse to hear a U.S. securities law claim because foreign courts may not be the most appropriate forums in which to bring such a claim. Even if a foreign court agrees to hear a claim, it may determine that the law of the jurisdiction in which the foreign court resides, and not U.S. law, is applicable to the claim. Further, if U.S. law is found to be applicable, the content of applicable U.S. law must be proved as a fact, which can be a time-consuming and costly process, and certain matters of procedure would still be governed by the law of the jurisdiction in which the foreign court resides. In particular, there is some doubt as to whether French courts would recognize and enforce certain civil liabilities under U.S. securities laws in original actions or judgments of U.S. courts based upon these civil liability provisions. In addition, awards of punitive damages in actions brought in the United States or elsewhere may be unenforceable in France. An award for monetary damages under the U.S. securities laws would be considered punitive if it does not seek to compensate the claimant for loss or damage suffered but is intended to punish the defendant. French law provides that a shareholder, or a group of shareholders, may initiate a legal action to seek indemnification from the directors of a corporation in the corporation's interest if it fails to bring such legal action it

The enforceability of any judgment in France will depend on the particular facts of the case as well as the laws and treaties in effect at the time. The United States and France do not currently have a treaty providing for recognition and enforcement of judgments (other than arbitration awards) in civil and commercial matters.

#### Our bylaws and French corporate law contain provisions that may delay or discourage a takeover attempt.

Provisions contained in our bylaws and French corporate law could make it more difficult for a third-party to acquire us, even if doing so might be beneficial to our shareholders. In addition, provisions of our bylaws impose various procedural and other requirements, which could make it more difficult for shareholders to effect certain corporate actions. These provisions include the following:

- under French law, the owner of 95% of voting rights of a public company listed on a regulated market in a Member State of the European Union or in a state party to the European Economic Area, or EEA, Agreement, including France, has the right to force out minority shareholders following a tender offer made to all shareholders;
- under French law, a non-resident of France as well as any French entity controlled by non-French residents may have to file an administrative
  notice with French authorities in connection with a direct or indirect investment in us, as defined by administrative rulings; see the section of this
  Annual Report on Form 20-F titled "Item 10.B—Memorandum and Articles of Association";
- a merger (i.e., in a French law context, a stock for stock exchange following which our company would be dissolved into the acquiring entity and our shareholders would become shareholders of the acquiring entity) of our company into a company incorporated in the European Union would require the approval of our board of directors as well as a two-thirds majority of the votes held by the shareholders present, represented by proxy or voting by mail at the relevant meeting;
- a merger of our company into a company incorporated outside of the European Union would require 100% of our shareholders to approve it;
- under French law, a cash merger is treated as a share purchase and would require the consent of each participating shareholder;
- our shareholders have granted and may grant in the future our board of directors broad authorizations to increase our share capital or to issue additional ordinary shares or other securities, such as warrants, to our shareholders, the public or qualified investors, including as a possible defense following the launching of a tender offer for our shares;

- our shareholders have preferential subscription rights on a *pro rata* basis on the issuance by us of any additional securities for cash or a set-off of cash debts, which rights may only be waived by the extraordinary general meeting (by a two-thirds majority vote) of our shareholders or on an individual basis by each shareholder;
- our board of directors has the right to appoint directors to fill a vacancy created by the resignation or death of a director, for the remaining duration of such director's term of office and subject to the approval by the shareholders of such appointment at the next shareholders' meeting, which prevents shareholders from having the sole right to fill vacancies on our board of directors;
- our board of directors can be convened by our chairman or our managing director, if any, or, when no board meeting has been held for more than two consecutive months, by directors representing at least one third of the total number of directors;
- our board of directors meetings can only be regularly held if at least half of the directors attend either physically or by way of videoconference or teleconference enabling the directors' identification and ensuring their effective participation in the board's decisions;
- our shares are nominative or bearer, if the legislation so permits, according to the shareholder's choice;
- approval of at least a majority of the votes held by shareholders present, represented by a proxy, or voting by mail at the relevant ordinary shareholders' general meeting is required to remove directors with or without cause;
- advance notice is required for nominations to the board of directors or for proposing matters to be acted upon at a shareholders' meeting, except that a vote to remove and replace a director can be proposed at any shareholders' meeting without notice;
- our bylaws can be changed in accordance with applicable laws;
- the crossing of certain thresholds has to be disclosed and can impose certain obligations; see the section of this Annual Report on Form 20-F titled "Item 10.B—Memorandum and Articles of Association";
- transfers of shares shall comply with applicable insider trading rules and regulations and, in particular, with the Market Abuse Directive and Regulation dated April 16, 2014; and
- pursuant to French law, our bylaws, including the sections relating to the number of directors and election and removal of a director from office, may only be modified by a resolution adopted by two-thirds of the votes of our shareholders present, represented by a proxy or voting by mail at the meeting.

#### Holders of our ADSs may not be able to exercise their right to vote the ordinary shares underlying such ADSs.

Holders of our ADSs may exercise voting rights with respect to the ordinary shares represented by the ADSs only in accordance with the provisions of the amended and restated deposit agreement. The amended and restated deposit agreement provides that, upon receipt of notice of any meeting of holders of our ordinary shares, the depositary will fix a record date for the determination of ADS holders who shall be entitled to give instructions for the exercise of voting rights. Upon timely receipt of notice from us, if we so request, the depositary shall distribute to the holders as of the record date (1) the notice of the meeting or solicitation of consent or proxy sent by us and (2) a statement as to the manner in which instructions may be given by the holders.

Holders of our ADSs may instruct the depositary of their ADSs to vote the ordinary shares underlying such ADSs. Otherwise, holders of our ADSs will not be able to exercise voting rights unless they withdraw the ordinary shares underlying the ADSs they hold. However, a holder of our ADSs may not know about the meeting far enough in advance to withdraw those ordinary shares. If we ask for a holder of our ADSs' instructions, the depositary, upon timely notice from us, will notify him or her of the upcoming vote and arrange to deliver our voting materials to him or her. We cannot guarantee to any holder of ADSs that he or she will receive the voting materials in time to ensure that he or she can instruct the depositary to vote his or her ordinary shares or to withdraw his or her ordinary shares so that he or she can vote them directly. If the depositary does not receive timely voting instructions from a holder of ADSs, it may give a proxy to a person designated by us to vote the ordinary shares underlying his or her ADSs. In addition, the depositary and its agents are not responsible for failing to carry out voting instructions or for the manner of carrying out voting instructions. This means that a holder of ADSs may not be able to exercise his or her right to vote, and there may be nothing he or she can do if the ordinary shares underlying his or her ADSs are not voted as he or she requested.

### The right as a holder of ADSs to participate in any future preferential subscription rights or to elect to receive dividends in shares may be limited, which may cause dilution to the holders of our ADSs.

Under French law, if we issue additional securities for cash, current shareholders will have preferential subscription rights for these securities on a pro rata basis unless they waive those rights at an extraordinary meeting of our shareholders (by a two-thirds majority vote) or individually by each shareholder. However, our ADS holders in the United States will not be entitled to exercise or sell such rights unless we register the rights and the securities to which the rights relate under the Securities Act or an exemption from the registration requirements is available. In addition, the amended and restated deposit agreement provides that the depositary will not make rights available to holders of our ADSs unless the distribution to ADS holders of both the rights and any related securities are either registered under the Securities Act or exempted from registration under the Securities Act. Further, if we offer holders of our ordinary shares the option to receive dividends in either cash or shares, under the amended and restated deposit agreement the depositary may require satisfactory assurances from us that extending the offer to holders of our ADSs does not require registration of any securities under the Securities Act before making the option available to holders of our ADSs. We are under no obligation to file a registration statement with respect to any such rights or securities act. Accordingly, ADS holders may be unable to participate in our rights offerings or to elect to receive dividends in shares and may experience dilution in their holdings. In addition, if the depositary is unable to sell rights that are not exercised or not distributed or if the sale is not lawful or reasonably practicable, it will allow the rights to lapse, in which case holders of our ADSs will receive no value for these rights.

#### Holders of our ADSs may be subject to limitations on the transfer of such ADSs and the withdrawal of the underlying ordinary shares.

ADSs, which may be evidenced by ADRs, are transferable on the books of the depositary. However, the depositary may close its books at any time or from time to time when it deems expedient in connection with the performance of its duties. The depositary may refuse to deliver, transfer or register transfers of ADSs generally when our books or the books of the depositary are closed, or at any time if we or the depositary think it is advisable to do so because of any requirement of law, government or governmental body, or under any provision of the amended and restated deposit agreement, or for any other reason subject to an ADS holder's right to cancel such ADSs and withdraw the underlying ordinary shares. Temporary delays in the cancellation of such ADSs and withdrawal of the underlying ordinary shares may arise because the depositary has closed its transfer books or we have closed our transfer books, the transfer of ordinary shares is blocked to permit voting at a shareholders' meeting or we are paying a dividend on our ordinary shares. In addition, a holder of ADSs may not be able to cancel his or her ADSs and withdraw the underlying ordinary shares when he or she owes money for fees, taxes and similar charges and when it is necessary to prohibit withdrawals in order to comply with any laws or governmental regulations that apply to ADSs or to the withdrawal of ordinary shares or other deposited securities.

### As a foreign private issuer, we are exempt from a number of rules under the U.S. securities laws and are permitted to file less information with the SEC than a U.S. company. This may limit the information available to holders of our ADSs or ordinary shares.

We are a foreign private issuer, as defined in the SEC's rules and regulations and, consequently, we are not subject to all of the disclosure requirements applicable to public companies organized within the United States. For example, we are exempt from certain rules under the U.S. Securities Exchange Act of 1934, as amended, or the Exchange Act, that regulate disclosure obligations and procedural requirements related to the solicitation of proxies, consents or authorizations applicable to a security registered under the Exchange Act, including the U.S. proxy rules under Section 14 of the Exchange Act. In addition, our officers and directors are exempt from the reporting and "short-swing" profit recovery provisions of Section 16 of the Exchange Act and related rules with respect to their purchases and sales of our securities. Moreover, while we currently make annual and semi-annual filings with respect to our listing on Euronext Paris and expect to continue to file such reports, we will not be required to file periodic reports and financial statements with the SEC as frequently or as promptly as U.S. public companies and will not be required to file quarterly reports on Form 10-Q or current reports on Form 8-K under the Exchange Act. Accordingly, there will be less publicly available information concerning our company than there would be if we were a U.S. domestic issuer.

# As a foreign private issuer, we are permitted and we follow certain home country practices in relation to corporate governance matters that differ significantly from Nasdaq's corporate governance standards. These practices may afford less protection to shareholders than they would enjoy if we complied fully with the corporate governance standards of the Nasdaq Global Select Market.

As a foreign private issuer listed on the Nasdaq Global Select Market, we are subject to Nasdaq's corporate governance standards. However, Nasdaq rules provide that foreign private issuers are permitted to follow home country corporate governance practices in lieu of Nasdaq's corporate governance standards as long as notification is provided to Nasdaq of the intention to take advantage of such exemptions. We currently rely on exemptions for foreign private issuers and follow French corporate governance practices in lieu of Nasdaq's corporate governance standards, to the extent possible. Certain

corporate governance practices in France, which is our home country, may differ significantly from Nasdaq corporate governance standards. For example, as a French company, neither the corporate laws of France nor our bylaws require a majority of our directors to be independent and we can include non-independent directors as members of our remuneration committee, and our independent directors are not required to hold regularly scheduled meetings at which only independent directors are present.

We are also exempt from provisions set forth in Nasdaq rules which require an issuer to provide in its bylaws for a generally applicable quorum, and that such quorum may not be less than one-third of the outstanding voting stock. Consistent with French law, our bylaws provide that a quorum requires the presence of shareholders having at least (1) 20% of the shares entitled to vote in the case of an ordinary shareholders' general meeting or at an extraordinary shareholders' general meeting where shareholders are voting on a capital increase by capitalization of reserves, profits or share premium, or (2) 25% of the shares entitled to vote in the case of any other extraordinary shareholders' general meeting.

As a foreign private issuer, we are required to comply with Rule 10A-3 of the Exchange Act, relating to audit committee composition and responsibilities. Under French law, the audit committee may only have an advisory role and appointment of our statutory auditors, in particular, must be decided by the shareholders at our annual meeting.

Therefore, our shareholders may be afforded less protection than they otherwise would have under Nasdaq's corporate governance standards applicable to U.S. domestic issuers.

### We are an "emerging growth company" under the JOBS Act and will be able to avail ourselves of reduced disclosure requirements applicable to emerging growth companies, which could make our ADSs less attractive to investors.

We are an "emerging growth company," as defined in the U.S. Jumpstart Our Business Startups Act of 2012, or the JOBS Act, and we intend to take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not "emerging growth companies," including not being required to comply with the auditor attestation requirements of Section 404(b) of the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved. In addition, Section 107 of the JOBS Act also provides that an emerging growth company can take advantage of the extended transition period provided in Section 7(a)(2)(B) of the U.S. Securities Act of 1933, as amended, or the Securities Act, for complying with new or revised accounting standards. We have elected not to take advantage of the extended transition period provided under Section 7(a)(2) (B) of the Securities Act for complying with new or revised accounting standards, the requirements for our compliance as a private company and as a public company are the same.

We cannot predict if holders of our ADSs will find the ADSs less attractive because we may rely on these exemptions. If some holders find the ADSs less attractive as a result, there may be a less active trading market for the ADSs and the price of the ADSs may be more volatile. We may take advantage of these reporting exemptions until we are no longer an emerging growth company. We will remain an emerging growth company until the earliest of (i) the last day of the fiscal year in which we have total annual gross revenue of \$1.07 billion or more; (ii) the last day of our fiscal year following the fifth anniversary of the date of the completion of the November 2017 global offering; (iii) the date on which we have issued more than \$1.0 billion in nonconvertible debt during the previous three years; and (iv) the date on which we are deemed to be a large accelerated filer under the rules of the SEC.

#### We may lose our foreign private issuer status in the future, which could result in significant additional cost and expense.

While we currently qualify as a foreign private issuer, the determination of foreign private issuer status is made annually on the last business day of our most recently completed second fiscal quarter and, accordingly, the next determination will be made with respect to us on June 30, 2018. In the future, we would lose our foreign private issuer status if we fail to meet the requirements necessary to maintain our foreign private issuer status as of the relevant determination date. We will remain a foreign private issuer until such time that more than 50% of our outstanding voting securities are held by U.S. residents and any of the following three circumstances applies: (i) the majority of our executive officers or directors are U.S. citizens or residents; (ii) more than 50% of our assets are located in the United States; or (iii) our business is administered principally in the United States.

The regulatory and compliance costs to us under U.S. securities laws as a U.S. domestic issuer would likely be significantly more than costs we incur as a foreign private issuer. If we lost our foreign private issuer status, we would be required to file periodic reports and registration statements on U.S. domestic issuer forms with the SEC, which are more detailed and extensive in certain respects than the forms available to a foreign private issuer. We would be required under current SEC rules to prepare our financial statements in accordance with U.S. GAAP, rather than IFRS, and modify certain of our policies to comply with corporate governance practices associated with U.S. domestic issuers. Such conversion of our financial statements to U.S. GAAP would involve significant time and cost. In addition, we would lose our ability to rely upon exemptions from certain corporate governance requirements on U.S. stock exchanges that are available to foreign private issuers such as the ones described herein and exemptions from procedural requirements related to the solicitation of proxies.

#### U.S. holders of our ADSs may suffer adverse tax consequences if we are characterized as a passive foreign investment company.

Generally, if, for any taxable year, at least 75% of our gross income is passive income, or at least 50% of the value of our assets is attributable to assets that produce passive income or are held for the production of passive income, including cash, we would be characterized as a passive foreign investment company, or PFIC, for U.S. federal income tax purposes. For purposes of these tests, passive income includes dividends, interest, and gains from the sale or exchange of investment property and rents and royalties other than rents and royalties which are received from unrelated parties in connection with the active conduct of a trade or business. If we are characterized as a PFIC, U.S. holders of the ADSs may suffer adverse tax consequences, including having gains realized on the sale of the ADSs treated as ordinary income, rather than capital gain, the loss of the preferential rate applicable to dividends received on the ADSs by individuals who are U.S. holders, and having interest charges apply to distributions by us and the proceeds of sales of the ADSs. See "Item 10. E. Taxation—Material U.S. Federal Income Tax Considerations—Passive Foreign Investment Company Considerations."

Our status as a PFIC will depend on the composition of our income (including whether we receive certain non-refundable grants or subsidies and whether such amounts and reimbursements of certain refundable research tax credits will constitute gross income for purposes of the PFIC income test) and the composition and value of our assets, which may be determined in large part by reference to the market value of the ADSs and our ordinary shares, which may be volatile, from time to time. Our status may also depend, in part, on how quickly we utilize the cash proceeds from the November 2017 global offering in our business. Based on certain estimates of our gross income and assets, and on the nature of our business, we do not expect to be characterized as a PFIC for our taxable year ending December 31, 2018; however, there can be no assurance that we will not be considered a PFIC for any taxable year. Our U.S. counsel expresses no opinion regarding our conclusions or expectations regarding our PFIC status.

# We have identified a material weakness in our internal control over financial reporting. If we are unable to remediate this material weakness, or if we experience additional material weaknesses in the future or otherwise fail to maintain an effective system of internal controls, we may not be able to accurately or timely report our financial condition or results of operations, which may adversely affect investor confidence in us and, as a result, the trading price of our ADSs or ordinary shares.

We have identified a material weakness in our internal control over financial reporting. A material weakness is a deficiency, or combination of deficiencies, in internal control over financial reporting such that there is a reasonable possibility that a material misstatement of our financial statements will not be prevented or detected on a timely basis.

If we are unable to remediate this material weakness, or if we experience additional material weaknesses in the future or otherwise fail to maintain an effective system of internal controls, we may not be able to accurately or timely report our financial condition or results of operations, which may adversely affect investor confidence in us and, as a result, the value of our securities.

In connection with the preparation of our financial results for the years ended December 31, 2016 and 2017, our management concluded that, as of December 31, 2017, our internal control over financial reporting was not effective as a result of a material weakness in our internal control over financial reporting. The material weakness remained unremediated as of December 31, 2017 and is described further below.

Our material weakness related to our having not designed and maintained controls over the operating effectiveness of information technology, or IT, general controls for information systems that are relevant to the preparation of our financial statements. Specifically, we did not design and maintain effective controls over program change management; user access, including segregation of duties; or computer operations. These IT deficiencies did not result in a material misstatement to our financial statements; however, the deficiencies, when aggregated, could impact the effectiveness of IT-dependent controls, such as automated controls that address the risk of material misstatement to one or more assertions, along with the IT controls and underlying data that support the effectiveness of system-generated data and reports.

These control deficiencies could result in a misstatement of these accounts or disclosures that would result in a material misstatement of our annual or interim consolidated financial statements that would not be prevented or detected, and accordingly, we determined that it constituted a material weakness.

We plan to initiate the following remediation efforts focused on improving our internal control over financial reporting and to specifically address the control deficiencies that led to our material weakness. These efforts include the following:

- hiring of finance and accounting personnel with experience in accounting operations, financial controls and SEC reporting;
- completing the implementation of a new enterprise resource planning, or ERP, system;
- initiating design and implementation of our financial control environment, including policies and procedures, controls, reporting and analysis, and segregation of duties; and
- implementation of formal disclosure controls and procedures.

We believe that these activities will further support the remediation of this material weakness. However, we cannot assure you that the measures we have taken to date, and actions we may take in the future, will be sufficient to remediate the control deficiencies that led to our material weakness in our internal control over financial reporting or that they will prevent or avoid potential future material weaknesses. In addition, neither our management nor an independent registered public accounting firm has ever performed an evaluation of our internal control over financial reporting in accordance with the provisions of the Sarbanes-Oxley Act because no such evaluation has been required. Had we or our independent registered public accounting firm performed an evaluation of our internal control over financial material weaknesses may have been identified. If we are unable to successfully remediate our existing or any future material weaknesses in our internal control over financial reporting, or identify any additional material weaknesses, the accuracy and timing of our financial reporting may be adversely affected, we may be unable to maintain compliance with securities law requirements regarding timely filing of reports in addition to applicable stock exchange listing requirements, investors may lose confidence in our financial reporting, and the trading price of our ADSs or ordinary shares may decline as a result.

### If we fail to establish and maintain proper internal controls, our ability to produce accurate financial statements or comply with applicable regulations could be impaired.

Section 404(a) of the Sarbanes-Oxley Act, or Section 404(a), requires that beginning with our second annual report following our U.S. initial public offering, management assess and report annually on the effectiveness of our internal control over financial reporting and identify any material weaknesses in our internal control over financial reporting. Although Section 404(b) of the Sarbanes-Oxley Act, or Section 404(b), requires our independent registered public accounting firm to issue an annual report that addresses the effectiveness of our internal control over financial reporting, we have opted to rely on the exemptions provided in the JOBS Act, and consequently will not be required to comply with SEC rules that implement Section 404(b) until such time as we are no longer an EGC.

We expect our first Section 404(a) assessment will take place for our annual report for the fiscal year ending December 31, 2018. The presence of material weaknesses could result in financial statement errors which, in turn, could lead to errors in our financial reports, delays in our financial reporting, which could require us to restate our operating results or our auditors may be required to issue a qualified audit report. We might not identify one or more material weaknesses in our internal controls in connection with evaluating our compliance with Section 404(a). In order to maintain and improve the effectiveness of our disclosure controls and procedures and internal control over financial reporting, we will need to expend significant resources and provide significant management oversight. Implementing any appropriate changes to our internal control may require specific compliance training of our directors and employees, entail substantial costs in order to modify our existing accounting systems, take a significant period of time to complete and divert management's attention from other business concerns. These changes may not, however, be effective in maintaining the adequacy of our internal control.

If either we are unable to conclude that we have effective internal control over financial reporting or, at the appropriate time, our independent auditors are unwilling or unable to provide us with an unqualified report on the effectiveness of our internal control over financial reporting as required by Section 404(b), investors may lose confidence in our operating results, the price of our ADSs or ordinary shares could decline and we may be subject to litigation or regulatory enforcement actions. In addition, if we are unable to meet the requirements of Section 404, we may not be able to remain listed on Nasdaq.

#### Item 4. Information on the Company.

#### A. History and Development of the Company

Our legal and commercial name is ERYTECH Pharma S.A. We were incorporated as a *société par actions simplifiée*, or S.A.S., under the laws of the French Republic on October 26, 2004 and became a *société anonyme*, or S.A., on September 29, 2005. We are registered at the Register of Commerce and Companies of Lyon (*Registre du commerce et des sociétés*) under the number 479 560 013. In April 2014, we incorporated our wholly-owned U.S. subsidiary, ERYTECH Pharma, Inc. In February 2016, we opened our U.S. office in Cambridge, Massachusetts.

Our principal executive offices are located at Bâtiment Adénine, 60 Avenue Rockefeller, 69008 Lyon, France. Our telephone number at our principal executive offices is +33 4 78 74 44 38. Our agent for service of process in the United States is ERYTECH Pharma, Inc. Our website address is *www.erytech.com*. The reference to our website is an inactive textual reference only and information contained in, or that can be accessed through, our website or any other website cited herein is not part of this Annual Report on Form 20-F.

Our actual capital expenditures for the years ended December 31, 2015, 2016 and 2017 amounted to 0.3 million, 1.8 million, and 1.7 million, respectively. These capital expenditures were related primarily to the buildup of our fixed assets for our pharmaceutical facility and laboratory and to a lesser extent to the purchase of office and computer equipment. We do not capitalize clinical research and development costs until we obtain marketing authorization for a product candidate. We expect our capital expenditures to increase in absolute terms in the near term as we continue to advance our research and development programs and grow our operations. We anticipate our capital expenditures in 2018 to be financed from the proceeds of our November 2017 global offering. For the near future, these investments will be located in France where our primary executive offices and our primary production facility are currently located, and in the United States for our secondary production facility.

#### **B. Business Overview**

We are a biopharmaceutical company developing innovative therapies for severe forms of cancer and orphan diseases. Leveraging our proprietary ERYCAPS platform, which uses a novel technology to encapsulate therapeutic drug substances inside erythrocytes, or red blood cells, we are developing a pipeline of product candidates targeting both solid and liquid tumors for patients with high unmet medical needs. Our lead product candidate eryaspase, which we also refer to as GRASPA, targets the metabolism of cancer cells by depriving the cells of asparagine, an amino acid necessary for their survival and critical in maintaining the cells' rapid growth rate. We are currently developing eryaspase for the treatment of severe solid tumors, including pancreatic cancer. and in acute lymphoblastic leukemia, or ALL. Following positive results obtained in a Phase 2b clinical trial of second-line treatment of patients with metastatic pancreatic cancer and based on the feedback we received from the FDA at our pre-IND meeting in October 2017 and from the feedback we received from the CHMP in February 2018, we are preparing for the launch of a pivotal Phase 3 clinical trial of eryaspase in this indication in the United States and Europe during the third quarter of 2018. Depending on our discussions with the FDA and the EMA, we may also initiate a clinical pivotal study of first line treatment of patients with ALL by the end of the third quarter 2018. We are also preparing for the launch of proof-of-concept clinical trials in first-line pancreatic cancer and other solid tumors, starting with TNBC. In ALL, eryaspase demonstrated positive efficacy and safety results in various clinical trials, including in a Phase 2/3 trial of relapsed or refractory ALL patients. In October 2017, we resubmitted to the European Medicines Agency, or EMA, our Marketing Authorization Application, or MAA, for GRASPA for relapsed or refractory ALL.

In addition to our product candidates based on L-asparaginase treatment, we believe that our ERYCAPS platform has broad potential application and can be used to encapsulate within red blood cells a wide range of therapeutic agents for which long-circulating therapeutic activity or rapid and specific targeting is desired. In addition to eryaspase, we are developing erymethionase, methionine-g-lyase encapsulated in red blood cells, to target the amino acid metabolism of cancer cells and induce tumor starvation. We are also exploring the use of our ERYCAPS platform for developing cancer immunotherapies (ERYMMUNE) and enzyme replacement therapies (ERYZYME).

#### Eryaspase—Our Lead Cancer Metabolism-Targeting Product Candidate

Eryaspase consists of the enzyme L-asparaginase encapsulated in red blood cells. L-asparaginase cleaves and reduces asparagine, a naturally occurring amino acid. All cells in the body need asparagine for their protein synthesis and growth. Normal cells are able to produce most of their asparagine requirements internally. Tumor cells, to ensure their aggressive growth, are highly dependent on asparagine and often lack the enzymes necessary to produce sufficient asparagine internally. They therefore must obtain this nutrient from circulating blood. While L-asparaginase injections have been used for decades as a cancer metabolism treatment in ALL, the toxicity profiles of current commercially available forms of non-encapsulated, or free-form, L-asparaginases have generally limited their use to patients with good performance status, such as pediatric ALL patients. Encapsulation of L-asparaginase, utilizing our proprietary ERYCAPS platform, is designed to prolong the activity and reduce the side effects of L-asparaginase, which we believe broadens the potential use of L-asparaginase outside the pediatric ALL setting, including for the treatment of aggressive solid and liquid tumors. Eryaspase has been tested in over 320 patients to date. In our clinical trials for the treatment of pancreatic cancer and ALL, patients treated with eryaspase have achieved improvements in efficacy endpoints compared to treatment with free-form L-asparaginase or standard of care chemotherapy, and treatment has generally been well tolerated.

We are currently developing eryaspase for the treatment of the following types of cancer:

#### Pancreatic Cancer

Pancreatic cancer is a disease in which solid tumors form in the tissues of the pancreas. We estimate there are approximately 150,000 new cases of pancreatic cancer diagnosed each year in the United States and Europe. Pancreatic cancer is a particularly aggressive cancer, with a five-year survival rate of less than 10%, and is one of the fastest growing cancer indications. According to



estimates published by the American Cancer Society, pancreatic cancer is currently the fourth largest cause of cancer deaths in the United States. According to an article published in the scientific journal *Cancer Research*, pancreatic cancer is projected to surpass colon and breast cancer to become the second largest cause of cancer deaths by 2030.

In September 2017, we announced the full results from our Phase 2b clinical trial of eryaspase combined with chemotherapy in 141 patients suffering from second-line metastatic pancreatic cancer. Data demonstrated improvements in both overall survival (OS) and progression-free survival (PFS). The hazard ratio for OS in the entire patient population was 0.60 (nominal p-value = 0.009), meaning that treatment with eryaspase reduced the risk of death rate by 40% compared to treatment with chemotherapy alone. The PFS hazard ratio was 0.59 (nominal p-value = 0.011). We believe this clinical trial represents the first time an asparaginase-based therapy has been reported to have a survival benefit in a solid tumor indication. We presented these results at the European Society for Medical Oncology, or ESMO, Congress in Madrid, Spain in September 2017.

Based on the feedback on trial design that we received from the FDA at our pre-IND meeting in October 2017 and based on the feedback from the CHMP that we obtained in February 2018, we are preparing for the launch of a pivotal Phase 3 clinical trial of eryaspase for second-line metastatic pancreatic cancer. The proposed Phase 3 trial will evaluate eryaspase in combination with standard chemotherapy, compared to standard chemotherapy alone, in approximately 500 patients in the United States and Europe. The primary endpoint will be overall survival (OS), and enrollment of the first patient in this trial is expected in the third quarter of 2018.

We are also considering the initiation of proof-of-concept studies in first-line pancreatic cancer patients as well as in other pancreatic cancer settings by the end of the first quarter of 2019. With this in mind, we have also initiated further preclinical work to assess the combinability of eryaspase with other compounds used in the treatment of first-line pancreatic cancer patients. We retain worldwide rights to commercialize eryaspase for the pancreatic cancer indication.

#### Triple Negative Breast Cancer

Following the results with eryaspase in the proposed treatment of second-line metastatic pancreatic cancer, we conducted a comprehensive evaluation to determine other potential solid-tumor indications for developing eryaspase and selected metastatic TNBC to evaluate as the next indication to potentially expand the use of eryaspase. TNBC is an aggressive and metabolically active form of breast cancer with high rates of symptomatic metastases. TNBC cells lack expression of estrogen receptor, progesterone receptor and do not overexpress a protein called human epidermal growth factor receptor 2 (HER2). The authors of a September 2017 article in the scientific journal *The Oncologist* estimate that approximately 10% to 20% of the 600,000 breast cancers that are diagnosed each year in the United States and Europe in aggregate are classified as TNBC. As commonly-utilized hormone therapy and HER2 targeting agents are not treatment options for women with TNBC, there is significant unmet need for novel therapeutic approaches in this subtype of breast cancer. We are preparing for the launch of a Phase 2 proof-of-concept clinical trial in this indication. We expect to enroll the first patient in the third quarter of 2018.

#### Acute Lymphoblastic Leukemia

ALL is a blood cancer affecting the lymphoid progenitor cells. ALL patients have excess cells derived from the lymphoid lineage, such as lymphoblast, B-cells, T-cells and natural killer cells. The American Cancer Society estimates that approximately 5,960 new cases of ALL will be diagnosed in the United States in 2018, resulting in approximately 1,470 deaths. Based on incidence data published in scientific literature, we estimate that there are at least as many new cases of ALL diagnosed each year in Europe as in the United States.

In 2014, we completed a multi-center, open-label pivotal Phase 2/3 clinical trial in 80 children and adults with relapsed or refractory ALL in which we evaluated the safety and efficacy of GRASPA compared to free-form L-asparaginase derived from the bacteria *E. coli*, also known as native L-asparaginase. In this European trial, patients without a history of allergies to native L-asparaginase treatments were randomized to receive standard chemotherapy plus either GRASPA or native L-asparaginase. Patients with a known allergy to native L-asparaginase treatments were treated with standard chemotherapy plus GRASPA. The patients treated with GRASPA experienced a mean duration of L-asparaginase activity that was more than twice as long as for patients receiving native L-asparaginase. None of the non-allergic patients who received GRASPA experienced an allergic reaction, compared to 46% of non-allergic patients who received native L-asparaginase. Only 11.5% of patients with a prior L-asparaginase allergy experienced a new allergic reaction after receiving GRASPA, with no patients in the trial experiencing a severe allergic reaction. Patients in the GRASPA treatment arm also had overall higher complete remission rates during induction, and GRASPA was also associated with fewer drug-related adverse events. After three years of follow-up, a nominal improvement in overall survival rates was observed.

In September 2015, we submitted an MAA to the EMA for GRASPA for the treatment of relapsed or refractory ALL. Based on the feedback we received from CHMP at Day 180, we decided to withdraw the MAA in November 2016. To address the outstanding issues, we conducted activities that are designed to provide data regarding immunogenicity and pharmacodynamics of eryaspase, as well as comparability of eryaspase produced with native versus recombinant asparaginase, and we resubmitted to the EMA our MAA for GRASPA for relapsed or refractory ALL in October 2017. We are expecting the CHMP's feedback on our resubmitted MAA by the end of 2018. If approved for the treatment of relapsed or refractory ALL, GRASPA is expected to be marketed in Europe by our commercial partner Orphan Europe, a subsidiary of Recordati S.p.A., an Italian-based pharmaceutical company, and in Israel by Teva Pharmaceuticals, Ltd., an Israeli pharmaceutical company, which we refer to in this Annual Report as Teva.

In the United States, we have completed a Phase 1 dose escalation trial of eryaspase as a potential first-line treatment for adult ALL patients and have determined a recommended dose of eryaspase (100 U per kilogram) for evaluation in Phase 3 clinical trials. We are planning on discussing with the FDA during the second quarter of 2018. We have retained the rights to commercialize eryaspase for the treatment of ALL outside of Europe and Israel, including in the United States.

#### **Our Additional ERYCAPS Product Candidates**

In addition to our product candidates based on L-asparaginase treatment, we believe that our ERYCAPS platform has broad potential application and can be used to encapsulate within red blood cells a wide range of therapeutic agents for which long-circulating therapeutic activity or rapid and specific targeting is desired.

- **Cancer Metabolism.** In addition to the development of eryaspase, we are developing erymethionase, methionine-g-lyase, or MGL, encapsulated in red blood cells (RBCs), as a potential novel amino acid agent targeting cancer metabolism. We presented preclinical data on our erymethionase product candidate at the American Society of Clinical Oncology's Gastrointestinal Cancers Symposium in January 2017 and at the American Association for Cancer Research's Annual Meeting in April 2017. Based on these preclinical studies, we believe that erymethionase represents a promising new treatment approach against a broad range of cancers that rely on methionine metabolism. We expect to commence a Phase 1 clinical trial in Europe by the end of 2018.
- Enzyme Replacement. Outside of the oncology field, we also are studying the use of our ERYCAPS platform to promote long-acting enzyme activity and targeting of specific cells, which we believe may result in attractive product development opportunities for enzyme therapies in the field of metabolic diseases. We refer to this program under the name ERYZYME. We believe that encapsulation of the therapeutic enzymes may reduce the potential for allergic reactions and allow the therapeutic substance to remain in the body longer when compared to non-encapsulated enzymes. In March 2017, we announced our entry into a research collaboration with the Fox Chase Cancer Center to advance the preclinical development of erymethionase for the treatment of homocystinuria, a rare and severe metabolic disorder of methionine metabolism. In July 2017, we announced our entry into a research collaboration with Queen's University to advance the preclinical development of eryminase specifically for the treatment of arginase-1 deficiency, a rare and severe metabolic disorder related to arginine metabolism. In September 2017, we presented early preclinical data on both programs at the 13th International Congress of Inborn Errors of Metabolism (ICIEM). We are also exploring the potential use of additional enzymes in the ERYZYME program.
- **Immunotherapy.** We have also initiated ERYMMUNE, a preclinical development program designed to explore the use of our ERYCAPS platform to encapsulate tumor antigens within red blood cells as an innovative approach to cancer immunotherapy. Based on our preclinical research, we believe that encapsulated tumor antigens can be targeted to key organs, such as the liver or spleen, in order to induce an immune response, resulting in sustained activation of the body's immune system to fight cancers. Preclinical proof-of-concept studies of ERYMMUNE are ongoing.

#### **Our ERYCAPS Platform Technology**

Our proprietary technology uses transfusion-grade, standard packed red blood cells of all four blood groups (O, A, B and AB), which we obtain from blood banks. We match the red blood cells used to the blood type of the patient receiving treatment. The red blood cells are subjected to osmotic stress, which opens and reseals pores on the surface of the cells and allows therapeutic compounds to be added and then trapped inside the cells. Encapsulation offers a number of benefits as compared to free-form compounds. By protecting the therapeutic substance from detection and clearance by the body's immune system, encapsulation is designed to reduce the potential for allergic reactions and to allow the therapeutic substance to remain in the body longer. The cellular membranes of the blood cells also protect the body against the direct toxicity of the drug substance, which results in a decreased incidence of side effects. In the case of L-asparaginase, encapsulation has been shown to extend the half-life of free-form L-asparaginase from one day to approximately two to three weeks, which should lead to fewer injections required for treatment and a lower overall dose. Another form of L-asparaginase derived from the bacteria *E.coli*, currently marketed under the brand name Oncaspar, has a half-life of eight days. We believe that these features make eryaspase a promising therapy for patients who may not be able to tolerate currently available free-form L-asparaginases.

We have automated our encapsulation process to allow for rapid turnaround and high reproducibility. The process for delivering eryaspase to patients, including the encapsulation of L-asparaginase into red blood cells, typically takes approximately 24 hours from the start of production to delivery of the product candidate to the hospital. We maintain a commercial-scale, cGMP-certified production facility in Lyon, France that we believe will be sufficient to supply our commercial requirements for approximately the first two years following the sales launch and commercialization of GRASPA in Europe for the treatment of ALL, if it is approved. We also maintain a smaller production facility in Philadelphia, Pennsylvania, on the premises of the American Red Cross, which is currently used for our clinical trial production. In 2018, we launched initiatives to further expand our production capacity with the addition of a new manufacturing site on the east coast of the United States, in addition to the Philadelphia facility.

Our intellectual property portfolio contains issued patents and patent applications in the United States and internationally, including 14 patent families directed to our production process, our ERYCAPS platform, our product candidates and related diagnostic tests. Our core patent covers eryaspase in the United States until 2030, with potential extension to 2035, and in Europe until 2025, with potential extension to 2030.

#### **Corporate Information**

In May 2013, we completed the initial public offering of our ordinary shares on Euronext Paris, raising  $\in$ 17.7 million in gross proceeds. In October 2014, December 2015, December 2016 and April 2017, we raised  $\in$ 30.0 million,  $\in$ 25.4 million,  $\notin$ 9.9 million and  $\notin$ 70.5 million, respectively, in gross proceeds from the issuances of additional ordinary shares. In November 2017, we completed a global public offering of our ordinary shares, including the full exercise of the underwriters' option to purchase additional shares, from which we raised gross proceeds of \$143.7 million. The November 2017 global offering consisted of a U.S. initial public offering of American Depositary Shares, or ADSs, each representing one ordinary share, and a concurrent private placement in Europe and other countries outside of the U.S. and Canada of our ordinary shares. Our ordinary shares are listed on Euronext Paris under the ticker symbol "ERYP" and our ADSs are listed on the Nasdaq Global Select Market under the symbol "ERYP."

#### **Our Strategy**

Our goal is to become a leading biopharmaceutical company focused on developing, manufacturing and commercializing innovative therapies to treat severe forms of cancer and orphan diseases. The key elements of our strategy to achieve this goal include the following:

- **Rapidly advance the clinical development of eryaspase for the treatment of pancreatic cancer in the United States and in Europe.** In March 2017, we reported positive top-line results from our Phase 2b clinical trial for the second-line treatment of metastatic pancreatic cancer. We presented the full results of this trial at the ESMO Congress in Madrid, Spain in September 2017. Based on the feedback we received from the FDA at our pre-IND meeting in October 2017 and the feedback we obtained from the CHMP in February 2018, we are preparing for a pivotal Phase 3 clinical trial of eryaspase for second-line metastatic pancreatic cancer in the United States and Europe during the third quarter of 2018. The proposed Phase 3 trial will evaluate eryaspase in combination with standard chemotherapy, compared to standard chemotherapy alone, in approximately 500 patients in the United States and Europe. The primary endpoint will be overall survival (OS), and enrollment of the first patient in this trial is expected in the third quarter of 2018. We are also considering the initiation of Phase 2 proof-of-concept studies for first-line pancreatic cancer patients and in other pancreatic cancer settings by the end of the first quarter of 2019.
- Develop eryaspase for the treatment of other solid tumor indications, including triple negative breast cancer. Based on the clinical trials conducted in Europe and on clinical trials to be launched in the United States, we plan to conduct other clinical trials and to seek regulatory authorizations for eryaspase in the United States and in Europe, for the treatment of other solid tumor indications. In February 2018, we announced the selection of TNBC as the next target indication for expanding the potential treatment scope of eryaspase. We are preparing a Phase 2 proof-of-concept clinical trial for this indication and expect to enroll the first patient in this trial in the third quarter of 2018.
- Complete the development of, obtain regulatory approval for and commercialize eryaspase in Europe and the United States for the treatment of ALL. In October 2017, we resubmitted to the EMA our MAA for GRASPA for relapsed or refractory ALL, and we are expecting CHMP feedback by the end of 2018. The MAA resubmission included the Phase 2/3 clinical trial data from children and adults with R/R ALL as well as additional data to address the outstanding questions of the CHMP. We also completed a Phase 1 dose-escalation clinical trial of eryaspase in the United States as a potential first-line therapy for the treatment of adults with ALL and announced in September 2017 that we determined a recommended pivotal Phase 2/3 dose for eryaspase. We intend to meet with the FDA to discuss next steps for ALL, including the design of a pivotal study, during the second quarter of 2018. Depending on our discussions with the FDA and the EMA, we may also initiate a pivotal clinical trial of GRASPA as a first-line treatment for ALL by the end of the third quarter of 2018.
- Leverage our ERYCAPS platform to develop additional innovative and novel therapeutics targeting cancer and orphan diseases. In addition to encapsulating L-asparaginase, the active ingredient in eryaspase, we plan to leverage the broad applicability of our ERYCAPS platform to develop additional product candidates that use other therapeutic drug substances. Based on our preclinical research, we have identified two other enzymes, MGL and ADI, which can be encapsulated within red blood cells in order to induce tumor starvation. We expect to commence a Phase 1 clinical trial in Europe by the end of 2018 evaluating the safety of administering encapsulated MGL in cancer patients. We also plan to expand our product pipeline to include other therapeutic approaches, such as cancer immunotherapy and enzyme replacement therapies. To support this strategy, we intend to continue to seek robust worldwide intellectual property protection for our ERYCAPS platform and our resulting product candidates.
- *Execute on research and development and commercialization opportunities that maximize the value of our proprietary ERYCAPS platform.* We seek to maximize shareholder value from our proprietary platform technology through a combination of in-house development and well-selected partnering opportunities. In some instances, we may elect to continue development and commercialization activities through the expansion of our in-house capabilities, but we will also evaluate and pursue collaborative arrangements with third parties for the development and distribution of our product candidates for specified indications and in specified territories where appropriate. We believe that we will benefit in this regard from our prior experience negotiating distribution arrangements with Orphan Europe for the treatment of ALL and AML in Europe and Teva for the treatment of ALL in Israel. We may also explore co-development or out-licenses of our platform technology to third parties and the creation of spin-out companies. As we move our product



candidates through development toward regulatory approval in the United States and Europe, we will evaluate several options for each product candidate's commercialization strategy, as we have retained all rights to commercialize our product candidates in the United States. These options include building our own internal sales force and distribution units or entering into collaborations with third parties for the distribution and marketing of any approved products.

#### **Our ERYCAPS Platform Technology**

Our ERYCAPS platform uses our proprietary technology to entrap active drug substances inside red blood cells using reversible hypotonic and hypertonic osmotic stress. Our platform technology uses transfusion-grade, standard packed red blood cells of all four blood groups (O, A, B and AB), taken from blood donors with a specific blood type and compatible with the blood type of the patient to be treated. To allow the therapeutic compounds to enter into the red blood cells, we subject the red blood cells to a hypotonic solution that causes water movement into the cells, which leads to swelling and opening of the pores on the cellular membrane. Once the desired concentration of molecules is reached inside the red blood cells, we subject the red blood cells to a hypertonic solution to restore the osmotic pressure to normal. This step causes water to flow out of the cell and the pores to close, rendering the cellular membrane impermeable to molecules above a specific size, including the molecules that have been trapped inside the cell.

The extent to which a red blood cell can swell, known as osmotic fragility, is not uniform and varies between packages of red blood cells. When we obtain a package of red blood cells from a blood bank, we identify a number of key hematological parameters, including the osmotic fragility of the particular sample. Based on the level of osmotic fragility measured, we are able to calculate the specific amount of osmotic pressure to apply in order to achieve the desired concentration of drug substance in each production batch. This patent-protected process allows us to reduce variations in the amount of drug substance to be encapsulated, which ensures that quantifiable amounts of drug substance can be captured in each batch. Our expertise in understanding osmotic fragility and optimizing the red blood cell encapsulation parameters is the cornerstone of our proprietary ERYCAPS platform.

We believe that our ERYCAPS platform technology is an innovative approach that offers several key benefits:

- **Prolonged duration of activity**. Red blood cells are biocompatible carriers that have a half-life of approximately one month in the body. This long half-life, coupled with the protection from the cellular membrane, allows encapsulated therapeutic drug substances to remain in the body longer, thereby increasing the duration of their therapeutic activity and their potential efficacy with lower dosages and fewer injections.
- *Decreased risk of side effects*. The red blood cell membrane protects the body from toxicities associated with the trapped drug substance, which reduces the potential for adverse side effects from the drug.
- *High reproducibility with rapid turnaround on commercial scale*. Our encapsulation process is automated and is designed to produce batches of loaded red blood cells in a highly reproducible, reliable and rapid manner, regardless of the initial characteristics and origin of the red blood cells used. At our cGMP-certified production facility, the process for delivering eryaspase to patients, including the encapsulation of L-asparaginase into red blood cells, typically takes approximately 24 hours from the start of production to delivery of the product candidate to the hospital. We have produced over 1,500 bags of eryaspase to date for use in clinical trials, and we estimate our current production facility will be sufficient for approximately the first two years of commercial-scale production of GRASPA following the sales launch and commercialization of GRASPA in Europe for the treatment of ALL, if it is approved.
- **Stability and ease of administration**. Once shipped from our production facility to the hospital, eryaspase has been shown to remain stable for five days in refrigeration followed by six hours at room temperature. This allows hospital staff to administer the required blood transfusion at an optimal time and to retain control over the administration process.
- **Broad applicability**. Our initial efforts have focused on encapsulating enzymes, such as L-asparaginase, that deplete nutrients necessary for the growth and proliferation of tumor cells, resulting in their starvation and death. Based on our preclinical studies and clinical experience to date, we believe that a variety of additional therapeutic molecules can be encapsulated within red blood cells to induce tumor starvation, both for blood cancers and solid tumors, and to develop cancer immunotherapy and enzyme replacement therapies.

#### **Our Product Development Pipeline**

Using our proprietary ERYCAPS platform, we are developing a pipeline of product candidates to treat severe cancer and orphan diseases. The following table summarizes our product development pipeline:

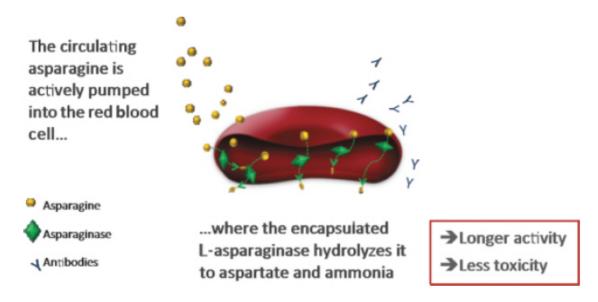
Mode of action	Product Candidate/ PROGRAM	Drug substance	Indication	Discovery	Pre- clinical	Phase 1	Phase 2	Phase 3/ Pivotal	Application for Regulatory Approval	Status/ Milestones	Commercial Rights						
Cancer metabolism Tumor starvation	eryaspase (GRASPA*)	Asparaginase	ALL							<ul> <li>EU: MAA resubmitted in October 2017 for r/r ALL</li> <li>US: Recommended P3 dose determined for first-line ALL in adults</li> <li>Next steps (US &amp; EU): Feedback from CHMP expected by end of 2018; subject to discussions with the FDA and EMA, preparation of potential P3 clinical trial by end of Q3 2018 for first-line ALL</li> </ul>	RECORDATI Europe TTTTT Israel erytech Se						
			PDAC							EU P2b: Full results presented in September 2017     Next steps (US & EU): Launch of P3 clinical trial expected during Q3 2018 for second-line metatastic pancreatic cancer; potential initiation of a P2 proof-of-concept studies in first-line pancreatic cancer setting	US & rest of the world						
											TNBC Solid tumor TBD						
	ery-methionase	Methionine-y- lyase	Solid tumors							- Preparing for launch of P1 study by end of 2018							
Enzyme therapies	ERYZYME	Therapeutic enzymes	Metabolic diseases							Preclinical proof-of-concept studies ongoing: additional     preclinical data expected during 2018							
Immuno- therapy	ERYMMUNE	Tumor antigens	TBD							- Preclinical proof-of-concept data expected by end of 2018							
Arrow indica	ates most advan	ced study within	an indication	or program;	more deta	il is provid	led in the	text sections	below.	·							

#### Our Lead Product Candidate Eryaspase—A Unique Approach to Cancer Treatment

Eryaspase, our first product candidate developed using our proprietary ERYCAPS platform, also known under the trade name GRASPA in Europe and Israel, consists of the enzyme L-asparaginase encapsulated inside an erythrocyte, or a red blood cell. L-asparaginase breaks down asparagine, a naturally occurring amino acid, into L-aspartic acid and ammonia. Asparagine is produced by healthy cells in the body for their own use in protein synthesis. Cancer cells also need asparagine to grow and proliferate, even more than normal cells, but most cancer cells do not produce enough asparagine and must rely on circulating asparagine in order to survive. Because L-asparaginase is capable of catalyzing circulating asparagine, thereby depriving cancer cells of a key nutrient and causing them to die, the use of L-asparaginase to deplete asparagine has become a well-established treatment for ALL patients, and L-asparaginase has been a common component of pediatric ALL treatment protocols for several decades. However, the use of L-asparaginase outside of the pediatric ALL setting is limited, due primarily to the toxicity of and allergies associated with free-form asparaginases, which inhibits their use in adult and elderly ALL patients, as well as in children with relapsed ALL. We believe that encapsulating L-asparaginase in red blood cells will expand the population of cancer patients that may be able to be treated with L-asparaginase.

Eryaspase is administered by intravenous infusion. Once administered, the red blood cells containing L-asparaginase circulate in the bloodstream and remove asparagine mainly through a mechanism of active transportation of asparagine into the red blood cells. Normal red blood cells contain two to three times more asparagine than in the surrounding plasma. When L-asparaginase is encapsulated in the red blood cells, it causes the inner concentration of asparagine to decrease, which activates a natural mechanism of the red blood cell to draw asparagine circulating in the blood plasma into the red blood cell. The asparagine is rapidly degraded inside the red blood cells as well. When maintained long enough, this pumping and degradation activity leads to a systemic depletion of asparagine levels in the bloodstream without releasing L-asparaginase into the bloodstream. The red blood cell membrane also protects the encapsulated L-asparaginase from antibodies present in the patient's blood that would substantially lessen or neutralize the enzyme's activity or cause an allergic reaction. As a result, the enzyme can remain active and potentially effective in the red blood cell for a longer period of time, while at the same time reducing the potential for toxicity and related side effects. Our research indicates that the encapsulation process does not significantly alter the life span of the red blood cell.

The following diagram illustrates the main mode of action of eryaspase:



#### Clinical Development of Eryaspase (GRASPA)

The table below sets forth summary information regarding our clinical trials of eryaspase conducted to date.



#### COMPLETED CLINICAL TRIALS

PHASE	TRIAL REFERENCE	# OF PATIENTS*	AGE	INDICATION	PRIMARY ENDPOINTS	DOSE	REGION	DESIGN
Metastatic Pancreatic Ca	incer							
2b	GRASPANC 2013-03	141	18+	Second-line	Efficacy (progression- free survival) or overall survival) of eryaspase in patients with low ASNS expression levels	100 U/kg	EU	Randomized, open label, controlled
1	GRASPANC 2008-02	12	18+	Second-line	Determination of the maximum tolerated dose (MTD) and recommended Phase 2 dose	25 / 50 / 100 / 150 U/kg	EU	Non-randomized, open label
Acute Lymphoblastic Leu 2/3	GRASPALL 2009-06	80	1 to 55	Relapsed/refractory	Mean duration	150 U/	EU	Randomized, open
					<ul> <li>(days) of ASNase activity &gt;100 U/L</li> <li>Incidence of allergic reactions (induction phase)</li> </ul>	kg		label
2a	GRAALL SA2-2008	30	55+	First-line	<ul> <li>Efficacy and safety of eryaspase with combination therapy and determination of the MTD in elderly</li> </ul>	50 / 100 / 150 U/kg	EU	Non-randomized, open label
1/2	GRASPALL 2005-01	24	1 to 55	Relapsed/refractory	Determination of the MTD and recommended Phase 2 dose	50 / 100 / 150 U/ kg	EU	Randomized, open label
1	GRASPALL 2012-09	14	18+	First-line	Determination of the MTD and recommended Phase 2 dose	50 / 100 / 150 / 200 U/ kg	US	Non-randomized, open label
Acute Myeloid Leukemia		100	05 05		0 "	100 11/		
2b	ENFORCE 1	123	65 to 85	First-line, unfit	<ul> <li>Overall survival</li> </ul>	100 U/ kg	EU	Multicenter, open label, randomized, controlled

#### ONGOING CLINICAL TRIALS

TRIAL ASE REFERENCE ute Lymphoblastic Leukemia	# OF <u>PATIENTS*</u>	AGE	INDICATION	PRIMA ENDPOI		REGION	DESIGN
2 NOPHO	30	1 to 45	Second-line post PEG-asparaginase	<ul> <li>PK / PD, and immunog</li> </ul>	, 0	EU	Single arm, open label
GRASPALL 2012-10-EAP	18	Up to 55	At risk - all lines	<ul> <li>Safety of eryaspase combinat polychen</li> </ul>	e in ion with	EU	Non-randomized, open label

\* Number of patients planned/enrolled.

#### Eryaspase for the Treatment of Pancreatic Cancer and Other Solid Tumors

Researchers have investigated the potential to target asparagine metabolism in solid tumor indications, and based on the observation that many solid tumors, like lymphoblasts, lack the asparagine synthetase, or ASNS, enzyme, a rationale for the use of asparaginase in solid tumors exists. L-asparaginase has been shown to have growth inhibitory effects in different solid tumor cell lines and in xenograft models. The toxicity profile of existing asparaginase products has, however, been prohibitive for their use in patients. Historically, Phase 1 clinical trials conducted by researchers have been modified or halted because of excess toxicity.

We selected pancreatic cancer as the first solid tumor indication for clinical development of eryaspase. After completion of a Phase 1 clinical trial, we commenced a Phase 2b clinical trial of eryaspase combined with chemotherapy in 141 patients suffering from second-line metastatic pancreatic cancer in 2014. In March 2017, we reported top-line results of the study showing improvement in overall and progression-free survival rates for patients treated with eryaspase in combination with chemotherapy as compared to treatment with eryaspase alone. The hazard ratio for overall survival in the entire patient population was 0.60 (nominal p-value = 0.009), meaning that treatment with eryaspase reduced the risk of death rate by 40% compared to treatment with chemotherapy alone. We presented the full results of this trial at the ESMO Congress in Madrid, Spain in September 2017. We believe this clinical trial represents the first time an asparaginase-based therapy has been reported to have a survival benefit in a solid tumor indication. This trial forms the basis for our strategy to explore the further development of eryaspase for the treatment of pancreatic cancer and other solid tumor indications.

#### Background and Potential for L-asparaginase as a Treatment for Pancreatic Cancer

We estimate there are approximately 150,000 new cases of pancreatic cancer diagnosed each year in Europe and the United States. Pancreatic cancer is a particularly aggressive cancer, with a five-year survival rate of less than 10%, and is one of the fastest growing cancer indications. According to estimates published by the American Cancer Society, pancreatic cancer is currently the fourth largest cause of cancer deaths in the United States. According to an article published in the scientific journal *Cancer Research*, pancreatic cancer is projected to surpass colon and breast cancer to become the second largest cause of cancer deaths by 2030. The following table summarizes the number of estimated cases and deaths in the United States in 2017 and 2030 in various solid tumor indications, as well as the five-year survival rate of each type of cancer for the years 2006 through 2012.

INDICATION		CASES (U.S., IN <u>THOUSANDS)</u> 2017 2030		DEATHS (U.S., IN THOUSANDS) 2017 2030	
Lung and bronchus	223	225	156	156	19%
Pancreas	54	88	43	63	9
Liver	41	83	29	51	18
Colon and rectum	135	114	50	47	66
Breast	255	294	41	37	91(1)
Prostate	161	228	27	24	99
Bladder	79	113	17	22	79
Brain and other nervous system	24	N/A	17	17	35
Oesophagus	17	N/A	16	17	21
Kidney	64	69	14	16	75
Ovary	22	N/A	14	14	46

#### (1) Refers to female survival rate.

#### Completed Phase 1 Clinical Trial of Eryaspase for the Treatment of Pancreatic Cancer

In 2011, we completed an open-label Phase 1 clinical trial in 12 patients with pancreatic cancer at four sites in France. The enrolled patients were separated into four cohorts of three subjects each. Eryaspase was administered as one injection of four different doses, 25 Units, or U, per kilogram, 50 U per kilogram, 100 U per kilogram or 150 U per kilogram. The primary endpoint of the trial was the determination of the maximum tolerated dose. Secondary endpoints included assessments of safety and exploratory measures of efficacy. No dose-limiting toxicities were reported, even at the highest dose administered in the trial.

#### Phase 2b Clinical Trial for Eryaspase for the Treatment of Second-Line Metastatic Pancreatic Cancer

In 2014, we commenced a multi-center, open-label, randomized Phase 2b clinical trial to evaluate the efficacy of eryaspase as a second-line treatment for patients with metastatic pancreatic cancer. The trial was conducted at 16 sites in France and performed in collaboration with the Groupe Coopérateur Multidisciplinaire en Oncologie. Professor Pascal Hammel, a gastroenterologist-oncologist at Beaujon Hospital in Paris, was the principal investigator of the trial. The original recruitment objective was 90 patients. In February 2016, we elected to continue to enroll patients to increase the statistical power of the trial. In September 2016, we completed enrollment of 141 patients in this trial. In March 2017, we reported positive top-line results from this trial, which also included three data safety monitoring board, or DSMB, safety reviews. In September 2017, we presented the full results of this trial at the ESMO Congress in Madrid, Spain.

#### Trial Design

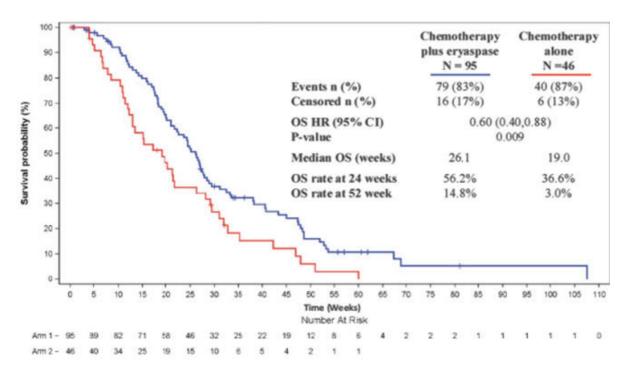
In this trial, patients in the active arm were treated with eryaspase in addition to the current standard of chemotherapy, consisting of either gemcitabine or FOLFOX, depending on which treatment the patient had received as first-line therapy. Patients in the control arm were patients treated with chemotherapy alone. Patients were randomized at a 2:1 ratio. Prior to enrolling each patient in this trial, we used a diagnostic test to assess the level of ASNS expression in such patient's cancer cells, indicating whether the cells were likely to respond to treatment with eryaspase. We included both patients with no or low ASNS expression levels and patients with normal or high ASNS expression levels in the trial.

#### Endpoints

The co-primary endpoints of the Phase 2b clinical trial were progression-free survival and overall survival rates, as measured by the hazard ratio, or HR, for the patients that were enrolled with no or low ASNS expression levels. The HR represents the chance of events occurring in the treatment arm relative to the chance of events occurring in the control arm. An HR of one means that there is no difference in survival between the two groups, while an HR of greater than one or less than one means that survival was better in one of the groups. The outcome of the trial would be considered positive if the HR was below 0.85 for the low or no ASNS expression group, irrespective of statistical significance. The secondary endpoints of the clinical trial included overall progression-free survival and overall survival rates, as measured by HR, in the entire patient population and for the patients enrolled with normal or high ASNS expression levels, as well as objective response rates and safety outcomes.

#### Efficacy Results

The primary objectives of the trial were met, with an overall survival HR of 0.65 and a progression-free survival HR of 0.72 in the patient population with no or low ASNS expression levels. This sub-group of the patient population constituted approximately 70% of the trial population. There was also an overall survival benefit in the entire patient population, with a statistically significant overall survival HR of 0.60 (nominal p-value = 0.009), meaning that a reduction in risk of death rate of 40% was observed. The graph below shows the Kaplan-Meier overall survival curve of the trial in the entire patient population. A Kaplan-Meier plot is a graphical statistical method commonly used to describe survival characteristics. Similar results were observed for progression-free survival.



The baseline characteristics and demographics in the patient population were balanced, and overall survival and progression-free survival results appeared to be consistent across different sub-groups, including age, gender and prior treatment.

An unexpected finding from these results was that the ASNS expression level in the patients did not appear to be predictive of treatment efficacy. However, ASNS does appear to be a prognostic factor. Patients with high ASNS expression levels appear to have a worse prognosis, and their relative response to eryaspase seems to be relatively higher in this group than the patients with no, low or normal ASNS expression levels. Based on this finding, we believe future clinical trials may be conducted in the entire patient population, independent of ASNS expression levels.

#### Next Steps and Phase 3 Clinical Trial Design

The next step in the development of eryaspase for the pancreatic cancer indication is the launch of a Phase 3 clinical trial in patients with second-line metastatic pancreatic cancer. Feedback on the design of the trial was obtained from the FDA and CHMP of the EMA. The proposed Phase 3 trial will evaluate eryaspase in combination with standard chemotherapy, compared to standard chemotherapy alone, in approximately 500 patients in the United States and Europe. The primary endpoint will be OS. We expect the main secondary endpoints will include progression-free survival, objective response rate, disease control rate, quality of life and safety. Enrollment of the first patient in this trial is expected in the third quarter of 2018.

We are also considering the initiation of proof-of-concept studies in first-line pancreatic cancer patients and in other pancreatic cancer settings by the end of the first quarter of 2019. With this in mind, we have also initiated further preclinical work to assess the combinability of eryaspase with other compounds used in the treatment of first-line pancreatic cancer patients. We retain worldwide rights to commercialize eryaspase for the pancreatic cancer indication.

Both the FDA and EMA have granted orphan drug designation for eryaspase or GRASPA for the treatment of pancreatic cancer. Orphan drug designation provides manufacturers with research grants, tax credits and eligibility for marketing exclusivity of up to seven years in the United States and 10 years in Europe.

#### Planned Clinical Development in Triple Negative Breast Cancer and Other Solid Tumors

Following the results with eryaspase in the proposed treatment of second-line metastatic pancreatic cancer, we conducted a comprehensive evaluation to determine other potential solid tumor indications and selected to evaluate metastatic TNBC as the next indication to expand the potential use of eryaspase in solid tumors. TNBC is an aggressive and metabolically active form of breast cancer with high rates of symptomatic metastases. TNBC cells lack expression of estrogen and progesterone receptors and do not overexpress HER2. Scientific literature estimates that approximately 10% to 20% of the 600,000 breast cancers that are diagnosed each year in the United States and Europe in aggregate are classified as TNBC. As commonly-utilized hormone therapy and HER2 targeting agents are not treatment options for women with TNBC, there is significant unmet need for novel therapeutic approaches in this subtype of breast cancer. We are preparing for the launch of a Phase 2 proof-of-concept clinical trial in this indication. Set-up activities have started and we expect to enroll the first patient in the third quarter of 2018.

Preclinical work is ongoing to identify other relevant solid tumor indications, including a review of the use of the product candidate in combination with chemotherapy and immunotherapy compounds.

#### Eryaspase for the Treatment of Acute Lymphoblastic Leukemia (ALL)

We are developing eryaspase (GRASPA) for the treatment of children and adults with ALL in combination with chemotherapy. We have completed three clinical trials in Europe in which a total of 134 patients with ALL enrolled, of which 102 patients were ultimately treated with eryaspase. We are also conducting additional clinical trials in Europe and in the United States to potentially broaden the application and use of GRASPA to include first-line treatment of patients with ALL.

Based on the positive efficacy and safety results from our Phase 2/3 pivotal trial, we submitted an MAA to the EMA for GRASPA for the treatment of relapsed or refractory ALL in September 2015. CHMP is the EMA committee responsible for reviewing the MAA. In September 2016, we received from CHMP a Day 180 List of Outstanding Issues. Following discussions with the EMA, we determined that the collection of the additional information requested by CHMP would take more time than allowed in the regulatory approval procedures. Accordingly, we decided to withdraw the MAA in November 2016. We conducted activities designed to provide data regarding immunogenicity and pharmacodynamics of eryaspase, as well as comparability of eryaspase produced with native versus recombinant asparaginase, and resubmitted our MAA in October 2017.

The EMA and the FDA have granted orphan drug designation for GRASPA for the treatment of ALL, providing us with the potential for marketing exclusivity for up to seven and 10 years, respectively, upon receipt of marketing approval.

#### Background and Market for ALL

Leukemia is a cancer of the bone marrow cells, sometimes called cancer of the blood. Leukemia is characterized by an abnormal and excessive proliferation of blood components that, in the absence of treatment, invade the bone marrow and then the blood. Leukemia characterized by a rapid proliferation of abnormal cells in the bone marrow and requiring urgent treatment is known as acute leukemia. On the other hand, chronic leukemia has a slow proliferation, with a clinical tolerance of cancer cells and a development that may take place over months or years.

ALL is a blood cancer affecting the lymphoid progenitor cells. ALL patients have excess cells derived from the lymphoid lineage, such as lymphoblasts, B-cells, T-cells and natural killer cells. Some mutations in bone marrow progenitors have been directly linked to the development of ALL, although the exact molecular alteration responsible for the disease is often unknown. In general, the development of ALL is difficult to anticipate and few major risk factors are known.

ALL is most prevalent for children between the ages of two and five, although adults are also affected. The American Cancer Society estimates that approximately 5,960 new cases of ALL will be diagnosed in the United States in 2018, resulting in approximately 1,470 deaths. Based on incidence data published in scientific literature, we estimate that there are at least as many new cases of ALL diagnosed each year in Europe as in the United States. The risk for developing ALL declines slowly after the age of five until the mid-20s and then begins to rise again slowly after the age of 50. Overall, approximately 40% of ALL cases occur in adults. Although most cases of ALL occur in children, approximately 80% of deaths from ALL occur in adults. Pediatric ALL patients have a five-year survival rate of approximately 90%, while the five-year survival rate for adults drops to approximately 30% and for seniors, to approximately 15%.

#### L-asparaginase for the Treatment of ALL

The treatment of childhood ALL relies heavily on chemotherapy regimens and the use of L-asparaginase due to a high rate of complete responses observed with these therapies. Adults are also treated with chemotherapy, but L-asparaginase use has generally been limited due to its toxicity, and elderly patients especially cannot tolerate L-asparaginase treatment. Children typically respond better to ALL treatment due to differences in the disease itself and the ability to better handle aggressive treatment regimens. Treatment of children with modern chemotherapy regimens can lead to complete response rates in the 90% range, although that rate

significantly drops as patients age. The identification of chromosomal translocations can also narrow down the exact disease subtype and lead to more targeted treatment options. One of these genetic anomalies, known as the Philadelphia chromosome, is present in approximately 5% of children with ALL and 20% to 25% of adults and seniors. For Philadelphia-negative patients, the administration of L-asparaginase has become the standard of care and is used as first-line treatment in conjunction with traditional chemotherapy regimens.

L-asparaginase is currently available in four forms, each described below. The use of each form depends upon the risk profile and age of the patient as well as the availability of a product in a specific market.

- *Native and recombinant L-asparaginase.* L-asparaginase purified from *E. coli* bacteria, also known as native L-asparaginase, has been part of the standard treatment for pediatric ALL patients since the 1970s. Native L-asparaginase has a half-life of about one day and is typically administered twice per week during the induction phase of chemotherapy treatment. In 2016, a new form of L-asparaginase purified from E. coli bacteria, known as recombinant L-asparaginase and marketed under the brand name Spectrila, was approved in Europe. Native and recombinant L-asparaginase remain the first-line, first-intention treatments for newly diagnosed pediatric ALL patients in many European countries.
- *PEG-asparaginase*. PEG-asparaginase is *E. coli* L-asparaginase that has been pegylated in order to reduce its toxicity and increase its half-life. In some countries, including the United States and the United Kingdom, PEG-asparaginase, marketed under the brand name Oncaspar, has almost completely replaced native L-asparaginase as the first-line, first-intention treatment for pediatric ALL patients, although its use for adults in conjunction with chemotherapy regimens is less universal due to toxicity concerns.
- *Chrysantaspase*. L-asparaginase can also be produced from the bacteria *E. chrysanthemi*. This form of L-asparaginase, marketed under the brand names Erwinase and Erwinaze, is typically used as an alternative treatment option in cases of hypersensitivity reactions to either the native or pegylated forms of *E. coli* L-asparaginase. This product was approved in the United Kingdom in 1985 and was approved in the United States in 2011.

Worldwide sales of the above free-form L-asparaginase products totaled approximately \$400 million in 2016.

#### Limitations of Free-Form L-asparaginase Administration

Despite its long history as a treatment for ALL, the direct administration of free-form L-asparaginase suffers from several limitations, including:

- *Allergic reactions*. The use of native L-asparaginase has been associated with the onset of serious and potentially fatal allergic reactions. In addition to safety concerns, allergies can lead to medical costs associated with treating the allergic reaction and switching to another L-asparaginase product. Oncaspar and Erwinaze were created to reduce the incidence of allergic reactions. While these products have reduced the frequency of allergic reactions, they have not eliminated them completely. Allergic reactions have been reported in up to 32% and 37% of patients who received Oncaspar or Erwinaze, respectively.
- Multiple injections required. With a half-life of approximately one day, native L-asparaginase requires up to eight injections per month at high doses. In addition, free-form L-asparaginase is often attacked by the body's immune system before it has had the opportunity to significantly deplete L-asparagine levels, thereby limiting the duration of its therapeutic activity. With its longer half-life, PEG-asparaginase has reduced the number of necessary injections to approximately two injections per month. However, despite its longer treatment duration, Oncaspar has not achieved progression-free survival rates that are superior to native L-asparaginase. The half-life of Erwinaze is less than that of native L-asparaginase, requiring up to 12 injections each month.
- *Toxicities and other side effects*. A significant number of ALL patients suffer from other adverse effects from administration of free-form L-asparaginase, including clotting disorders, pancreatitis, liver damage and brain damage.

Eryaspase has been designed to reduce the potential for allergic reactions and other side effects, and to allow the therapeutic substance to remain in the body longer. The encapsulation of L-asparaginase has also been shown to extend the half-life of free-form L-asparaginase from one day to approximately two to three weeks, which should lead to fewer injections required for treatment and a lower overall dose. Accordingly, we believe eryaspase has the potential to overcome some of the limitations of free-form L-asparaginase and that a large number of additional patients would benefit from an improved L-asparaginase product.

#### Clinical Development of Eryaspase for the Treatment of ALL

#### Completed Phase 1/2 Clinical Trial in Europe in Adults and Children with Relapsed or Refractory ALL

Between 2006 and 2009, we conducted an open-label, multi-center, randomized Phase 1/2 clinical trial of GRASPA in 24 children and adults up to age 55 with relapsed ALL. The trial was conducted at 24 investigator sites in Europe and was designed to evaluate the efficacy of GRASPA compared to native L-asparaginase in terms of duration of L-asparagine depletion, as well as the safety of GRASPA by examining the side effects associated with treatment. The results of this Phase 1/2 clinical trial supported our hypothesis that GRASPA could deplete circulating L-asparagine at a similar level as free-form L-asparaginase but with fewer injections and potentially reduced side effects.

#### Completed Pivotal Phase 2/3 Clinical Trial in Europe in Adults and Children with Relapsed or Refractory ALL

In 2014, we completed an open-label, randomized, multi-center pivotal Phase 2/3 clinical trial known as the GRASPIVOTALL trial in 80 children and adults with relapsed ALL. The trial began in 2009 and was transitioned into a Phase 3 portion in 2013 upon the positive review by an independent DSMB of the safety results from the first 60 patients. The trial was conducted at 58 investigator sites in France, Belgium and Spain.

#### Trial Design

Patients between the ages of one year and 55 years who had experienced a first relapse of Philadelphia-negative ALL after treatment with native L-asparaginase were eligible to participate in the trial. There were 52 males and 28 females enrolled. The 80 patients in the trial were divided into three treatment arms, depending on whether or not the patients had a known allergy to native L-asparaginase. The 26 patients enrolled in the trial with a known allergy were treated with chemotherapy plus GRASPA. Of the remaining 54 patients in the trial, 26 patients were treated with chemotherapy plus GRASPA, while a control group consisting of the other 28 patients received chemotherapy plus Kidrolase, a native L-asparaginase. The chemotherapy regimen for all patients was a standard protocol known as COOPRALL. During the induction phase of chemotherapy, patients received one or two injections of GRASPA, depending on the severity of disease. During the consolidation phase of chemotherapy, patients received an injection of GRASPA at each time that a block of chemotherapy was given, for up to eight cycles. For patients randomized to the control group, native L-asparaginase was administered up to eight times per month during the induction phase, for up to eight cycles.

#### Endpoints

The primary endpoints of the trial were the duration of L-asparagine activity and the incidence of allergic reactions with GRASPA as compared to the native L-asparaginase control group. The threshold for L-asparaginase activity was established at 100 U per liter, and the number of continuous days with at least that level of activity in the blood was measured. Secondary efficacy endpoints included complete remission rates, existence of minimal residual disease, progression-free survival rates and overall survival rates.

#### Efficacy Results

After one year of patient monitoring, researchers concluded that GRASPA had achieved, both of its primary endpoints for the trial:

- Lower Incidence of Allergic Reactions. Among the non-allergic patients, none of the 26 patients treated with GRASPA experienced an allergic reaction during the induction phase, compared to 13 patients out of 28, or 46%, of those treated with native L-asparaginase in the control group. This result had a statistically significant p-value of less than 0.001. P-value is a conventional statistical method for measuring the statistical significance of clinical trial results. A p-value of less than 0.05 is generally considered to represent statistical significance, meaning that there is a less than five percent likelihood that the observed results occurred by chance. Among the 26 patients with known allergies to L-asparaginase, only three patients, or 12%, experienced an allergy, none of which was determined to be at or above Grade 3 severity.
- Superior Duration of L-Asparaginase Activity. Among the non-allergic patients, the patients treated with GRASPA maintained a mean duration of L-asparaginase activity above 100 U per liter for 18.9 days, with a standard deviation of 5.3 days, with at most two injections during the first month of treatment. This result compared to a mean duration of activity of 8.5 days, with a standard deviation of 6.6 days, in the control group, who received up to eight injections of native L-asparaginase. This comparative result was also statistically significant, with a p-value of less than 0.001. The duration of activity was similar in the allergic patient group, with those patients receiving GRASPA having a mean duration of activity of 17.2 days, with a standard deviation of 6.3 days.

Based on further analysis<sup>1</sup>, GRASPA was also observed to have an improved clinical benefit as compared to native L-asparaginase based on its achievement of the secondary efficacy endpoints:

- *Higher Complete Remission Rate*. At the end of the induction phase, the non-allergic patients in the GRASPA treatment arm, or 76%, had achieved complete remission, or the disappearance of all signs of cancer in response to treatment, as compared to 46.4%, in the control arm. Among the allergic patients, 60% achieved complete remission after treatment with GRASPA.
- *Improved Minimal Residual Disease Rate*. Among the non-allergic patients, nine out of 26, or 35%, achieved low levels of residual leukemic cells classified as minimal residual disease, or MRD, at the end of the induction phase, as compared to seven out of 28, or 25%, of those in the control group. Among the allergic patients, six out of 26, or 23%, achieved MRD after treatment with GRASPA.
- *Improved Overall Survival Rates*. 12-month overall survival rates among the non-allergic patients treated with GRASPA were 76.9%, compared to 67.9%, for those in the control group. 12-month overall survival in the allergic group of patients was 50%. Based on three years of follow-up, a nominal improvement of overall survival was observed (HR = 0.73).
- 1 Following amendment to the statistical analysis plan and use of a different database and statistical program due to the change of vendor

#### Safety Results

Treatment with GRASPA was generally well tolerated. Drug-related adverse events generally consisted of allergic reactions, clotting problems, liver toxicities and pancreas disorders. None of the 52 patients receiving GRASPA during the trial had an adverse event leading to discontinuation of the trial, as compared to 13 out of the 28 patients, or 46%, in the control arm. A total of three patients out of the 52 patients treated with GRASPA during the trial experienced serious adverse events determined to be drug-related.

Among the non-allergic patients in the GRASPA treatment arm, 3 out of 26, or 11.5%, experienced study drug-related coagulation disorders (including impaired coagulation parameters, thromboembolic and hemorrhagic events), compared to 20 out of 28, or 71.4%, in the non-allergic patients in the control group. Similarly, only seven out of the 26 allergic patients, or 26.9%, experienced coagulation disorders. Among the non-allergic patients in the GRASPA treatment arm, nine out of 26, or 34.6%, experienced study drug-related pancreatic events, compared to 13 out of 28, or 46.4%, in the non-allergic patients in the GRASPA treatment arm, 8 out of 26, or 30.8%, experienced study drug-related hepatic events, compared to 13 out of 28, or 46.4%, of the non-allergic patients in the GRASPA treatment arm, 8 out of 26, or 30.8%, experienced study drug-related hepatic events, compared to 13 out of 28, or 46.4%, of the non-allergic patients in the control group. Similarly, only 10 out of the 26 allergic patients, or 38.5%, experienced hepatic events.

#### Completed Phase 2 Clinical Trial in France in Elderly ALL Patients as First-Line Treatment

In 2009, we commenced a Phase 2, open-label, dose-escalation clinical trial of GRASPA as a first-line treatment in 30 patients over the age of 55 with newly diagnosed, Philadelphia-negative ALL. This trial was conducted at 20 sites in France and was completed in 2012. The main objective of this trial was to determine the maximum tolerated and effective dose of GRASPA in combination with chemotherapy. The trial also evaluated the side effects related to treatment with GRASPA, as well as its pharmacokinetic and pharmacodynamic parameters and the rate of complete remission after treatment. We observed in the trial that GRASPA was generally well tolerated and the frequency of adverse events was similar to what was expected in this fragile population of senior patients. The most frequently reported adverse events were elevated pancreatic enzyme levels and coagulation disorders. In addition, this trial demonstrated that GRASPA® (100U/kg) resulted in a complete remission of 77% of patients with an improved median survival of 6 months compared to historical data. No allergic reactions were reported in any of the GRASPA treatment groups. Subject to our discussions with the FDA and EMA, we may also initiate a pivotal clinical trial of GRASPA as a first-line treatment for ALL by the end of the third quarter of 2018.

#### Completed Phase 1 Clinical Trial in the United States in Adult ALL Patients as First-Line Treatment

In March 2013, we initiated a Phase 1 clinical trial in the United States evaluating eryaspase in escalating doses as a potential first-line therapy in patients over the age of 18 with Philadelphia-negative ALL. We enrolled 14 patients at five clinical sites. In this trial, eryaspase was administered starting at 50 U per kilogram, and the dose was increased to 100 U per kilogram and 150 U per kilogram in later cohorts. The primary endpoint of this trial is the number of dose-limiting toxicities. Secondary endpoints include safety, tolerability and serum concentrations of L-asparagine and L-asparaginase. In September 2017, we announced that all patients had been treated in the third dose escalation cohort. The steering committee of the trial reviewed the safety data from all three cohorts and selected a recommended pivotal Phase 2/3 dose of eryaspase (100 U per kilogram).

#### Ongoing Expanded Access Program in Europe for Allergic ALL Patients

In the course of conducting our European clinical trials in pediatric and adult ALL patients, several clinical investigators identified ALL patients who were unable to be treated in our clinical trials due to allergies to other asparaginase formulations (native L-asparaginase, Oncaspar, or Erwinaze). After discussion with French regulatory authorities, in 2014, we commenced a clinical trial in France to allow these allergic patients to be treated with GRASPA as part of an expanded access program, or EAP. Patients up to 55 years of age, with either newly diagnosed or relapsed or refractory ALL, are eligible to participate in the EAP. Patients in the EAP receive GRASPA in conjunction with a standard chemotherapy regimen and are followed for 12 months after completion of chemotherapy. We have enrolled 18 patients to date in the EAP and we received a favorable review by an independent DSMB in October 2017 of the first seven patients treated.

#### Ongoing Phase 2 Clinical Trial in the Nordic Countries of Europe for Treatment of Patients Allergic to Pegylated Asparaginase

In April 2017, we commenced an investigator-initiated Phase 2 clinical trial to evaluate GRASPA in patients with ALL, which is expected to enroll approximately 30 patients at 23 sites across seven Nordic and Baltic countries, including Denmark, Finland, Norway, Sweden, Iceland, Lithuania and Estonia. This trial will be conducted in collaboration with the Nordic Society of Pediatric Hematology and Oncology, or NOPHO. The main objectives of this trial are to evaluate the pharmacokinetic and pharmacodynamic activity, safety and immunogenicity profile of eryaspase in combination with NOPHO's 2008 multi-agent chemotherapy protocol for ALL, administered as second-intention treatment for children or adult ALL patients, one year to 45 years of age, who experience hypersensitivity reactions to PEG-asparaginase or silent inactivation. This trial is expected to continue for approximately two years.

#### Next Steps in ALL

Based on the results of our completed clinical trials for the treatment of ALL, we resubmitted an MAA to the EMA in October 2017 for GRASPA, and expect CHMP feedback on our MAA by the end of 2018.

We expect to discuss next steps for eryaspase in ALL with the FDA in the second quarter of 2018. Subject to our discussions with the FDA and EMA, we may initiate a pivotal clinical trial of GRASPA as a first-line treatment for ALL by the end of the third quarter of 2018 that could become the basis for seeking approval of eryaspase in the United States.

#### **Other ERYCAPS Development Programs**

In addition to our product pipeline centered on L-asparaginase treatment, we are using our proprietary patent-protected ERYCAPS platform to identify additional enzymes that could induce tumor starvation. We have received funding from BPI France for a research program, known as the TEDAC program, intended to identify additional tumor starvation agents and to identify companion diagnostic tests. In preclinical studies performed under the TEDAC program, we have identified two other amino acids, methionine and arginine, and their respective enzymes, methionine-g-lyase, or MGL, and arginine deiminase, or ADI, that we believe may be promising treatments when encapsulated inside red blood cells.

In 2017, we presented preclinical data with our product candidate erymethionase, which consists of MGL in red blood cells, at the American Society of Clinical Oncology Gastrointestinal Cancers Symposium and the American Association for Cancer Research conferences. We are performing preclinical toxicology studies and are planning to start a Phase 1 clinical trial by the end of 2018 with erymethionase. We are also evaluating eryminase, which consists of ADI encapsulated inside red blood cells, as a potential product candidate for further clinical development.

In addition, we currently have two other preclinical development programs ongoing. ERYZYME is a preclinical development program designed to use our proprietary ERYCAPS platform for enzyme-based therapies beyond oncology. We encapsulate therapeutic enzymes inside donor-derived red blood cells using our proprietary ERYCAPS platform in order to create ERYZYME product candidates to target certain metabolic diseases. We believe that the encapsulation of the therapeutic enzymes in the red blood cells may be able to reduce the potential for allergic reactions and to allow the therapeutic substance to remain in the body longer as compared to non-encapsulated enzymes. In 2017, we entered into a research collaboration with the Fox Chase Cancer Center to advance the preclinical development of erymethionase for the treatment of homocystinuria and with Queen's University of Canada to advance the preclinical development of erymethionase for the treatment of arginase-1-deficiency. In September 2017, we presented early preclinical data on both programs at the 13th International Congress of Inborn Errors of Metabolism (ICIEM).

ERYMMUNE is a preclinical development program exploring the use of our proprietary ERYCAPS platform to encapsulate tumor antigens within red blood cells as an innovative approach to cancer immunotherapy. Based on our preclinical research, we believe that encapsulated tumor antigens can be targeted to the spleen, in order to induce an immune response, resulting in sustained activation of the body's immune system to fight cancers. In preclinical studies with three different antigens loaded in red blood cells, we have observed promising proof-of-concept data in three different tumor models. In these studies, we observed significantly increased antigen-specific CD8+ and CD4+ T-cell responses and delays in tumor growth when the encapsulated antigens were injected in mice with tumors, as compared to the injection of the unloaded antigens alone. We plan to continue incubating this platform in order to confirm our earlier preclinical data and to determine our development strategy for these earlier-stage programs. Proof-of-principle studies of ERYMMUNE are ongoing, and will be the basis on which we will decide on the best way to value creation for this technology.

#### **Manufacturing and Supply**

We currently operate two manufacturing facilities to manufacture our product candidates. Our primary production facility for Europe is based in Lyon, France, and includes 19 employees. This production facility complies with European cGMP. We estimate that our current manufacturing capacity in Lyon is approximately three thousand bags annually, which we believe will be adequate for approximately the first two years after commercial launch of GRASPA in Europe for the treatment of ALL. For our current and future clinical trials to be conducted in the United States, we use a qualified production unit in Philadelphia, Pennsylvania in conjunction with the American Red Cross from which we buy the red blood cells bags. Since the beginning of 2018, we launched initiatives to further expand our production capacity with the addition of a new manufacturing site on the east coast of the United States, in addition to the Philadelphia facility and are evaluating strategy for capacity expansion in Europe Our operations at our U.S. production facility are similar to those at our French production facility and are in compliance with FDA regulations. We oversee production and controls for this unit jointly with the American Red Cross. In Europe, we purchase packed red blood cells from *Établissement Français du Sang*, the French Blood Establishment.

In the case of eryaspase, we have the manufacturing and logistics in place to deliver eryaspase to patients, including the encapsulation of L-asparaginase into red blood cells, in approximately 24 hours from the start of production to delivery of the product candidate to the hospital. Once a prescription is written, we receive an order for eryaspase from the hospital. We then purchase a pack of red blood cells compatible with the patient's blood type from a blood bank. We identify the key parameters of the red blood cell sample, including number of cells, blood type, osmotic fragility and other hematological parameters, in order to achieve the desired concentration of L-asparaginase. We encapsulate the L-asparaginase into the red blood cells using an automated process that takes three to eight hours, depending on the number of washing steps required. Before release, the product must meet a number of quality control specifications, including the number of red blood cells in the packed product, the level of L-asparaginase activity, the amount of extracellular L-asparaginase in the blood and the integrity of the container holding the red blood cells. We then deliver the product to the hospital using a third-party commercial overnight delivery service. We ship the product at a refrigerated temperature of between two and eight degrees Celsius, or approximately 36 to 46 degrees Fahrenheit. At this temperature, the product has been shown to remain stable for five days. Once removed and ready for administration, the product remains stable for six hours at room temperature.

For the supply of the L-asparaginase, we entered into a worldwide supply agreement with medac GmbH, or Medac, in December 2008, as subsequently amended on August 19, 2009 and July 25, 2016, which we refer to as the 2008 Medac Agreement. The 2008 Medac Agreement has a term of 20 years and provides for the supply of free-form L-asparaginase at tiered pricing, including a maximum annual number of units at a reduced price for use in our clinical trials. Pursuant to the July 2016 amendment, as of January 1, 2018, Medac may suspend its performance under the 2008 Medac Agreement in the event its supplier of L-asparaginase discontinues supply to Medac and may terminate the 2008 Medac Agreement upon a complete denial of our MAA for GRASPA, upon withdrawal of our MAA for GRASPA or if we substitute L-asparaginase for a recombinant formulation of L-asparaginase.

In May 2011, we entered into a second worldwide supply agreement, as subsequently amended on April 4, 2014 and July 25, 2016, which we refer to as the 2011 Medac Agreement, under which Medac has agreed to supply us with a new, recombinant free-form L-asparaginase that Medac is developing. The 2011 Medac Agreement includes an exclusivity period, starting from the date of commercial authorization of eryaspase/GRASPA for a duration of five years. The term of the 2011 Medac Agreement is until December 2028, provided, that Medac is entitled, upon expiration of the five-year exclusivity period, to terminate the agreement, upon five years' notice, in the event its supplier of the recombinant formulation of L-asparaginase discontinues supplying to Medac. The July 2016 amendment nullified the clauses providing that we could have been forced to refrain from any form of promotion of eryaspase/GRASPA if such product was produced from a new formulation of L-asparaginase registered and marketed prior to eryaspase/GRASPA as a first-line treatment. We have begun using exclusively this new recombinant formulation of L-asparaginase in eryaspase for new indications, including our ongoing clinical trials for pancreatic cancer and do not intend to use the native form of asparaginase for eryaspase anymore.

Additionally, pursuant to the July 2016 amendment of the 2011 Medac Agreement, we granted Medac a second negotiation right for the marketing of GRASPA in the indications of ALL and AML and in certain territories such as Turkey and Russia, assuming Orphan Europe fails to exercise its right of negotiation or we and Orphan Europe do not enter into a subsequent agreement.

We have also entered into a collaboration with Invetech, developer of cGMP manufacturing solutions for cell and advanced therapies, under which Invetech is assisting us in the development of systems to improve the efficiency of the future commercial-scale manufacture of product candidates based on our proprietary ERYCAPS platform and to accommodate production volume needs for commercialization of our product candidates following the receipt of the necessary regulatory approvals.

#### Commercialization

We have not yet established a sales, marketing or product distribution infrastructure. With the exception of eryaspase under the brand name GRASPA for the treatment of ALL and AML in Europe and for the treatment of ALL in Israel, to which we have granted certain marketing and distribution rights to Orphan Europe and Teva, respectively, as described below, we generally expect to retain full commercial rights to our product candidates and we evaluate different commercialization strategies for each product candidate or indication. These options include building our own internal sales force and distribution units or entering into collaborations with third parties for the distribution and marketing of any approved products.

We may also explore co-development or out-licenses of our platform technology to third parties or the creation of spin-out companies. As we move our product candidates through development toward regulatory approval in the United States and Europe, we will evaluate and consider the proper commercialization strategy for each product candidate, as we have retained all rights to commercialize our product candidates in the United States.

#### Agreement with Orphan Europe

In November 2012, we entered into an exclusive license and distribution agreement with Orphan Europe to market and distribute GRASPA for the treatment of ALL and AML in 38 countries in Europe, including all of the countries in the European Union. Under this agreement, we are responsible for obtaining regulatory approval for GRASPA for the treatment of ALL in the European Union, and Orphan Europe is responsible for regulatory activities for the 10 countries not part of the European Union. If GRASPA is approved, Orphan Europe will be responsible for obtaining pricing and reimbursement approvals, subject to our reasonable input. Orphan Europe has agreed to, at its expense, use commercially reasonable efforts to market and promote GRASPA after it has been approved. We have agreed to use commercially reasonable efforts to manufacture and supply GRASPA in the quantities requested by Orphan Europe, based on forecasts that Orphan Europe will provide to us. We are responsible for delivering GRASPA to the customers directly.

We received a payment of  $\pounds$ 5 million upon signing the agreement. In addition, in 2012, we issued  $\pounds$ 5 million in convertible bonds to Recordati S.p.A. which, along with accrued interest, converted into 945,018 of our ordinary shares at the time of our 2013 initial public offering on Euronext Paris. Our agreement with Orphan Europe provides for sharing in the development costs for GRASPA in AML, and we may be entitled to receive future payments of up to  $\pounds$ 37.5 million, subject to our achievement of specified clinical regulatory and commercial milestones. Once on the market, we will receive a combined supply price and royalties up to 45% of net product sales.

We have granted Orphan Europe rights of first negotiation for the commercialization of GRASPA in additional indications beyond ALL and AML in Europe, and for the commercialization of GRASPA in all indications in additional territories consisting of Turkey, Russia, specified countries in the Middle East and all countries in Africa. Orphan Europe has agreed not to be involved in the development or marketing of any competing products containing L-asparaginase for the treatment of ALL and AML.

The term of the agreement varies on a country-to-country basis. For countries that are part of the European Union, the term is 10 years from the date of marketing approval for GRASPA for the treatment of ALL, and will automatically be extended to 10 years from the date of marketing approval for the treatment of AML if that occurs by the end of 2019. For countries that are not part of the European Union, the term is 10 years from the date of marketing approval for GRASPA in the treatment of either ALL or AML, but not longer than three years after the expiration of the term for the countries in the European Union. At the end of the term, Orphan Europe is entitled to request additional 10-year renewals as long as it is in material compliance with the agreement. If we refuse to renew the agreement in specified circumstances, we may be subject to financial penalties as set forth in the agreement. In addition, the agreement provides that Orphan Europe may automatically terminate the agreement, recoup certain expenses and reduce milestone payments in the event that the intellectual property we license to them under the agreement is deemed invalid.

#### Agreement with Teva

In March 2011, we entered into an exclusive distribution agreement with Abic Marketing Limited, an affiliate of Teva Pharmaceutical Industries Ltd., an Israeli pharmaceutical company, which we refer to in this Annual Report as Teva. We granted Teva an exclusive license to seek regulatory approval for and commercialize GRASPA in Israel. We are responsible for the manufacturing and for transporting any products directly to the customer. Teva is responsible for all regulatory and commercial efforts and has agreed to reimburse us for part of our transportation expenses. We do not expect Teva to pursue regulatory approval in Israel until we have obtained marketing approval for GRASPA in the European Union. If we receive European marketing approval for GRASPA in indications other than ALL, Teva may choose to extend its commercial rights within Israel to those additional indications. Under the agreement, we received an upfront payment of €40,000 upon signing the agreement and are eligible to earn up to €45,000 in potential milestone payments upon achievement of specified regulatory milestones as well as a share of Teva's operating profit if Teva extends its distribution rights to other indications. We will receive a transfer price equal to half of total sales of GRASPA in Israel, calculated as set forth in the agreement. The agreement has a term of 10 years and will automatically renew for successive five-year terms unless either party gives at least six months' notice of non-renewal.

We retain the rights to commercialize eryaspase for the treatment of ALL outside Europe and Israel, including in the United States, and for the treatment of all other indications outside of Israel. We retain worldwide commercial rights for all other product candidates.

#### **Intellectual Property**

Our patent portfolio includes pending patent applications and issued patents in the United States and foreign countries. These patents and applications include 14 patent families we own in our own name, summarized below:

TECHNOLOGY	NUMBER OF PATENT FAMILIES	EXPIRATION YEARS FOR EACH PATENT FAMILY *	COUNTRIES IN WHICH PATENTS ARE ISSUED
Our production process		2024 - 2030	Japan, Europe, Australia, China, United
	2	2033 - 2034	States, Korea, India, Canada
Eryaspase	3	2027 - 2029 2032 - 2033 2028 - 2029	Europe, United States, Australia, Singapore, Israel, Japan, Korea, China, India
Other tumor starvation enzymes	3	2026 2034 - 2035 2035 - 2036	Europe, Japan, China, Canada, Korea, Australia, United States
Eryzyme	3	2028 2033 - 2034 2037 - 2038	Europe, Israel
Immune modulation platform	2	2030 2027 - 2028	Australia, Singapore, France, China, Israel, Korea, Europe, United States, Japan
Other technologies/candidates	1	2028 - 2029	Europe, Israel, China, Australia, Singapore, Korea, Canada

\* This expiration year does not take into account supplementary patent protection that could be obtained for some of our patents in the United States, Europe and other countries. Expiration dates for U.S. patents not yet granted may be subject to patent term adjustment.

Of our 14 patent families, ten currently include at least one issued patent.

The term of a U.S. patent may be eligible for patent term restoration under the Hatch-Waxman Act to account for at least some of the time the drug or method of manufacture is under development and regulatory review after the patent is granted. With regard to a drug or method of manufacture for which FDA approval is the first permitted marketing of the active ingredient, the Hatch-Waxman Act allows for extension of the term of one U.S. patent. The extended patent term cannot exceed the shorter of five years beyond the non-extended expiration of the patent or 14 years from the date of the FDA approval of the drug or method of manufacture. Some foreign jurisdictions have analogous patent term extension provisions that allow for extension of the term of a patent that covers a device approved by the applicable foreign regulatory agency. In the future, if and when our product candidates receive FDA approval, we expect to apply for patent term extensions on the patents that we believe will provide the best exclusivity position if extended.

In addition to patent protection, we have trademark protection in many countries for our name, logo and several product candidates. None of our trademarks are subject to a third-party license, except under our distribution agreements with Teva and Orphan Europe with respect to the trademark GRASPA.

#### Patent License from U.S. Public Health Service

In August 2012, we entered into a license agreement with the Public Health Service of the Department of Health and Human Services of the United States, or PHS, under which PHS has granted us an exclusive license to a patent family including two U.S. patents directed to ASNS and asparaginase therapies in the United States. We intend to use the patent rights licensed from PHS to develop a companion diagnostic test for eryaspase and other product candidates we may develop based on our ERYCAPS platform.

#### Competition

The biotechnology and pharmaceutical industries are highly competitive and subject to significant and rapid technological change as researchers learn more about diseases and develop new technologies and treatments. Significant competitive factors in our industry include product efficacy and safety; quality and breadth of an organization's technology; skill of an organization's employees and its ability to recruit and retain key employees; timing and scope of regulatory approvals; government reimbursement rates for, and the average selling price of, products; the availability of raw materials and qualified manufacturing capacity; manufacturing costs; intellectual property and patent rights and their protection; and sales and marketing capabilities. We cannot ensure you that any of our products that we successfully develop will be clinically superior or scientifically preferable to products developed or introduced by our competitors.

Our competitors may also succeed in obtaining EMA, FDA or other regulatory approvals for their product candidates more rapidly than we are able to do, which could place us at a significant competitive disadvantage or deny us marketing exclusivity rights.

Market acceptance of our product candidates will depend on a number of factors, including:

- potential advantages over existing or alternative therapies or tests;
- the actual or perceived safety of similar classes of products;
- the effectiveness of our sales, marketing, and distribution capabilities; and
- the scope of any approval provided by the FDA or foreign regulatory authorities.

Although we believe our product candidates possess attractive attributes, we cannot ensure that our product candidates will achieve regulatory or market acceptance, or that we will be able to compete effectively in the biopharmaceutical drug markets. If our product candidates fail to gain regulatory approvals and acceptance in their intended markets, we may not generate meaningful revenues or achieve profitability.

The competition for our lead product candidate eryaspase is expected to come mainly from other asparaginase products, and from novel immunotherapy agents.

L-asparaginase is currently available in four forms, each described below.

#### Native L-asparaginase

Native L-asparaginase has been part of the standard treatment for pediatric ALL patients since the 1970s. Native L-asparaginase remains the first-line, firstintention treatment for newly diagnosed pediatric ALL patients in many European countries. However, because of its general toxicity, this native form is rarely used in fragile patients. In the United States, the native form, with the brand name Elspar, was removed from the market in 2013 due to production problems and competition from other forms of L-asparaginase.

#### Recombinant L-asparaginase

In 2016, recombinant L-asparaginase was approved in Europe. The product was developed by our partner Medac as a bioequivalent product to native L-asparaginase, and is being launched by Medac under the brand name Spectrila. Recombinant L-asparaginase has a half-life of about one day and is also typically administered twice per week, similar to native L-asparaginase.

#### PEG-asparaginase

PEG-asparaginase is *E. coli* L-asparaginase that has been pegylated in order to reduce its toxicity and increase its half-life. Pegylation refers to the attachment of a polyethylene glycol group to the enzyme, which creates a protective shell around the enzyme to partially protect it from immune cell destruction. This pegylation extends the half-life of the L-asparaginase from one day to approximately five to seven days. PEG-asparaginase, currently marketed under the brand name Oncaspar, was approved by the FDA in 1994 and was granted EU marketing authorization in 2016 for the treatment of ALL patients with a hypersensitivity to native L-asparaginase. Oncaspar is typically administered twice per month, with one injection replacing four injections of native L-asparaginase. The label was expanded in 2006 to include first-line treatment of ALL in combination with chemotherapy. In some countries, including the United States and the United Kingdom, PEG-asparaginase has almost completely replaced native L-asparaginase as the first-line, first-intention treatment for pediatric ALL patients, although its use for adults in conjunction with chemotherapy regimens is less universal due to toxicity concerns. We estimate that worldwide sales of Oncaspar were approximately \$204 million in 2016.

#### Erwinaze

L-asparaginase can also be produced from the bacteria *E. chrysanthemi*. This form of L-asparaginase, marketed under the brand names Erwinase and Erwinaze, is typically considered as an alternative treatment in cases of hypersensitivity reactions to either the native or pegylated forms of *E. coli* L-asparaginase. The product was approved in the United Kingdom in 1985 and was approved in the United States in 2011. Worldwide sales of Erwinaze were approximately \$200 million in 2016

Each of these products corresponds to a different formulation or different production process and, as a result, has a separate profile, particularly in terms of activity duration, frequency of injections and side effects. We currently do not intend to compete directly with native L-asparaginase or Oncaspar where such treatments are prescribed as first-line treatments for newly diagnosed or relapsed or refractory patients. Our initial target market is for patients who have either relapsed or failed first-line treatment with current forms of asparaginases or who have developed an allergic hypersensitivity to those forms of L-asparaginase.

Medac has developed a recombinant L-asparaginase that has been granted marketing approval in Europe. Medac's recombinant product was observed in latestage clinical trials to have efficacy, a life span and a side effect profile similar to that of native L-asparaginase. Medac is also developing a PEG-asparaginase product candidate that is currently in early clinical trials. In addition, Jazz Pharmaceuticals Inc. is developing a pegylated form of Erwinaze, although its clinical development is currently on hold. In addition, Jazz Pharmaceuticals is evaluating early stage asparaginase product candidates with the goal of an improved profile, including a recombinant crisantaspase candidate and other asparaginase product candidates using XL-protein GmbH's PASylation<sup>®</sup> technology. Jazz has also obtained an option to negotiate a license to Pfenex's recombinant pegaspargase candidate.

In addition to currently available forms of L-asparaginase or new forms in development, our product candidates may also compete with other immunotherapy products or development candidates that could be used in the treatment of ALL or AML. These potential treatments include monoclonal antibodies, bispecific monoclonal antibodies and chimeric antigen receptor, or CAR, T-cells approaches. Recent regulatory approvals for the treatment of relapsed or refractory B-cell ALL include Amgen's bispecific antibody, BLINCYTO (blinatumomab), Pfizer's antibody-drug conjugate, BESPONSA (inotuzumab ozogamicin) and Novartis' chimeric antigen receptor T cell (CAR-T) therapy, Kymriah (tisagenlecleucel). Several large pharmaceutical and biotechnology companies, including Amgen Inc., Pfizer, Inc. and Novartis AG, are developing these types of therapies for the treatment of Philadelphia-negative patients with relapsed or refractory B-cell precursor ALL. Continued approval for this indication may be contingent upon verification of clinical benefit in subsequent trials. Amgen Inc. has also recently been granted a conditional MAA from the EMA for BLINCYTO. Other products in later-stage clinical trials include immunotherapy drugs targeting multiple immune mechanisms, such as inotuzumab, an antibody-drug conjugate from Pfizer Inc., and CAR T-cells products from Cellectis S.A., Kite Pharma, Inc. and Novartis AG. These product candidates consist of patients' own immune cells, engineered to recognize and attack their tumors. These new treatments have yielded positive results when used as salvage therapy, but their use has been restricted to small clinical trials to date.

Many of the companies against which we are competing, or against which we may compete in the future, have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved drugs than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

#### **Government Regulation**

Government authorities in the United States at the federal, state and local level and in other countries extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, post-approval monitoring and reporting, marketing and export and import of drug and biological products, or biologics, such as our product candidates. Generally, before a new drug or biologic can be marketed, considerable data demonstrating its quality, safety and efficacy must be obtained, organized into a format specific to each regulatory authority, submitted for review and approved by the regulatory authority.

#### U.S. Biological Product Development

In the United States, the FDA regulates biologics under the Federal Food, Drug, and Cosmetic Act, or FDCA, and the Public Health Service Act, or PHSA, and their implementing regulations. Biologics are also subject to other federal, state and local statutes and regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval, may subject an applicant to administrative or judicial sanctions. These sanctions could include, among other actions, the FDA's refusal to approve pending applications, withdrawal of an approval, a clinical hold, untitled or warning letters, product recalls or withdrawals from the market, product seizures, total or partial suspension of production or distribution injunctions, fines, refusals of government contracts, restitution, disgorgement, reputational harm, and/or civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on us.

Our product candidates must be approved by the FDA through the Biologics License Application, or BLA, process before they may be legally marketed in the United States. The process required by the FDA before a biologic may be marketed in the United States generally involves the following:

- completion of extensive nonclinical, sometimes referred to as preclinical laboratory tests, preclinical animal studies and formulation studies in
  accordance with applicable regulations, including the FDA's Good Laboratory Practice, or GLP, regulations;
- submission to the FDA of an IND, which must become effective before human clinical trials may begin;
- performance of adequate and well-controlled human clinical trials in accordance with applicable IND and other clinical trial-related regulations, sometimes referred to as good clinical practices, or GCPs, to establish the safety and efficacy of the proposed product candidate for its proposed indication;
- submission to the FDA of a BLA;
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities where the product is produced to assess compliance with the FDA's cGMP requirements to assure that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality, purity and potency;
- potential FDA audit of the preclinical and clinical trial sites that generated the data in support of the BLA; and
- FDA review and approval of the BLA prior to any commercial marketing or sale of the product in the United States.

The data required to support a BLA is generated in two distinct development stages: preclinical and clinical. The preclinical development stage generally involves laboratory evaluations of drug chemistry, formulation and stability, as well as studies to evaluate toxicity in animals, which support subsequent clinical testing. The conduct of the preclinical studies must comply with federal regulations, including GLPs. The sponsor must submit the results of the preclinical studies, together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical protocol, to the FDA as part of the IND. An IND is a request for authorization from the FDA to administer an investigational drug product to humans. The central focus of an IND submission is on the general investigational plan and the protocol(s) for human trials. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA raises concerns or questions regarding the proposed clinical trials and places the IND on clinical hold within that 30-day time period. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. The FDA may also impose clinical holds on a product candidate at any time before or during clinical trials due to safety concerns or non-compliance. Accordingly, we cannot be sure that submission of an IND will result in the FDA allowing clinical trials to begin, or that, once begun, issues will not arise that could cause the trial to be suspended or terminated.

The clinical stage of development involves the administration of the product candidate to healthy volunteers or patients under the supervision of qualified investigators, generally physicians not employed by or under the trial sponsor's control, in accordance with GCPs, which include the requirement that all research subjects provide their informed consent for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria, and the parameters to be used to monitor subject safety and assess efficacy. Each protocol, and any subsequent amendments to the protocol, must be submitted to the FDA as part of the IND. Further, each clinical trial must be reviewed and approved by an independent institutional review board, or IRB, at or servicing each institution at which the clinical trial will be conducted. An IRB is charged with protecting the welfare and rights of trial participants and considers such items as whether the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the informed consent form that must be provided to each clinical trial subject or his or her legal representative and must monitor the clinical trial until completed.

There are also requirements governing the reporting of ongoing clinical trials and completed clinical trial results to public registries. Sponsors of clinical trials of FDA-regulated products, including biologics, are required to register and disclose certain clinical trial information, which is publicly available at www.clinicaltrials.gov. Information related to the product, patient population, phase of investigation, study sites and investigators, and other aspects of the clinical trial is then made public as part of the registration. Sponsors are also obligated to discuss the results of their clinical trials after completion. Disclosure of the results of these trials can be delayed until the new product or new indication being studied has been approved.

Clinical trials are generally conducted in three sequential phases that may overlap, known as Phase 1, Phase 2 and Phase 3 clinical trials. Phase 1 clinical trials generally involve a small number of healthy volunteers who are initially exposed to a single dose and then multiple doses of the product candidate. The primary purpose of these clinical trials is to assess the metabolism, pharmacologic action, side effect tolerability and safety of the product candidate and, if possible, to gain early evidence on effectiveness. Phase 2 clinical trials typically involve studies in disease-affected patients to determine the dose required to produce the desired benefits. At the same time, safety and further pharmacokinetic and pharmacodynamic information is collected, as well as identification of possible adverse effects and safety risks and preliminary evaluation of efficacy. Phase 3 clinical trials generally involve large numbers of patients at multiple sites, in multiple countries, from several hundred to several thousand subjects, and are designed to provide the data necessary to demonstrate the efficacy of the product for its intended use and its safety in use, and to establish the overall benefit/risk relationship of the product and provide an adequate basis for product approval. Phase 3 clinical trials may include comparisons with placebo and/or other comparator treatments. The duration of treatment is often extended to mimic the actual use of a product during marketing. Generally, two adequate and well-controlled Phase 3 clinical trials are required by the FDA for approval of a BLA.

Post-approval trials, sometimes referred to as Phase 4 clinical trials, may be conducted after initial marketing approval. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication. In some instances, FDA may condition approval of a BLA on the sponsor's agreement to conduct additional clinical trials to further assess the biologic's safety and effectiveness after BLA approval.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and written IND safety reports must be submitted to the FDA and the investigators for serious and unexpected suspected adverse events or any finding from tests in laboratory animals that suggests a significant risk for human subjects. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, if at all. The FDA, the IRB, or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board or committee. This group provides authorization for whether or not a trial may move forward at designated intervals based on access to certain data from the trial. We may also suspend or terminate a clinical trial based on evolving business objectives and/or competitive climate. Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the product candidate as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, must develop methods for testing the identity, strength, quality and purity of the final product. Additionally, appropriate packaging must be selected and tested and stability studies must be cond

#### BLA and FDA Review Process

Following trial completion, trial data is analyzed to assess safety and efficacy. The results of preclinical studies and clinical trials are then submitted to the FDA as part of a BLA, along with proposed labeling for the product and information about the manufacturing process and facilities that will be used to ensure product quality, results of analytical testing conducted on the chemistry of the product candidate, and other relevant information. The BLA is a request for approval to market the biologic for one or more specified indications and must contain proof of safety, purity, potency and efficacy, which is demonstrated by extensive preclinical and clinical testing. The application includes both negative or ambiguous results of preclinical and clinical trials, as well as positive findings. Data may come from company-sponsored clinical trials intended to test the safety and efficacy of a use of a product, or from a number of alternative sources, including studies initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and efficacy of the investigational product to the satisfaction of the FDA. FDA approval of a BLA must be obtained before a biologic may be offered for sale in the United States.

Under the Prescription Drug User Fee Act, or PDUFA, as amended, each BLA must be accompanied by a significant user fee, which is adjusted on an annual basis. PDUFA also imposes an annual product fee for human drugs and an annual establishment fee on facilities used to manufacture prescription drugs. Fee waivers or reductions are available in certain circumstances, including a waiver of the application fee for the first application filed by a small business.

Once a BLA has been accepted for filing, which occurs, if at all, 60 days after the BLA's submission, the FDA's goal is to review BLAs within 10 months of the filing date for standard review or six months of the filing date for priority review, if the application is for a product intended for a serious or life-threatening disease or condition and the product, if approved, would provide a significant improvement in safety or effectiveness. The review process is often significantly extended by FDA requests for additional information or clarification.

After the BLA submission is accepted for filing, the FDA reviews the BLA to determine, among other things, whether the proposed product candidate is safe and effective for its intended use, and whether the product candidate is being manufactured in accordance with cGMP to assure and preserve the product candidate's identity, strength, quality, purity and potency. The FDA may refer applications for novel drug product candidates or drug product candidates which present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions. The FDA will likely re-analyze the clinical trial data, which could result in extensive discussions between the FDA and us during the review process.

The review and evaluation of a BLA by the FDA is extensive and time consuming and may take longer than originally planned to complete, and we may not receive a timely approval, if at all.

Before approving a BLA, the FDA will conduct a pre-approval inspection of the manufacturing facilities for the new product to determine whether they comply with cGMPs. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. In addition, before approving a BLA, the FDA may also audit data from clinical trials to ensure compliance with GCP requirements. After the FDA evaluates the application, manufacturing process and manufacturing facilities, it may issue an approval letter or a Complete Response Letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A Complete Response Letter indicates that the review cycle of the application is complete and the application is not ready for approval. A Complete Response Letter usually describes all of the specific deficiencies in the BLA identified by the FDA. The Complete Response Letter may require additional clinical data and/or an additional pivotal Phase 3 clinical trial(s), and/or other significant and time-consuming requirements related to clinical trials, preclinical studies or manufacturing. If a Complete Response Letter is issued, the applicant may either resubmit the BLA, addressing all of the deficiencies identified in the letter, or withdraw the application. Even if such data and information is submitted, the FDA may ultimately decide that the BLA does not satisfy the criteria for approval. Data obtained from clinical trials are not always conclusive and the FDA may ultimately decide that the BLA does not satisfy the criteria for approval. Data obtained from clinical trials are not always conclusive and the FDA may ultimaterpret data differently than we interpret the same data.

There is no assurance that the FDA will ultimately approve a product for marketing in the United States, and we may encounter significant difficulties or costs during the review process. If a product receives marketing approval, the approval may be significantly limited to specific populations, severities of allergies, and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. Further, the FDA may require that certain contraindications, warnings or precautions be included in the product labeling or may condition the approval of the BLA on other changes to the proposed labeling, development of adequate controls and specifications, or a commitment to conduct post-market testing or clinical trials and surveillance to monitor the effects of approved products. For example, the FDA may require Phase 4 testing, which involves clinical trials designed to further assess the product's safety and effectiveness and may require testing and surveillance programs to monitor the safety of approved products that have been commercialized. The FDA may also place other conditions on approvals including the requirement for a Risk Evaluation and Mitigation Strategy, or REMS, to assure the safe use of the product. If the FDA concludes a REMS is needed, the sponsor of the BLA must submit a proposed REMS. The FDA will not approve the NDA without an approved REMS, if required. A REMS could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. Any of these limitations on approval or marketing could restrict the commercial promotion, distribution, prescription or dispensing of products. Product approvals may be withdrawn for non-compliance with regulatory standards or if problems occur following initial marketing.

#### Other U.S. Regulatory Matters

Manufacturing, sales, promotion and other activities following product approval are also subject to regulation by numerous regulatory authorities in addition to the FDA, including, in the United States, the Centers for Medicare & Medicaid Services, or CMS, other divisions of the Department of Health and Human Services, the Drug Enforcement Administration, the Consumer Product Safety Commission, the Federal Trade Commission, the Occupational Safety & Health Administration, the Environmental Protection Agency and state and local governments. In the United States, sales, marketing and scientific or educational programs must comply with state and federal fraud and abuse laws, data privacy and security laws, transparency laws, and pricing and reimbursement requirements in connection with governmental payor programs, among others. The handling of any controlled substances must comply with the U.S. Controlled Substances Act and Controlled Substances Import and Export Act. Products must meet applicable child-resistant packaging requirements under the U.S. Poison Prevention Packaging Act. Manufacturing, sales, promotion and other activities are also potentially subject to federal and state consumer protection and unfair competition laws. The distribution of pharmaceutical products is subject to additional requirements and regulations, including extensive record-keeping, licensing, storage and security requirements intended to prevent the unauthorized sale of pharmaceutical products.

The failure to comply with regulatory requirements subjects' entities to possible legal or regulatory action. Depending on the circumstances, failure to meet applicable regulatory requirements can result in criminal prosecution, fines or other penalties, injunctions, recall or seizure of products, total or partial suspension of production, denial or withdrawal of product approvals, or refusal to allow an entity to enter into supply contracts, including government contracts. In addition, even if an entity complies with FDA and other regulatory requirements, new information regarding the safety or efficacy of a product could lead the FDA to modify or withdraw product approval. Prohibitions or restrictions on sales or withdrawal of future products marketed by us could materially affect our business in an adverse way.

Changes in regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example: (i) changes to our manufacturing arrangements, and/or our commercial operations; (ii) additions or modifications to product labeling; (iii) the recall or discontinuation of our products; or (iv) additional record-keeping and/or documentation requirements. If any such changes were to be imposed, they could adversely affect the operation of our business.

#### U.S. Patent Term Restoration and Marketing Exclusivity

Depending upon the timing, duration and specifics of the FDA approval of our product candidates, some of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent term restoration period is generally one-half the time between the effective date of an IND and the submission date of a BLA plus the time between the submission date of a BLA and the approval of that application. Only one patent applicable to an approved drug is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent. The U.S. Patent and Trademark Office, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, we may apply for restoration of patent term for our currently owned or licensed patents to add patent life beyond their current expiration dates, depending on the expected length of the clinical trials and other factors involved in the filing of the relevant BLA.

An abbreviated approval pathway for biological products shown to be similar to, or interchangeable with, an FDA-licensed reference biological product was created by the Biologics Price Competition and Innovation Act of 2009, which was part of the Affordable Care Act. This amendment to the PHSA attempts to minimize duplicative testing. Biosimilarity, which requires that the biological product is highly similar to the reference product notwithstanding minor differences in clinically inactive components and that there be no clinically meaningful differences between the product and the reference product in terms of safety, purity, and potency, can be shown through analytical studies, animal studies, and a clinical trial or trials. Interchangeability requires that a biological product is biosimilar to the reference product and the product can be expected to produce the same clinical results as the reference product and, for products administered multiple times, the product and the reference product may be switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biological product. However, complexities associated with the larger, and often more complex, structure of biological products, as well as the process by which such products are manufactured, pose significant hurdles to implementation that are still being worked out by the FDA.

A reference biological product is granted 12 years of exclusivity from the time of first licensure of the reference product. The first biological product submitted under the abbreviated approval pathway that is determined to be interchangeable with the reference product has exclusivity against other biologics submitting applications under the abbreviated approval pathway for the lesser of one year after the first commercial marketing, 18 months after approval if there is no legal challenge, 18 months after the resolution in the applicant's favor of a lawsuit challenging the biologic's patents if an application has been submitted, or 42 months after the application has been approved if a lawsuit is ongoing within the 42-month period.

Pediatric exclusivity is another type of regulatory market exclusivity in the United States. Pediatric exclusivity, if granted, adds six months to existing exclusivity periods and patent terms. This six-month exclusivity, which runs from the end of other exclusivity protection or patent term, may be granted based on the voluntary completion of a pediatric trial in accordance with an FDA-issued "Written Request" for such a trial.

#### **European Union Drug Development**

In the European Union, our product candidates may also be subject to extensive regulatory requirements. As in the United States, medicinal products can only be marketed if a marketing authorization from the competent regulatory agencies has been obtained.

Similar to the United States, the various phases of preclinical and clinical research in the European Union are subject to significant regulatory controls. Clinical trials of medicinal products in the European Union must be conducted in accordance with European Union and national regulations and the International Conference on Harmonization, or ICH, guidelines on Good Clinical Practices, or GCP. Although the EU Clinical Trials Directive 2001/20/EC has sought to harmonize the European Union clinical trials regulatory framework, setting out common rules for the control and authorization of clinical trials in the European Union, the EU Member States have transposed and applied the provisions of the Directive differently. This has led to significant variations in the Member State regimes. To improve the current system, Regulation (EU) No 536/2014 on clinical trials on medicinal products for human use, which repealed Directive 2001/20/EC, was adopted on April 16, 2014 and published in the European Official Journal on May 27, 2014. The Regulation aims at harmonizing and streamlining the clinical trials authorization process, simplifying adverse event reporting procedures, improving the supervision of clinical trials, and increasing their transparency. Although the Regulation entered into force on June 16, 2014, it will not be applied before 2019 (its enactment will occur six months after the publication of a notice delivered by the European Commission on the European Union clinical trial portal and database, expected for 2019 according to the European Commission's website). Until then the Clinical Trials Directive 2001/20/EC will still apply. In addition, the transitory provisions of the new Regulation offer the sponsors the possibility to choose between the requirements of the Directive and the Regulation for one year from the entry into application of the Regulation.

Under the current regime, before a clinical trial can be initiated it must be approved in each of the EU Member States where the trial is to be conducted by two distinct bodies: the National Competent Authority, or NCA, and one or more Ethics Committees, or ECs. Under the current regime all suspected unexpected serious adverse reactions, or SUSARs, to the investigated drug that occur during the clinical trial have to be reported to the NCA and ECs of the Member State where they occurred.

#### European Union Drug Review and Approval

In the European Economic Area, or EEA (which is comprised of the 28 Member States of the European Union plus Norway, Iceland and Liechtenstein), medicinal products can only be commercialized after obtaining a Marketing Authorization, or MA. Marketing Authorizations may be granted either centrally (Community MA) or nationally (National MA).

The Community MA is issued centrally by the European Commission through the Centralized Procedure, based on the opinion of the CHMP of the EMA and is valid throughout the entire territory of the EEA. The Centralized Procedure is mandatory for certain types of products, such as biotechnology medicinal products, orphan medicinal products, and medicinal products containing a new active substance indicated for the treatment of AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and viral diseases. The Centralized Procedure is optional for products containing a new active substance not yet authorized in the EEA, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the European Union.

National MAs are issued nationally by the competent authorities of the Member States of the EEA and only cover their respective territory. National MAs are available for products not falling within the mandatory scope of the Centralized Procedure. We do not foresee that any of our current product candidates will be suitable for a National MA as they fall within the mandatory criteria for the Centralized Procedure. Therefore, our product candidates will be approved through Community MAs.

Under the above-described procedures, before granting the MA, the EMA or the competent authorities of the Member States of the EEA make an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy.

Pursuant to Regulation (EC) No. 1901/2006, all applications for marketing authorization for new medicines must include to be valid, in addition to the particulars and documents referred to in Directive 2001/83/EC, the results of all studies performed and details of all information collected in compliance with a pediatric investigation plan agreed between regulatory authorities and the applicant, unless the medicine is exempt because of a deferral or waiver of the EMA.

Before the EMA is able to begin its assessment of a Community MA application, it will validate that the applicant has complied with the agreed pediatric investigation plan. The applicant and the EMA may, where such a step is adequately justified, agree to modify a pediatric investigation plan to assist validation. Modifications are not always possible; may take longer to agree than the period of validation permits; and may still require the applicant to withdraw its marketing authorization application and to conduct additional non-clinical and clinical studies. Products that are granted a MA on the basis of the pediatric clinical trials conducted in accordance with the PIP are eligible for a six-month extension of the protection under a supplementary protection certificate (if any is in effect at the time of approval) or, in the case of orphan medicinal products, a two-year extension of the orphan market exclusivity. This pediatric reward is subject to specific conditions and is not automatically available when data in compliance with the PIP are developed and submitted.

#### Orphan Drugs

In the European Union, Regulation (EC) No 141/2000 of the European Parliament and of the Council of December 16, 1999 on orphan medicinal products, as amended, states that a drug shall be designated as an orphan drug if its sponsor can establish:

- that it is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting not more than five
  in ten thousand persons in the European Union when the application is made, or that it is intended for the diagnosis, prevention or treatment of a
  life-threatening, seriously debilitating or serious and chronic condition in the European Union and that without incentives it is unlikely that the
  marketing of the drug in the European Union would generate sufficient return to justify the necessary investment; and
- that there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorized in the European Union or, if such method exists, that the drug will be of significant benefit to those affected by that condition.

Pursuant to Regulation (EC) No. 847/2000 of April 27, 2000 laying down the provisions for implementation of the criteria for designation of a medicinal product as an orphan medicinal product and definitions of the concepts "similar medicinal product" and "clinical superiority", an application for the designation of a drug as an orphan drug must be submitted at any stage of development of the drug before filing of a MA application.

The European Union provides opportunities for market exclusivity. Pursuant to abovementioned Regulation (EC) No. 141/2000, products receiving orphan designation in the European Union can obtain market exclusivity for a certain number of years in the European Union following the marketing approval.

If a Community MA in respect of an orphan drug is granted pursuant to Regulation (EC) No. 726/2004 or where all the Member States have granted marketing authorizations for this product, in accordance with the procedures for mutual recognition, regulatory authorities will not, for a period of usually 10 years, accept another application for a MA, or grant a MA or accept an application to extend an existing MA, for the same therapeutic indication, in respect of a similar drug. This period may however be reduced to six years if, at the end of the fifth year, it is established, in respect of the drug concerned, that the above-mentioned criteria for orphan drug designation are no longer met, in other words, when it is shown on the basis of available evidence that the product is sufficiently profitable not to justify maintenance of market exclusivity.

Pursuant to Regulation No. 1901/2006, for orphan medicinal products, instead of an extension of the supplementary protection certificate, the 10 year period of orphan market exclusivity should be extended to 12 years if the requirement for data on use in the pediatric population is fully met (i.e. when the request contains the results of all studies carried out under the approved Pediatric Investigation Plan or PIP and when the declaration attesting the conformity of the request to this PIP is included in the marketing authorization).

Notwithstanding the foregoing, a MA may be granted, for the same therapeutic indication, to a similar drug if:

- the holder of the MA for the original orphan drug has given its consent to the second applicant;
- the holder of the MA for the original orphan drug is unable to supply sufficient quantities of the drug; or
- the second applicant can establish in the application that the second drug, although similar to the orphan drug already authorized, is safer, more effective or otherwise clinically superior.

The abovementioned Regulation (EC) No. 141/2000 provides for other incentives regarding orphan medicinal products. It notably provides for a protocol assistance. The sponsor of an orphan medicinal product may indeed, prior to the submission of an application for marketing authorization, request advice from EMA on the conduct of the various tests and trials necessary to demonstrate the quality, safety and efficacy of the medicinal product. Besides, EMA shall draw up a procedure on the development of orphan medicinal products, covering regulatory assistance for the definition of the content of the application for authorization.

Regulation (EC) No. 141/2000 also provides that medicinal products designated as orphan medicinal products under the provisions of this Regulation shall be eligible for incentives made available by the Community and by the Member States to support research into, and the development and availability of, orphan medicinal products and in particular aid for research for small- and medium-sized undertakings provided for in framework programs for research and technological development.

#### Post-Approval Controls

The holder of a MA must establish and maintain a pharmacovigilance system and appoint an individual qualified person for pharmacovigilance, or QPPV, who is responsible for oversight of that system. Key obligations include expedited reporting of suspected serious adverse reactions and submission of periodic safety update reports, or PSURs.

All new MAAs must include a risk management plan, or RMP, describing the risk management system that the company will put in place and documenting measures to prevent or minimize the risks associated with the product. The regulatory authorities may also impose specific obligations as a condition of the MA. Such risk-minimization measures or post-authorization obligations may include additional safety monitoring, more frequent submission of PSURs, or the conduct of additional clinical trials or post-authorization safety studies. RMPs and PSURs are routinely available to third parties requesting access, subject to limited redactions. All advertising and promotional activities for the product must be consistent with the approved summary of product characteristics, and therefore all off-label promotion is prohibited. Direct-to-consumer advertising of prescription medicines is also prohibited in the European Union. Although general requirements for advertising and promotion of medicinal products are established under EU directives, the details are governed by regulations in each EU Member State and can differ from one country to another.

#### **Other European Regulatory Matters**

#### French Regulatory Framework

In the European Union, pending the entry into force of Regulation No. 536/2014, the regulation governing clinical trials is currently based on European Directive No. 2001/20/EC of April 4, 2001 relative to the implementation of good clinical practices in the conduct of clinical trials on medicinal products for human use. Each Member State of the European Union had to transpose this Directive into national law, which resulted in Member States adapting it to their own regulatory framework.

In France, for example, Directive No. 2001/20/EC has been implemented by Law 2004-806 of August 9, 2004 regarding the public health policy and Decree 2006-477 of April 26, 2006, modifying the section of the Public Health Code, or PHC, on biomedical research. The Act of August 9, 2004 was notably amended by Law No. 2012-300 of March 5, 2012, or the "Loi Jardé," related to

biomedical research involving human subjects, and French Order No. 2016-800 of June 16, 2016 related to clinical trials of medicinal products for human use, which has recently adapted French law to the new provisions of Regulation No. 536/2014 of the European Parliament and of the Council of April 16, 2014 related to clinical trials of medicinal products for human use, which repealed Directive 2001/20/EC. The Jardé Act was inapplicable for a long time, and applicable since November 18, 2016, date of its enforcement decree.

Law 2004-806 abolishes the prior notification procedure introduced by the Law Huriet-Sérusclat of December 20, 1988. Indeed, Article L. 1121-4 of the PHC, as amended by Law 2004-806, establishes a system of prior authorization. This authorization is granted by the French Medicines Agency, or ANSM, provided that the competent Ethics Committee issued a favorable opinion. All research now requires a prior favorable opinion from an ethics committee. Under Article L. 1123-7 of the PHC, the competent Ethics Committee—selected randomly by drawing lots under Article L. 1123-6 of the PHC—shall notably assess whether the conditions in which the trial will be conducted are valid. This assessment should be based on whether: adequate protection is offered to individuals, in particular to participants; adequate information is provided to the participants and appropriate procedure is in place to obtain their informed consent; the project is relevant; the benefits/risks assessment is satisfactory; the objectives of the trial are adequate to the means implemented; the qualification of the investigator(s) is satisfactory; the conditions and amount of patients' remuneration is compliant; and the method for recruiting participants is adequate. The ANSM, after submission of the complete file containing not only information on the clinical protocol, but also specific product data and its quality control, as well as results of preclinical studies, may inform the sponsor that it objects to the implementation of the research. The sponsor can then modify the contents of its research project and submit this amended or supplemented request to the ANSM. If the sponsor does not alter the content of its request, the request is considered rejected. Under Article R. 1123-38 of the PHC, the time limit for the examination of a request for authorization cannot exceed 60 days from the receipt of the complete file. Finally, under Article L. 1123-11, in the event of risk to public health or if the ANSM considers that the conditions in which the research is implemented no longer correspond to the conditions indicated in the request for authorization or does not comply with the provisions of the Public Health Code, it may at any time request changes to procedures for the realization of research, and suspend or ban this research. The decision of November 24, 2006 sets the rules for Good Clinical Practice, or GCPs, for clinical trials on medicines for human use as referred to in Article L. 1121-3 of the PHC. GCPs aim to ensure both the reliability of data arising from clinical trials and the protection of the persons participating in these clinical trials. GCPs apply to all clinical trials, including pharmacokinetics, bioavailability and bioequivalence studies in healthy volunteers as well as Phase 2 to Phase 4 clinical trials.

The processing of personal data collected during clinical trials should comply with the simplified standards adopted in this respect by the *Commission Nationale de l'Informatique et des Libertés*, or CNIL (i.e. the "Reference Methodologies"), and the sponsor of the trial shall file with the CNIL a compliance undertaking with these Reference Methodologies, as applicable, through a simplified notification procedure. Patients then always shall have a right to access and correct their personal data, and to object to their processing/withdraw their consent, pursuant to Act No. 78-17 of January 6, 1978, as amended. As from the entry into force of the GDPR on May 25, 2018, the current regime should remain pretty much the same, as the draft bill "CNIL 2" still provides for the obligation to comply with standards adopted by the CNIL, and file simplified formalities in this respect.

The main French legislative and regulatory texts relating to the conduct of clinical trials are as follows (which are mainly codified in the French Public Health Code (Articles L. 1121-1 to L. 1126-12 and Articles R. 1121-1 to R. 1125-26)):

- Decree No. 2017/884 of May 9, 2017 modifying regulatory provisions related to research involving human subjects;
- Decree No. 2016-1538 of November 16, 2016 on the Unique Agreement for the implementation of commercial clinical trials involving human beings in health care institutions;
- Decree No. 2016-1537 of November 16, 2016 related to research involving human beings;
- Order No. 2016-800 of June 16, 2016 related to research involving human beings;
- Loi Jardé, Law No. 2012-300 of March 5, 2012, related to biomedical research involving human subjects;
- Law 2004-806 of August 9, 2004 related to the public health policy;
- Decision of December 29, 2015 establishing the rules of Good Manufacturing Practice;
- Law 78-17 of January 6, 1978, as amended, on data protection and its implementing decrees;
- Law 2002-303 of March 4, 2002 and its implementing decrees regarding patient's rights and the quality of the healthcare system;
- Decision No. 2016-262 of July 21, 2016 concerning the standard methodology for the processing of personal data carried out within the context
  of clinical trials (standard methodology MR-001);
- Decision No. 2016-263 of July 21, 2016 concerning the approval of a standard methodology for processing personal data in the context of research in the field of health, which does not require the express consent of the person involved (methodology MR-003);
- Law 2011-2012 of December 29, 2011 strengthening the safety of medicines and health products;

- Law 2000-230 of March 13, 2000, Decree 2001-272 of March 30, 2001 as amended, and Decree 2002-535 of April 18, 2002, relating to
  electronic signatures;
- Decree No. 2016-1871 of December 28, 2016 concerning the processing of personal data on the new "National Health Data System" of France;
- Decision of November 24, 2006 establishing the rules for Good Clinical Practice; and
- Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data which will enter into force on 25 May 2018.

#### Protection of Clinical Trial Subjects

Under French law, a clinical trial may be undertaken only if (i) it is based on the latest stage of scientific knowledge and on sufficient preclinical testing, (ii) the foreseeable risk incurred by the subjects is outweighed by the benefit expected for these persons or the interest of the research, (iii) it aims at expanding scientific knowledge and the means possible to improve the human condition and (iv) the research was designed to reduce the pain, inconveniences, fear and other predictable inconvenience connected to the disease or to the research, by taking into account in particular the degree of maturity of minors and the capacity of understanding of adults unable to express an informed consent. All these conditions must be fulfilled in order to start a clinical trial. A clinical trial may be undertaken under the following technical conditions: (a) under the direction and the supervision of a qualified physician and (b) under adapted material and technical conditions, compatible with the rigorous imperatives of science and the safety of the clinical trial subjects. Two documents must be provided to clinical trial subjects before the conduct of the trial. First, the patient must receive a patient information sheet which must contain in particular a description of the objective, the methodology and the time period of the research, as well as a description of the alternative treatments, the number of subjects expected to take part in the study, the anticipated benefits, the constraints and the foreseeable risks resulting from the administration of the products that are the object of the clinical trials but also the favorable opinion of the ethics committee and the authorization of the ANSM, and information on processing of personal data. The information communicated must be summarized in a written document delivered to the patient prior to any administration of products by the investigator or a physician. Second, the patient must confirm his or her agreement to participate in the clinical study by signing an informed consent form. For each study, patient information must include a right to refuse to participate and to withdraw consent at any time and by any means without further consequences or prejudice. A clinical trial on a minor may be undertaken only if, in particular, the informed consent of the parents or legal representative has been obtained. Furthermore, a clinical trial on adults under guardianship requires the informed consent of the adult's legal representative.

#### Declaration of Financial Interests

Act No. 2011-2012 of December 29, 2011, aimed at strengthening the health safety of medicinal and health products, as amended (and its implementing decrees), introduced into French law certain provisions regarding transparency of fees received by some healthcare professionals from industries, i.e. companies manufacturing or marketing health products that are reimbursed under the French social security system (Article L.4113-6 of the French Public Health Code). These provisions have been recently extended and redefined by Decree No. 2016-1939 of December 28, 2016, which clarified French "Sunshine" regulations. The decree notably provides that companies manufacturing or marketing health care products (medicinal products, medical devices, etc.) in France shall publicly disclose (mainly on a specific public website available at: https://www.entreprises-transparence.sante.gouv.fr) the advantages and fees paid to healthcare professionals amounting to 10 euros or above, as well as the agreements concluded with the latter, along with detailed information about each agreement (the precise subject matter of the agreement, the date of signature of the agreement, its end date, the total amount paid to the healthcare professional, etc.). Act No. 2011-2012 also reinforced the French anti-gift rules and Order No. 2017-49 of January 19, 2017 amended the law and expanded the scope of the general prohibition of payments from pharmaceutical and device manufacturers to healthcare professionals. The changes of the anti-gift rules will only enter into force after the publication of implementing measures, which is expected to occur by July 2018.

Please note in this regard that under French law, parties to a clinical trial agreement or CTA must use a CTA template ("unique agreement" or *convention unique* in French) to organize the conduct of interventional clinical trials with commercial purpose, as well as specific template exhibits to this agreement (Articles L.1121-16-1 and R.1121-3-1 of the PHC). Once concluded, the CTA shall be communicated for information by the sponsor to the French national board of physicians (*Ordre national des médecins* in French) without delay.

#### French Pharmaceutical Company Status

We have the regulated status of pharmaceutical establishment and operating company, which allows us to manufacture and market our product candidates. Obtaining a pharmaceutical establishment license, either as a distributor or as a manufacturer requires the submission of an application dossier to the ANSM. The application package will vary depending on the type of application (distribution license or manufacturing license). The ANSM grants such license after verifying that the company has adequate premises, the necessary personnel and adequate procedures to carry out the proposed pharmaceutical activities.

#### Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any product candidates for which we obtain regulatory approval. In the case of GRASPA, we have entered into distribution arrangements with Orphan Europe and Teva for marketing in Europe and Israel, respectively, and those third parties will be responsible for obtaining coverage and reimbursement for GRASPA in those territories if it is approved. Sales of our products will depend, in part, on the extent to which our products, once approved, will be covered and reimbursed by third-party payors, such as government health programs, commercial insurance and managed healthcare organizations. These third-party payors are increasingly reducing reimbursement levels for medical products and services. The process for determining whether a third-party payor will provide coverage for a drug product typically is separate from the process for setting the price of a drug product or for establishing the reimbursement rate that a payor will pay for the drug product once coverage is approved. Third-party payors may limit coverage to specific drug products on an approved list, also known as a formulary, which might not include all of the approved drugs for a particular indication.

To secure coverage and reimbursement for any product candidate that might be approved for sale, we may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product candidate, in addition to the costs required to obtain FDA or other comparable regulatory approvals. Whether or not we conduct such studies, our product candidates may not be considered medically necessary or cost-effective. A third-party payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a product does not assure that other payors will also provide coverage, and adequate reimbursement, for the product. Third-party reimbursement may not be sufficient to enable us to maintain price levels high enough to realize an appropriate return on our investment in product development.

The containment of healthcare costs has become a priority of federal and state governments, and the prices of drugs have been a focus in this effort. The U.S. government, state legislatures and foreign governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement, utilization management and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit our net revenue and results. Decreases in third-party reimbursement for our product candidates or a decision by a third-party payor to not cover our product candidates could reduce physician usage of the product candidates and could have a material adverse effect on our sales, results of operations and financial condition.

For example, the Patient Protection and Affordable Care Act, or ACA, enacted in the United States in March 2010, has already had, and is expected to continue to have, a significant impact on the health care industry. The ACA has expanded coverage for the uninsured while at the same time containing overall healthcare costs. With regard to pharmaceutical products, among other things, the ACA expanded and increased industry rebates for drugs covered under Medicaid programs and made changes to the coverage requirements under the Medicare Part D program. Some of the provisions of the ACA have vet to be implemented, and there have been judicial and Congressional challenges to certain aspects of the ACA, as well as recent efforts by the Trump administration to repeal or replace certain aspects of the ACA. Since January 2017, President Trump has signed two Executive Orders and other directives designed to delay the implementation of certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. Concurrently, Congress has considered legislation that would repeal or repeal and replace all or part of the ACA. While Congress has not passed comprehensive repeal legislation, two bills affecting the implementation of certain taxes under the ACA have been signed into law. The Tax Cuts and Jobs Act of 2017 includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate". Additionally, on January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain ACA-mandated fees, including the so-called "Cadillac" tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the medical device excise tax on non-exempt medical devices. Further, the Bipartisan Budget Act of 2018, or the BBA, among other things, amends the ACA, effective January 1, 2019, to increase from 50 percent to 70 percent the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole." The prospects for further Congressional action remain uncertain. We continue to evaluate the effect that the ACA and its possible repeal or repeal and replacement will have on our business. We cannot predict the full impact of the ACA on pharmaceutical companies, as many of the ACA reforms require the promulgation of detailed regulations implementing the statutory provisions, which has not yet occurred.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. For example, on August 2, 2011, the Budget Control Act of 2011 among other things, created measures for spending reductions by Congress. Specifically, the Joint Select Committee on Deficit Reduction was created to recommend to Congress proposals in spending reductions. The Joint Select Committee on Deficit Reduction did not achieve a targeted deficit reduction of at least \$1.2 trillion for the years 2012 through 2021, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, started in April 2013 and which, due to subsequent legislative amendments, including the BBA, will stay in effect through 2027 unless additional Congressional action is taken. Additionally, on January 2, 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Recently, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products. Such scrutiny has resulted in several recent U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the cost of drugs under Medicare and reform government program reimbursement methodologies for drug products. At the federal level, the Trump administration's budget proposal for fiscal year 2019 contains further drug price control measures that could be enacted during the 2019 budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. While any proposed measures will require authorization through additional legislation to become effective, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, legislatures are increasingly passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

We expect that additional federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, and in turn could significantly reduce the projected value of certain development projects and reduce our profitability.

In addition, in some foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, the European Union provides options for its Member States to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A Member State may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. For example, in France, effective market access will be supported by agreements with hospitals and products may be reimbursed by the Social Security Fund. The price of medicines is negotiated with the Economic Committee for Health Products, or CEPS. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our product candidates. Historically, products launched in the European Union do not follow price structures of the United States and generally prices tend to be significantly lower.

#### Other Healthcare Laws and Compliance Requirements

Our business operations in the United States and our arrangements with clinical investigators, healthcare providers, consultants, third party payors and patients may expose us to broadly applicable federal and state fraud and abuse and other healthcare laws. These laws may impact, among other things, our research, proposed sales, marketing and education programs of our product candidates that obtain marketing approval. The laws that may affect our ability to operate include, among others:

- the U.S. federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, receiving, offering or paying remuneration (including any kickback, bribe or rebate), directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, lease, order, or recommendation of, an item, good, facility or service reimbursable under a federal healthcare program, such as the Medicare and Medicaid programs;
- federal civil and criminal false claims laws and civil monetary penalty laws, including the federal civil False Claims Act, which impose penalties
  and provide for civil whistleblower or qui tam actions against individuals and entities for, among other things, knowingly presenting, or causing
  to be presented, claims for payment from Medicare, Medicaid, or other third-party payers that are false or fraudulent, or making a false statement
  or record material to payment of a false claim or avoiding, decreasing, or concealing an obligation to pay money to the federal government,
  including for example, providing inaccurate billing or coding information to customers or promoting a product off-label;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created additional federal criminal statutes that
  prohibit knowingly and willfully executing or attempting to execute a scheme to defraud any healthcare benefit program, knowingly and willfully
  embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense, and knowingly
  and willingly falsifying, concealing or covering up a material fact or making materially false statements, fictitious, or fraudulent statements in
  connection with the delivery of or payment for healthcare benefits, items, or services;
- the federal Physician Payments Sunshine Act, enacted as part of the ACA, which requires applicable manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid, or the Children's Health Insurance Program, with specific exceptions, to track and annually report to CMS payments and other transfers of value provided to physicians and teaching hospitals and certain ownership and investment interests held by physicians or their immediate family members;
- HIPAA, as amended by the Health Information Technology and Clinical Health Act, or HITECH, and its implementing regulations, which
  imposes certain requirements on covered entities and their business associates that perform functions or activities that involve HIPAA Protected
  Health Information on their behalf relating to the privacy, security and transmission of individually identifiable health information; and



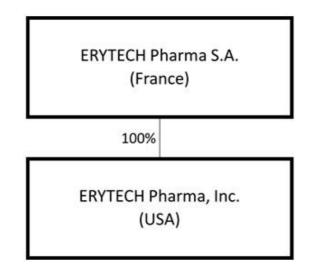
• State and/or foreign equivalents of each of the above federal laws and regulations, such as: state anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payor, including commercial insurers; state marketing and/or transparency laws applicable to manufacturers that may be broader in scope than the federal requirements; state laws that require biopharmaceutical companies to comply with the biopharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government; and state and/or foreign laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect as HIPAA, thus complicating compliance efforts.

The ACA broadened the reach of the federal fraud and abuse laws by, among other things, amending the intent requirement of the U.S. federal Anti-Kickback Statute and certain federal criminal healthcare fraud statutes. Pursuant to the statutory amendment, a person or entity no longer needs to have actual knowledge of those statutes or specific intent to violate them in order to have committed a violation. In addition, the ACA provides that the government may assert that a claim including items or services resulting from a violation of the U.S. federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act or the civil monetary penalties statute.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to, for example, significant administrative, civil, and/or criminal penalties, damages, fines, disgorgement, contractual damages, reputational harm, diminished profits and future earnings, individual imprisonment, exclusion from government funded healthcare programs, such as Medicare and Medicaid, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws and the curtailment or restructuring of our operations. If the physicians or other healthcare providers or entities with whom we expect to do business are found to be not in compliance with applicable laws, they may be subject to administrative, civil, and/or criminal sanctions, including exclusions from government funded healthcare programs.

## C. Organizational Structure.

The following diagram illustrates our corporate structure:



## **D.** Property, Plants and Equipment.

Our principal executive offices are located at Bâtiment Adénine, 60 Avenue Rockefeller, 69008 Lyon, France. We lease office and laboratory space, which together consist of approximately 1,800 square meters, in Lyon, France. The lease for this facility expires in June 2024, and we have the ability to terminate the lease early in either June 2019 or June 2021. We have entered into another lease in Lyon for additional offices and laboratory space due to our increasing headcount, which together will consist of approximately 2,430 square meters. This new facility is under construction and we anticipate taking occupancy in June 2019. The lease for this facility expires on June 2029 and we will have the ability to terminate the lease either in June 2025 or June 2028. We believe our current leased space is sufficient to meet our current needs in Europe.

In February 2016, we opened our U.S. office in Cambridge, Massachusetts. We currently lease 6,289 square feet of office space in Cambridge, Massachusetts under a lease that expires in January 2023. We anticipate leasing additional office and manufacturing space in the United States in connection with the expansion of our clinical trials and preparing for commercialization activities.

In addition, we have an agreement with the American Red Cross that provides us with a production facility in Philadelphia, Pennsylvania.

## Item 4A. Unresolved Staff Comments.

Not applicable.

## Item 5. Operating and Financial Review and Prospects.

You should read the following discussion of our operating and financial review and prospects in conjunction with our audited consolidated financial statements and the related notes thereto included elsewhere in this Annual Report on Form 20-F. In addition to historical information, the following discussion and analysis contains forward-looking statements that reflect our plans, estimates and beliefs. Our actual results and the timing of events could differ materially from those anticipated in the forward-looking statements. Factors that could cause or contribute to these differences include those discussed below and elsewhere in this Annual Report on Form 20-F, particularly in sections titled "Risk Factors" and "Special Note Regarding Forward-Looking Statements."

#### Overview

We are a biopharmaceutical company developing innovative therapies for severe forms of cancer and orphan diseases. Leveraging our proprietary ERYCAPS platform, which uses a novel technology to encapsulate therapeutic drug substances inside erythrocytes, or red blood cells, we are developing a pipeline of product candidates targeting both solid and liquid tumors for patients with high unmet medical needs. Our lead product candidate eryaspase, which we also refer to as GRASPA, targets the metabolism of cancer cells by depriving the cells of asparagine, an amino acid necessary for their survival and critical in maintaining the cells' rapid growth rate. We are currently developing eryaspase for the treatment of certain solid tumors, including pancreatic cancer and acute lymphoblastic leukemia, or ALL. Following positive results obtained in a Phase 2b clinical trial of second-line treatment of patients with metastatic pancreatic cancer, we are preparing for the launch of a pivotal Phase 3 clinical trial of eryaspase in this indication in the United States and Europe during the third quarter of 2018. We are also preparing for the launch of proof-of-concept clinical trials in first-line pancreatic cancer and other solid tumors, starting with TNBC. In ALL, eryaspase demonstrated positive efficacy and safety results in various clinical trials, including in a Phase 2/3 trial of relapsed or refractory ALL patients. In October 2017, we resubmitted to the European Medicines Agency, or EMA, our Marketing Authorization Application, or MAA, for GRASPA for relapsed or refractory ALL.

In addition to our product candidates based on L-asparaginase treatment, we believe that our ERYCAPS platform has broad potential application and can be used to encapsulate within red blood cells a wide range of therapeutic agents for which long-circulating therapeutic activity or rapid and specific targeting is desired. In addition to eryaspase, we are developing erymethionase, methionine-g-lyase encapsulated in red blood cells, to target the amino acid metabolism of cancer cells and induce tumor starvation. We are also exploring the use of our ERYCAPS platform for developing cancer immunotherapies (ERYMMUNE) and enzyme replacement therapies (ERYZYME).

We have never generated any revenues from product sales. We do not expect to generate material revenue from product sales unless and until we successfully complete development of, obtain marketing approval for and commercialize our product candidates. Clinical development, regulatory approval and commercial launch of a product candidate can take several years and are subject to significant uncertainty. Historically, we have financed our operations and growth through issuances of share capital and convertible bonds and through conditional advances and subsidies from Bpifrance Financement (formerly Oséo), part of BPI France, a French public investment bank and from research tax credits. In May 2013, we completed the initial public offering of our ordinary shares on Euronext Paris, from which we raised  $\in$ 17.7 million in cash proceeds, and in October 2014, we raised an additional  $\in$ 30 million in gross proceeds from the issuance of additional ordinary shares. We also conducted three private placements with institutional investors in the United States and in Europe in December 2015, December 2016 and April 2017, raising  $\notin$ 25.4 million,  $\notin$ 9.9 million and  $\notin$ 70.5 million in gross proceeds, respectively.

In November 2017, we completed a global offering of an aggregate of 6,180,137 ordinary shares, including the full exercise of the underwriters' options to purchase additional shares, for gross proceeds of \$143.7 million. The global offering consisted of a U.S. initial public offering of 5,389,021 American Depositary Shares, each representing one ordinary share and a concurrent private placement in Europe and other countries outside of the U.S. and Canada of 791,116 ordinary shares. Our net proceeds from the global offering were approximately  $\pounds$ 112.1 million (\$130.4 million). In connection with our 2017 global offering, our share capital increased by  $\pounds$ 618,013.70 with a corresponding increase of  $\pounds$ 122,984,726 in our share premium.

Since our inception in 2004, we have incurred significant operating losses. Our net loss was  $\leq 15.0$  million,  $\leq 21.9$  million and  $\leq 33.5$  million for the years ended December 31, 2015, 2016 and 2017, respectively. We had an accumulated deficit of  $\leq 113.5$  million as of December 31, 2017, and we expect to incur significant expenses and substantial operating losses over the next several years as we continue our research and development efforts and advance our clinical development programs in Europe and the United States. Our net losses may fluctuate significantly from quarter to quarter and year to year, depending on the timing of our clinical trials, the receipt of milestone payments, if any, under our collaborations with Orphan Europe and Teva, and our expenditures on other research and development activities. We anticipate that our expenses will increase substantially in connection with our ongoing activities, as we:

- initiate and conduct our planned clinical trials of eryaspase in Europe and in the United States;
- continue the research and development of our other product candidates, including planned and future clinical trials;
- seek to discover and develop additional product candidates;
- seek regulatory approvals for any product candidates that successfully complete clinical trials;
- scale-up our manufacturing capabilities to support the launch of additional clinical studies and the commercialization of our product candidates, if approved;
- establish a sales and marketing infrastructure for the commercialization of our product candidates, if approved;
- maintain, expand and protect our intellectual property portfolio;
- hire additional clinical, medical, regulatory, quality control and scientific personnel; and
- add operational, financial and management information systems and personnel, including personnel to support our product development, manufacturing and commercialization efforts and our operations as a public company listed in the United States.

Until such time that we can generate substantial revenue from product sales, we expect to finance these expenses and our operating activities through our existing cash and cash equivalents. If we are unable to generate revenue from product sales, in particular from GRASPA for ALL in Europe, in accordance with our expected timeframes, we will need to raise additional capital through the issuance of our shares, through other equity or debt financings or through collaborations or partnerships with other companies. However, we may be unable to raise additional funds or enter into other funding arrangements when needed on favorable terms, or at all, which would have a negative impact on our financial condition and could force us to delay, limit, reduce or terminate our development programs or commercialization efforts or grant other rights to develop or market product candidates that we would otherwise prefer to develop and market ourselves.

Although it is difficult to predict future liquidity requirements, we believe that our existing cash and cash equivalents as at December 31, 2017, together with interest thereon, will be sufficient to fund our operations for at least the next 24 months. However, our ability to successfully transition to profitability will be dependent upon achieving a level of revenues adequate to support our cost structure. We cannot assure you that we will ever be profitable or generate positive cash flow from operating activities.

As indicated in Note 3 of our consolidated financial statements for the years ended December 31, 2015, 2016 and 2017 due to the listing of our ordinary shares on Euronext Paris and in accordance with the European Union's regulation No. 1606/2002 of July 19, 2002, statutory consolidated financial statements were prepared in accordance with IFRS, as adopted by the European Union for the years ended December 31, 2015, 2016 and 2017 and were approved and authorized for issuance by our board of directors on February 19, 2016, March 1, 2017 and March 9, 2018, respectively.

The consolidated financial statements as of and for the years ended December 31, 2015, 2016 and 2017 included in this Annual Report on Form 20-F have been prepared in accordance with IFRS as issued by the IASB with no difference with the statutory consolidated financial statements and were approved and authorized for issuance by our board of directors on March 9, 2018.

#### **Financial Operations Overview**

## **Operating Income**

Our operating income consists of other income.

#### Revenues

To date, we have not generated any revenue from the sale of products. Our ability to generate product revenue and to become profitable will depend upon our ability to successfully develop and commercialize GRASPA and our other product candidates. Because of the numerous risks and uncertainties associated with product development and regulatory approval, we are unable to predict the amount or timing of product revenue.

#### **Other Income**

Our other income consists of research tax credits, grants from BPI France for our preclinical research programs and reimbursements from Orphan Europe for some of the internal costs we incur under our distribution agreement with them.

#### Research Tax Credit

The research tax credit (*crédit d'impôt recherche*), or CIR, is granted to companies by the French tax authorities in order to encourage them to conduct technical and scientific research. Companies demonstrating that they have expenses that meet the required criteria, including research expenses located in France or, since January 1, 2005, within the European Union or in another state that is a party to the agreement in the European Economic Area that has concluded a tax treaty with France that contains an administrative assistance clause, receive a tax credit which can be used against the payment of the corporate tax due the fiscal year in which the expenses were incurred and during the next three fiscal years, or, as applicable, can be reimbursed for the excess portion. The expenses taken into account for the calculation of the CIR only involve research expenses.

The main characteristics of the CIR are the following:

- the CIR results in a cash inflow from the tax authorities paid directly to us as we are not subject to corporate income tax;
- a company's corporate income tax liability does not limit the amount of the CIR—a company that does not pay any corporate income tax can request direct cash payment of the research tax credit; and
- the CIR is not included in the determination of the corporate income tax.

As a result, we have concluded that the CIR meets the definition of a government grant as defined in IAS 20, *Accounting for Government Grants and Disclosure of Government Assistance*, and, as a result, it has been classified as other income within operating income in our statement of income (loss).

We will request the reimbursement of the 2017 CIR under the community tax rules for small and medium firms in compliance with the current regulations.

#### Subsidies and Conditional Advances

We have received financial assistance from BPI France and other governmental organizations in connection with the development of our product candidates. BPI France's mission is to provide assistance and support to emerging French enterprises to facilitate the development and commercialization of innovative technologies. Such funding, in the form of non-refundable subsidies and conditional advances, is intended to finance our research and development efforts and the recruitment of specific personnel.

We account for non-refundable subsidies as other income ratably over the duration of the funded project. Funds are recognized in other income in our consolidated statement of income (loss) for the fiscal year in which the financed expenses were recorded. Since our inception in 2004 through December 31, 2017, we have received  $\leq 2,738$  thousand in nonrefundable subsidies, mainly from BPI France. For the years ended December 31, 2016 and 2015, we recorded  $\leq 463$  and  $\leq 368$  thousand, respectively, as other income in the condensed consolidated statement of income (loss) based on research and development expenses incurred for the period. We had no similar income for the year ended December 31, 2017. We record the remaining balance of subsidies received but not yet expended as deferred revenue on our consolidated statement of financial position. There was no deferred revenue balance as of December 31, 2017.

Funds received from BPI France in the form of conditional advances are recognized as financial liabilities, as we are obligated to reimburse BPI France for such conditional advances in cash based on a repayment schedule if specified conditions are met. Our advances from BPI France are summarized below under "Liquidity and Capital Resources— Non-refundable Subsidies and Conditional Advances from BPI France."

## Reimbursements from Orphan Europe

Under our distribution agreement with Orphan Europe, we are reimbursed by Orphan Europe for some of our internal clinical costs, such as personnel costs associated with the management of clinical trials, or personnel involved in the production of batches necessary for our ongoing clinical trial of GRASPA for AML patients and for the NOPHO clinical trial. These invoiced internal costs are classified as "other income" in our consolidated statement of income and amounted to &341 thousand, &327 thousand and &178 thousand for the years ended December 31, 2015, 2016 and 2017, respectively.

#### **Operating Expenses**

Since our inception in 2004, our operating expenses have consisted primarily of research and development activities and general and administrative costs.

#### **Research and Development**

We engage in substantial research and development efforts to develop innovative pharmaceutical product candidates. Research and development expense consists primarily of:

- sub-contracting, collaboration and consultant expenses, that primarily include the cost of third-party contractors such as contract research organizations, or CROs, who conduct our non-clinical studies and clinical trials;
- personnel costs, including salaries, related benefits and share-based compensation, for our employees engaged in scientific research and development functions;
- licensing and intellectual property costs;
- purchases, real-estate leasing costs as well as conferences and travel costs; and
- depreciation and amortization.

Since 2015, our research and development efforts have been related primarily to our completed and ongoing clinical trials of eryaspase for the treatment of pancreatic cancer, ALL and AML.

Our direct research and development expenses consist principally of external costs, such as manufacturing expenses, non-clinical studies, fees paid to consultants, laboratories and CROs in connection with our clinical trials, and costs related to our collaborations, which we allocate to our specific research programs. We also allocate some personnel-related costs, depreciation and other indirect costs to specific programs, although costs for some scientific personnel associated with the development of our ERYCAPS platform generally are not allocated to specific programs.

Research and development activities are central to our business model. Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. We expect that our research and development expenses will continue to increase in the foreseeable future as we initiate clinical trials for certain product candidates and pursue later stages of clinical development of other product candidates.

We cannot determine with certainty the duration or costs of the current or future clinical trials of our product candidates or if, when, or to what extent we will generate revenue from the commercialization and sale of any of our product candidates that obtain regulatory approval. We may never succeed in achieving regulatory approval for any of our product candidates. The duration, costs and timing of clinical trials and development of our product candidates will depend on a variety of factors, including:

- the scope, rate of progress and expense of our ongoing, as well as any additional, non-clinical studies, clinical trials and other research and development activities;
- clinical trial and early-stage results;
- the terms and timing of regulatory approvals;
- the expense of filing, prosecuting, defending and enforcing patent claims and other intellectual property rights; and
- the ability to market, commercialize and achieve market acceptance for GRASPA or any other product candidate that we may develop in the future.

A change in the outcome of any of these variables with respect to the development of product candidates that we are developing could mean a significant change in the costs and timing associated with the development of such product candidates. For example, if the FDA, the EMA or other regulatory authority were to require us to conduct non-clinical and clinical studies beyond those which we currently anticipate will be required for the completion of clinical development, or if we experience significant delays in enrollment in any clinical trials, we could be required to spend significant additional financial resources and time on the completion of clinical development.

#### Agreement with Orphan Europe

Under our exclusive license and distribution agreement with Orphan Europe related to the development of GRASPA for the treatment of AML, we re-invoiced, with no margin, some of the clinical costs that we incur from external providers. In application of IAS 18, *Revenue*, we consider that, within the context of our agreement with Orphan Europe, we act as agent regarding these re-invoiced external costs, as:

- We do not have primary responsibility for provision of the goods or services, and the majority of services are provided by third parties. Costs of CROs are the most significant external costs, and such costs are directly invoiced to Orphan Europe. We are directly invoiced only for secondary services.
- We bear no inventory risk.
- We have no capacity to determine prices, all of the external costs are re-invoiced for the exact amount of the initial invoice, with no margin, and we are not affected by any price changes applied by the suppliers.
- We bear a credit risk that we do not consider to be significant.

Consequently, the re-invoicing of these external costs to Orphan Europe is presented as a decrease in corresponding research and development expenses incurred by us. For the years ended December 31, 2015 and 2016, the amount of external costs re-invoiced within the context of our agreement with Orphan Europe totaled &341 thousand and &327 thousand, respectively. We did not record any external costs that were re-invoiced during the year ended December 31, 2017.

# General and Administrative

General and administrative expense consists primarily of personnel costs including share-based compensation for personnel other than employees engaged in scientific research and development functions. General and administrative expense also consists of fees for professional services, mainly related to audit, IT, accounting, recruitment and legal services, communication and travel costs, real-estate leasing costs, office furniture and equipment costs, allowance for amortization and depreciation, directors' attendance fees, insurance costs and overhead costs, such as postal and telecommunications expenses.

We anticipate that our general and administrative expenses will increase in the future as we grow our support functions for the expected increase in our research and development activities and the potential commercialization of our product candidates. We also anticipate increased expenses associated with being a public company in the United States, including costs related to audit, legal, regulatory and tax-related services associated with maintaining compliance with U.S. exchange listing and SEC requirements, director and officer insurance premiums, and investor relations costs.

## Financial Income (Expense)

Financial income (expense) relates primarily to interest and other expense for loans and other financial debts, including leases, offset by income received from cash and cash equivalents, as well as foreign exchange gains and losses related to exchange rate differences on cash held in U.S. dollars as of December 31, 2017 and our purchases of services in U.S. dollars.

Our cash and cash equivalents have been deposited primarily in cash accounts, money market funds and term deposit accounts with short maturities and therefore generate only a modest amount of interest income. We expect to continue this investment philosophy in the future. Interest income from short-term deposits was  $\in$ 631 thousand,  $\in$ 558 thousand and  $\in$ 539 thousand for the years ended December 31, 2015, 2016 and 2017, respectively. Financial expenses were  $\in$ 64 thousand,  $\in$ 70 thousand and  $\in$ 3,211 thousand for the years ended December 31, 2015, 2016 and 2017, respectively. In 2017, our financial expenses were mainly related to losses resulting from exchange rate differences on the U.S. dollars held in our bank account.

## **A. Operating Results**

# Comparison of the Years Ended December 31, 2016 and 2017

# **Operating** Income

We generated operating income of  $\notin$ 4,138 thousand in 2016 and  $\notin$ 3,364 thousand in 2017, a decrease of 18.7%. The components of our operating income are set forth in the table below. Other income was primarily generated by the CIR, subsidies received from BPI France for our research projects and re-invoicing of clinical trials co-financed by our partner Orphan Europe.

	EN DECEN 2016	HE YEAR DED 1BER 31, 2017 usands)
Revenues	€ —	€ —
Other income		
Research Tax Credit	3,347	3,187
Subsidies	463	
Other income	327	178
Total operating income	€4,138	€3,364

As no research and development expenditure is capitalized before obtaining a marketing authorization, the CIR related to a research program is entirely recognized as operating income.

The CIR recognized for the year ended December 31, 2017 is expected to be received in cash in 2018.

Grants recorded in operating income represents non-reimbursable subsidies. The amounts recorded in 2016 relate to grants associated with the preclinical research programs in partnership with BPI France. In the context of this research program, no subsidy has been recorded in 2017.

Other income totaled &327 thousand and &178 thousand in 2016 and 2017, respectively. These amounts represent the sum of internal costs incurred by us within the context of the AML and the NOPHO studies, which were re-invoiced to Orphan Europe.

#### Research and Development Expenses

In 2017, our research and development expenses increased from  $\pounds$ 19,720 thousand to  $\pounds$ 25,463 thousand, an increase of 29.0% compared to 2016. While most of our research and development expenses related to completed and ongoing clinical trials of eryaspase, we have also incurred preclinical costs in connection with the discovery of additional enzymes beyond L-asparaginase for development as potential therapies to treat cancers. This research program, known as TEDAC, has resulted in the identification of our early-stage product candidate, erymethionase. We are pursuing the preclinical development of erymethionase and are preparing for the potential launch of a Phase 1 clinical trial of this product candidate by the end of 2018.

Our research and development expenses are broken down in the table below. Our research and development expenses consist principally of external costs, such as startup fees paid to investigators, consultants, central laboratories and CROs in connection with our clinical studies, and costs related to acquiring and manufacturing clinical study materials. We do not allocate personnel-related costs, costs associated with our general platform improvements, depreciation or other indirect costs to specific projects, as they are deployed across multiple projects under development.

	FOR THE DECI		
	2016 (in t	2017 housands)	% <u>CHANGE</u>
ERYASPASE / GRASPA	€ 5,636	€ 10,264	82%
TEDAC (ERYMETHIONASE / ERYMINASE)	3,120	2,378	(24%)
ERYMMUNE	139	146	(5%)
ERYZYME	15	99	560%
Total direct research and development expenses	8,910	12,887	45%
Consumables	2,071	663	68%
Rental and maintenance	645	628	(3%)
Services, subcontracting and consulting fees	2,499	3,028	21%
Personnel expenses (1)	5,282	7,916	50%
Depreciation and amortization expense	277	81	(71%)
Other	35	259	640%
Total indirect research and development expenses	10,810	12,575	16%
Total research and development expenses (2)	€ 19,720	€ 25,463	29%

(1) Includes €688 thousand and €833 thousand related to share-based compensation expense for 2016 and 2017, respectively.

(2) Of which €14,397 thousand and €19,476 thousand are related to clinical studies for 2016 and 2017, respectively.

The increase in research and development expenditures from 2016 to 2017 was primarily the result of a  $\notin$ 4,628 thousand increase in costs related to eryaspase due to the additional work performed as requested by the EMA prior to our resubmission of the MAA for GRASPA in October 2017. Personnel expenses increased from  $\notin$ 5,282 thousand in 2016 to  $\notin$ 7,916 thousand in 2017. The increase of  $\notin$ 2,634 thousand was mainly due to increased wages of research and development personnel as we increased headcount in connection with our ongoing and planned clinical trials. Services, subcontracting and consulting fees, including third-party fees and other service provider fees for our manufacturing and clinical trials, also increased to  $\notin$ 3,028 in 2017, reflecting an increase of  $\notin$ 529 thousand as compared to 2016. This increase was primarly related to additional activities in connection with our resubmitted MAA and expenses related to our pancreatic clinical trial. We also experienced a  $\notin$ 1,408 thousand decrease in consumables costs, which was primarily the result of a decrease in production of GMP batches for use in pre-clinical development.

#### General and Administrative Expenses

In 2017, our general and administrative expenses increased from &6,808 thousand to &8,791 thousand, an increase of 29% compared to 2016. The increase of &1,983 thousand in general and administrative expenses was primarily due to an increase of &1,269 thousand in personnel expenses in 2017, partly as a result of an increase in share-based compensation expense and partly related to our increase in headcount. The increase in our general and administrative costs was also due to an increase in the amount of rental and maintenance fees we incurred related to the development of our offices in both Lyon (France) and in Cambridge (United States).

Our general and administrative expenses are broken down as follows:

	FOR THE YEAR ENDED DECEMBER 31,				
	2	2016 (in the	ousands)	2017	% <u>CHANGE</u>
Consumables	€	66	€	148	124%
Rental and maintenance		511		894	75%
Services, subcontracting, and consulting fees		2,793		2,867	3%
Personnel expenses (1)		2,713		3,982	47%
Depreciation and amortization expense		148		266	80%
Other (2)		577		633	10%
Total general and administrative expenses	€	6,808	€	8,791	29%

(1) Includes €490 thousand and €936 thousand related to share-based compensation expense for 2016 and 2017, respectively.

(2) Includes €37 thousand and €300 thousand related to share-based compensation expense (warrants allocated to directors) for 2016 and 2017, respectively.



The increase in general and administrative expenses in 2017 by €1,983 thousand is due to:

- an increase in personnel expenses in the amount of €1,269 thousand;
- an increase of rental and maintenance costs in the amount of €383 thousand, primarily related to our new leased office space in Lyon, fixtures and fittings, as well as IT service costs; and
- an increase in "other" costs related to share-based compensation expense in the amount of €325 thousand to warrants allocated to directors and board fees.

## Financial Income (Loss)

Our financial income resulted in a loss of €2,644 thousand in 2017, as compared to a profit of €488 thousand in 2016 and is broken down as follows:

	YEAR	R THE ENDED MBER 31,
	2016	2017
	(in the	ousands)
Financial expenses	€(70)	€(3,183)
Financial income	558	539
Net financial income (loss)	€488	€(2,644)

In 2016 and 2017, our financial income consisted primarily of (i) interest earned on interest-bearing accounts as well as (ii) foreign exchange gains related to purchases of services in U.S. dollars and funds held in our bank account in U.S. dollars.

In 2017, our financial expense consisted primarily of a foreign exchange loss resulting from the conversion of our cash and cash equivalents positions denominated in U.S. dollars.

# Comparison of the Years Ended December 31, 2015 and 2016

# **Operating** Income

We generated operating income of €2,929 thousand in 2015 and €4,138 thousand in 2016, an increase of 41.3%. The components of our operating income are set forth in the table below. Other income was primarily generated by the CIR and by subsidies received from BPI France for our research projects.

	EN DECEM 2015	IE YEAR DED <u>1BER 31,</u> <u>2016</u> uusands)
Revenues	€ —	€ —
Other income		
Research Tax Credit	2,219	3,347
Subsidies	368	463
Other income	341	327
Total operating income	€2,929	€4,138

As no research and development expenditure is capitalized before obtaining a marketing authorization, the CIR related to a research program is entirely recognized as operating income.

Grants recorded in operating income represents non-reimbursable subsidies. The amounts recorded in 2015 and 2016 relate to grants associated with the preclinical research programs in partnership with BPI France.

Other income totaled  $\notin$  341 thousand and  $\notin$  327 thousand in 2015 and 2016, respectively. These amounts represent the sum of internal costs incurred by us within the context of our clinical studies, which were re-invoiced to Orphan Europe.

#### Research and Development Expenses

Between 2015 and 2016, the total amount recorded by us for research and development expenses increased from  $\pounds$ 10,776 thousand to  $\pounds$ 19,720 thousand, an increase of 83.0%. While most of our research and development expenses related to completed and ongoing clinical trials of eryaspase, we have also incurred preclinical costs in connection with the discovery of additional enzymes beyond L-asparaginase for development as potential therapies to treat cancers. This research program, known as TEDAC, has resulted in the identification of our early-stage product candidate, erymethionase. We are pursuing the preclinical development of erymethionase and are preparing for the launch of a Phase 1 clinical trial of the product candidate by the end of 2018.

Our research and development expenses are broken down as set forth in the table below. Our direct research and development expenses consist principally of external costs, such as startup fees paid to investigators, consultants, central laboratories and CROs in connection with our clinical studies, and costs related to acquiring and manufacturing clinical study materials. We do not allocate personnel-related costs, costs associated with our general platform improvements, depreciation or other indirect costs to specific projects, as they are deployed across multiple projects under development.

	,,	%
		CHANGE
€ 1,805	€ 5,636	212%
1,523	3,120	105
	139	
	15	—
3,328	8,910	168
805	2,071	157
304	645	112
1,896	2,499	32
3,977	5,282	33
250	277	11
216	35	(84)
7,448	10,810	45
€ 10,776	€ 19,720	83
	DECEM 2015 (in those 1,805 1,523  3,328 805 304 1,896 3,977 250 216 7,448	(in thousands)         €       1,805       €       5,636         1,523       3,120          139          15         3,328       8,910         805       2,071         304       645         1,896       2,499         3,977       5,282         250       277         216       35         7,448       10,810

(1) Includes €822 thousand and €688 thousand related to share-based compensation expense for 2015 and 2016, respectively.

(2) Of which €6,745 thousand and €14,397 thousand are related to clinical studies for 2015 and 2016, respectively.

The increase in research and development expenditures from 2015 to 2016 was primarily the result of a  $\leq$ 1,597 thousand increase in costs related to the TEDAC program and a  $\leq$ 3,831 thousand increase in costs related to eryaspase due to additional work as requested by the EMA in connection with its review of the MAA we submitted for GRASPA in September 2015. Personnel expenses increased from  $\leq$ 3,977 thousand to  $\leq$ 5,282 thousand from 2015 to 2016. The increase of  $\leq$ 1,305 thousand was mainly due to wages of research and development personnel related to the increase in our R&D staffing. Services, subcontracting and consulting fees, including third-party fees and other service provider fees for our manufacturing and clinical trials, resulted in an increase of  $\leq$ 603 thousand as compared to 2015. We also experienced a  $\leq$ 1,266 thousand increase in consumables costs, which was primarily the result of increased production batches for use in clinical development.

# General and Administrative Expenses

Between 2015 and 2016, our general and administrative expenses decreased from  $\notin$ 7,736 thousand to  $\notin$ 6,808 thousand, a decrease of 12%. The decrease of  $\notin$ 928 thousand in general and administrative expenses was primarily due to a decrease of  $\notin$ 2,050 thousand in other costs, as a result of a decrease in sharebased compensation for warrants allocated to directors ( $\notin$ 37 thousand in 2016, compared to  $\notin$ 1,593 thousand in 2015). The decrease in our general and administrative costs was also due to a decrease in the amount of services, subcontracting and consulting fees we incurred related to the development of our clinical strategy in the United States.

Our general and administrative expenses are broken down as follows:

	FOR THE YEAR ENDED DECEMBER 31,				
	_	2015 (in th	ousands	2016 5)	% <u>CHANGE</u>
Consumables	€	36	€	66	83%
Rental and maintenance		304		511	68
Services, subcontracting, and consulting fees		3,022		2,793	(8)
Personnel expenses (1)		1,627		2,713	67
Depreciation and amortization expense		120		148	23
Other (2)		2,627		577	(78)
Total general and administrative expenses	€	7,736	€	6,808	(12)

(1) Includes €301 thousand and €490 thousand related to share-based compensation expense for 2015 and 2016, respectively.

(2) Includes €1,593 thousand related to share-based compensation expense (warrants allocated to directors) for 2015.

## Financial Income (Loss)

Our financial income resulted in a profit of €488 thousand in 2016, as compared to a profit of €567 thousand in 2015 and is broken down as follows:

	FOR YEAR I DECEM	ENDED
	2015	2016
	(in thou	isands)
Financial expense	€ (64)	€ (70)
Financial income	631	558
Net financial income (loss)	€ 567	€ 488

In 2015 and 2016, our financial income consisted primarily of (i) interest earned on interest-bearing accounts as well as (ii) foreign exchange gains related to purchases of services in U.S. dollars.

#### **Critical Accounting Policies and Estimates**

Our consolidated financial statements are prepared in accordance with IFRS. Some of the accounting methods and policies used in preparing our consolidated financial statements under IFRS are based on complex and subjective assessments by our management or on estimates based on past experience and assumptions deemed realistic and reasonable based on the circumstances concerned. The actual value of our assets, liabilities and shareholders' equity and of our earnings could differ from the value derived from these estimates if conditions change and these changes had an impact on the assumptions adopted. We believe that the most significant management judgments and assumptions in the preparation of our consolidated financial statements are described below. See Note 4 to our consolidated financial statements for a description of our other significant accounting policies.

# Share-Based Compensation

We have four share-based compensation plans for employees and non-employees, the 2012 Plan, the 2014 Plan, the 2016 Plan and the 2017 Plan.

As of December 31, 2017, we have granted share-based compensation under these plans to certain employees as well as to members of our board of directors in the form of free shares (*Actions gratuites*, or AGA), stock options, or SOs, share warrants (*Bons de Souscription d'Actions*, or BSA) and founder's share warrants (*Bons de Souscription de Parts de Créateur d'Entreprise*, or BSPCE) with the following exercise prices and on each of the grant dates reflected below.

WARRANTS	GRANT DATE	NUMBER OF WARRANTS GRANTED	I	ERCISE PRICE PER HARE	SI MA V SI AT	DINARY HARE FAIR ARKET ALUE PER HARE GRANT DATE
BSA 2012	May 31, 2012	2,027	€	7.362		
BSPCE 2012	May 31,2012	7,434	€	7.362		_
BSA 2012	August 3, 2012	1,539	€	7.362		
BSA 2012	July 18, 2013	459	€	7.362	€	10.27
BSPCE 2012	July 18, 2013	13,177	€	7.362	€	10.27
BSPCE 2014	January 22, 2014	12,000	€	12.250	€	12.77
BSA 2012	July 17, 2014	1,000	€	7.362	€	14.90
BSPCE 2012	July 17, 2014	13,176	€	7.362	€	14.90
BSA 2012	April 29, 2015	2,150	€	7.362	€	31.19
BSPCE 2014	June 23, 2015	2,500	€	12.250	€	32.75
BSA 2014	June 23, 2015	3,000	€	12.250	€	32.75
BSA 2012	August 31, 2015	3,585	€	7.362	€	37.52
BSPCE 2014	May 6, 2016	5,000	€	12.250	€	24.75
AGA 2016	October 3, 2016	111,261		—	€	18.52
SO 2016	October 3, 2016	44,499	€	18.520	€	18.52
BSA 2016	October 3, 2016	45,000	€	18.520	€	18.52
AGA 2016	January 8, 2017	15,000		—	€	13.60
BSA 2016	January 8, 2017	15,000	€	13.60	€	13.60
SO 2016	January 8, 2017	3,000	€	15.65	€	15.65
AGA 2016	June 27, 2017	8,652		—	€	26.47
SOP 2016	June 27, 2017	18,000	€	26.47	€	26.47
AGA 2017	June 27, 2017	74,475		—	€	26.47
SOP 2017	June 27, 2017	22,200	€	26.47	€	26.47
BSA 2017	June 27, 2017	55,000	€	26.47	€	26.47
AGA 2016	October 3, 2017	16,650		—	€	24.48
SOP 2016	October 3, 2017	30,000	€	23.59	€	23.59

The share-based compensation granted under the 2016 Plan and 2017 Plan by our board of directors at meetings held on January 8, 2017, June 27, 2017 and October 3, 2017 was valued using Monte Carlo, Black and Scholes, Cox Ross Rubinstein methods. Assumptions were updated at the grant date.

Following the resignation of Yann Godfrin, our former Chief Scientific Officer, in January 2016, 1,000 BSPCE<sub>2014</sub> of the 3,000 BSPCE<sub>2014</sub> initially allocated on January 22, 2014 will not be granted.

Following the resignation of certain other employees, our Chief Executive Officer acknowledged on October 3, 2017 that 1,017 AGA 2016 shares of *Tranche 1* allocated on October 3, 2016 would not be granted to these employees and would be forfeited for those employees.

We account for share-based compensation in accordance with the authoritative guidance on share-based compensation, IFRS 2 *Share-based payment*, or IFRS 2. Under the fair value recognition provisions of IFRS 2, share-based compensation is measured at the grant date based on the fair value of the award and is recognized as an expense, net of estimated forfeitures, over the requisite service period, which is generally the vesting period of the respective award.

Determining the fair value of share-based awards at the grant date requires judgment. We use the Black-Scholes option-pricing model to determine the fair value of certain warrants and for our stock options. We use the Monte-Carlo and Cox-Ross-Rubinstein option-pricing models to determine the fair value of free shares and certain warrants, respectively. The determination of the grant date fair value of warrants using an option-pricing model is affected by assumptions regarding a number of complex and subjective variables. These variables include the fair value of our ordinary shares on the date of grant, the expected term of the awards, our share price volatility, risk-free interest rates and expected dividends. We estimate these items as follows:

*Fair Value of Our Ordinary Shares.* As our ordinary shares are publicly traded on Euronext Paris, for purposes of determining the fair value of our ordinary shares we have established a policy of using the closing sales price per ordinary share as quoted on Euronext Paris on the date of the grant by the *Conseil d'Administration* or the shareholders' meeting.

*Expected Term.* The expected term represents the period that our share-based awards are expected to be outstanding. As we do not have sufficient historical experience for determining the expected term of the warrant awards granted, we have based our expected term on the simplified method, which represents the average period from vesting to the expiration of the award.

*Expected Volatility.* We use the historical volatility of the Next Biotech index observed on Euronext Paris for the 2014 Plan and the historical volatility of our ordinary shares on Euronext Paris for the 2016 Plan and the 2017 Plan.

*Risk-Free Interest Rate.* The risk-free interest rate is based on the yields of French government bonds with maturities similar to the expected term of the warrants for each warrant group.

*Dividend Yield*. We have never declared or paid any cash dividends and do not presently plan to pay cash dividends in the foreseeable future. Consequently, we have used an expected dividend yield of zero.

If any of the assumptions used in the Black-Scholes, Monte-Carlo and Cox-Ross-Rubinstein models change significantly, share-based compensation for future awards may differ materially compared with the awards granted previously.

The following table presents the weighted-average assumptions used to estimate the fair value of options granted during the periods presented:

	2012 PLAN	2014 PLAN		2016 PLAN	2017 PLAN SIX
	YEAR ENDED DECEMBER 31,		ENDED IBER 31,	YEAR ENDED DECEMBER 31,	MONTHS ENDED JUNE 30,
	2015	2015	2016	2016	2017
Volatility	20.5% - 22.5%	19.59% - 21.55%	21.25% - 22.27%	45%	48%
Risk free interest rate	(0.07)% - (0.08)%	0.21% - 0.40%	(0.18)% - (0.11)%	0%	0%
Expected life (in years)	2.4 - 2.5	4.3 - 5.3	5 - 5.51	6 - 6.5	
Dividend yield		—	—	_	

For the years ended December 31, 2015, 2016 and 2017, we recorded share-based compensation expense of  $\pounds$ 2,716 thousand,  $\pounds$ 1,178 thousand and  $\pounds$ 1,769 thousand, respectively.

## **B. Liquidity and Capital Resources**

We have financed our operations since our inception through several rounds of public and private financings. Through 2012, we raised an aggregate of  $\pounds$ 17.7 million from the issuance of ordinary and preference shares and an additional  $\pounds$ 9.0 million from the issuance of convertible bonds. In 2013, we issued ordinary shares in our initial public offering on Euronext Paris, raising net proceeds of  $\pounds$ 14.7 million and in 2014, we issued additional ordinary shares, raising net proceeds of  $\pounds$ 28.4 million. In 2015, we raised  $\pounds$ 23.5 million of net proceeds through the issuance of ordinary shares in our December 2015 offering. In December 2016, we raised an additional  $\pounds$ 9.2 million of net proceeds through the issuance of ordinary shares. In April 2017, we raised an additional  $\pounds$ 65.2 million of net proceeds through the issuance of ordinary shares. In April 2017, we raised an additional  $\pounds$ 65.2 million of net proceeds through the issuance of ordinary shares, including the full exercise of the underwriters' options to purchase additional shares, for net proceeds of \$130.4 million. The global offering consisted of a U.S. initial public offering of American Depositary Shares and a concurrent private placement of ordinary shares in Europe and other countries outside of the United States and Canada. Our net proceeds from the November 2017 global offering were approximately  $\pounds$ 112.1 million (\$130.4 million).

We have also financed our operations through an aggregate of  $\leq 12.4$  million in research tax credits since our inception in 2004 through December 31, 2017, as well as  $\leq 2.7$  million in non-refundable grants from BPI France since 2005 and  $\leq 2.0$  million in conditional advances received from BPI France since our inception in 2004 through December 31, 2017.

In 2016, we entered into an unsecured bank loan with Société Générale for a total amount of €1.9 million. The outstanding amount drawn at December 31, 2017 was €1.9 million.

We are potentially eligible to earn a significant amount of milestone payments and royalties under our agreement with Orphan Europe in the event that we are able to obtain European marketing approval for GRASPA. However, our ability to earn these payments and their timing will, in part, be dependent upon the outcome of Orphan Europe's activities, which is uncertain at this time.

# Cash Flows

The table below summarizes our sources and uses of cash for the years ended December 31, 2015, 2016 and 2017.

	December 31,		
	2015	2016	2017
	(Amount	ts in thousands of	Euros)
Net cash flows used in operating activities	(14,578)	(17,614)	(24,702)
Net cash flows used in investing activities	(284)	(1,786)	(1,791)
Net cash flows from financing activities	23,524	11,393	177,545
Net currency exchange variation	(16)	19	(3,183)
Net increase in cash and cash equivalents	8,646	(7,988)	147,869

Our net cash flows used in operating activities were  $\leq 14,578$  thousand,  $\leq 17,614$  thousand and  $\leq 27,386$  thousand for the years ended December 31, 2015, 2016 and 2017, respectively. During 2016 and 2017, our net cash flows used in operating activities increased due to our efforts in advancing our research and development programs in both preclinical and clinical research.

Our net cash flows used in investing activities were  $\leq 284$  thousand,  $\leq 1,786$  thousand and  $\leq 1,791$  thousand in the years ended December 31, 2015, 2016 and 2017, respectively. The slight increase for 2017 mainly reflected fixtures and fittings acquired for our offices in Cambridge and Lyon together with our project to develop and optimize our second-generation production facility. The costs related to the second-generation production were not incurred in 2015.

Our net cash flows from financing activities increased to &177.5 million in 2017 from &11.4 million in 2016. The increase to &177.5 million in 2017 from &11.4 million in 2016 was primarily the result of our November 2017 underwritten global offering, which included the issuance of ordinary shares and ADSs. In November 2015, we completed a private placement which resulted in net proceeds of &25.4 million. We continue to hold 2,500 shares as treasury shares from our former liquidity account.

#### Non-refundable Subsidies and Conditional Advances from BPI France

Since our inception in 2004 through December 31, 2017, we have received non-refundable subsidies from BPI France in the amount of  $\notin$ 2.7 million in connection with our preclinical research programs.

Since our inception in 2004 through December 31, 2017, we have also received three conditional advances from BPI France in relation to the development of our encapsulation platform technology. These conditional advances are recorded under the "proceeds from borrowings" line item in our consolidated statements of cash flows. The TEDAC research program, which is funded by one of these three conditional advances, will be funded according to a specified schedule set forth in the contract, subject to completion of milestones. As the program advances, we will provide BPI France with interim progress reports and a final report when the funded project ends. Based on these reports, we are entitled to conditional advances, each award of an advance being made to help fund a specific development milestone. The total amount of the conditional advances to be granted is €5,711 thousand, of which we have received an aggregate of €1,998 thousand through December 31, 2017. During the year ended December 31, 2016, we repaid advances in the amount of €508 thousand. No similar advances were repaid for the year ended December 31, 2017.

We recognize advances as current or non-current liabilities, as applicable, in the statement of financial position, based on the repayment schedule.

The remaining milestones that we may achieve generally relate to development of product candidates such as erymethionase and eryminase under the TEDAC research program. If and to the extent that we earn these conditional advances, we will be obligated to make repayments based on the achievement of specified sales levels as well as a percentage of sales.

# **Operating Capital Requirements**

We believe our existing cash and cash equivalents at December 31, 2017 will enable us to fund our operating expenses and capital expenditure requirements for at least the next 24 months. We have based this estimate on assumptions that may prove to be wrong, and we could use our capital resources sooner than we currently expect. Until we can generate a sufficient amount of revenue from our product candidates, if ever, we expect to finance our operating activities through our existing cash and cash equivalents.

Our present and future funding requirements will depend on many factors, including, among other things:

- the size, progress, timing and completion of our clinical trials for eryaspase or GRASPA and any other current or future product candidates;
- the number of potential new product candidates we identify and decide to develop;
- the costs involved in filing patent applications and maintaining and enforcing patents or defending against claims of infringement raised by third parties;
- the time and costs involved in obtaining regulatory approval for our product candidates and any delays we may encounter as a result of evolving regulatory requirements or adverse results with respect to any of these product candidates;



- selling and marketing activities undertaken in connection with the anticipated commercialization of eryaspase or GRASPA and any other current
  or future product candidates, including other product candidates in preclinical development, together with the costs involved in the creation of an
  effective sales and marketing organization; and
- the amount of revenues, if any, we may derive either directly, or in the form of royalty payments from any future potential collaboration agreements, from our ERYCAPS platform or relating to our other product candidates.

For more information as to the risks associated with our future funding needs, see the section entitled "Item 3.D—Risk Factors."

# **Capital Expenditures**

Our main capital expenditures in the years ended December 31, 2015, 2016 and 2017 were related primarily to the buildup of our fixed assets for our pharmaceutical facility and laboratory and to a lesser extent to the purchase of office and computer equipment. We do not capitalize clinical research and development costs until we obtain marketing authorization for a product candidate.

Our non-current assets are broken down as follows:

		December 31,		
	2015	2016	2017	
	(Amour	(Amounts in thousands of Euros)		
Intangible assets	61	57	53	
Property, plant and equipment	918	2,245	3,406	
Other non-current financial assets	97	132	234	
Total	1,076	2,434	3,693	

For the year ended December 31, 2015, we capitalized costs related to general equipment in the amount of  $\leq 174$  thousand and related to fittings and to technical and industrial equipment in the amount of  $\leq 31$  thousand

For the year ended December 31, 2016, we capitalized costs related to our new production facility in the amount of €830 thousand, which have been recognized as tangible assets in progress as of December 31, 2016 and fixtures, fittings and office equipment for our offices in Lyon, France and Cambridge, Massachusetts in the amount of €864 thousand.

For the year ended December 31, 2017, we capitalized costs related to the new production facility in the amount of &868 thousand, which have been recognized as tangible assets in progress as of December 31, 2017, general equipment and computer equipment in the amount of &407 thousand and building improvements in the amount of &389 thousand.

Non-current financial assets relate to deposits paid on bank collateral and operating leases for our premises in Lyon, France and in Cambridge, Massachusetts for all periods presented.

## **C. Research and Development**

For a discussion of our research and development activities, see "Item 4.B—Business Overview" and "Item 5.A—Operating Results."

#### **D. Trend Information**

For a discussion of trends, see "Item 5.A—Operating Results" and "Item 5.B—Liquidity and Capital Resources."

#### **E. Off-Balance Sheet Arrangements**

During the periods presented, we did not and do not currently have any off-balance sheet arrangements as defined under Securities and Exchange Commission rules, such as relationships with other entities or financial partnerships, which are often referred to as structured finance or special purpose entities, established for the purpose of facilitating financing transactions that are not required to be reflected on our balance sheet.

The off-balance sheet commitments related to operating leases as of December 31, 2017 amounted to €726 thousand, of which €484 thousand is due within a year and the balance between one and five years. These commitments relate primarily to leases of buildings.

#### F. Tabular Disclosure of Contractual Obligations

The following table discloses aggregate information about our material contractual obligations and the periods in which payments were due as of December 31, 2017. Future events could cause actual payments and timing of payments to differ from the contractual cash flows set forth below.

	LESS THAN <u>1 YEAR</u>	1 TO 3 YEARS	3 TO 5 YEARS (in thousand	MORE THAN 5 YEARS	TOTAL
Bank loans	€ 735	€ 799	(III tilousand	í c	£1 E24
Dalik ioalis	€ /35	€ /99	£ —	ŧ —	€1,534
Conditional advances				1,182	1,182
Pension and employee benefits	—			214	214
Operating lease agreements	484	242	_	—	726
Finance lease agreements	79	39		—	117
Total	€1,298	€1,080	€ —	€ 1,396	€3,773

The amounts of contractual obligations set forth in the table above are associated with contracts that are enforceable and legally binding and that specify all significant terms, fixed or minimum services to be used, fixed, minimum or variable price provisions, and the approximate timing of the actions under the contracts. The table does not include obligations under agreements that we can cancel without a significant penalty.

#### G. Safe Harbor.

This Annual Report on Form 20-F contains forward-looking statements within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act and as defined in the Private Securities Litigation Reform Act of 1995. See "Special Note Regarding Forward-Looking Statements."

## Item 6. Directors, Senior Management and Employees.

#### A. Directors and Senior Management.

The following table sets forth information concerning our executive officers and directors as of March 31, 2018. Unless otherwise stated, the address for our executive officers and directors is Bâtiment Adénine, 60 Avenue Rockefeller 69008 Lyon France.

NAME	AGE	POSITION(S)
Executive Officers		
Gil Beyen	56	Chief Executive Officer and Chairman of the Board
Eric Soyer	51	Chief Financial Officer and Chief Operating Officer
Jean-Sébastien Cleiftie (1)	44	Chief Business Officer
Iman El-Hariry, M.D., Ph.D. (1)	57	Chief Medical Officer
Alexander Scheer, Ph.D.	55	Chief Scientific Officer
Jérôme Bailly, Pharm.D.	39	Vice President and Director of Pharmaceutical Operations and Qualified Person
Non-Employee Directors		
Sven Andréasson (2)(3)(4)	65	Director
Philippe Archinard, Ph.D. (2)(3)(5)	58	Director
Allene Diaz (3)(5)	53	Director
Luc Dochez, Pharm.D. (2)(5)	43	Director
Martine Ortin George, M.D. <sup>(5)</sup>	69	Director
Hilde Windels (2)(6)	52	Director

(1) Employee of our wholly-owned U.S. subsidiary, ERYTECH Pharma, Inc.

(2) Member of the audit committee.

(3) Member of the remunerations and appointment committee.

(4) As representative of Galenos SPRL, the legal entity that holds this board seat.

(5) Member of the clinical strategy committee.

(6) As representative of BVBA Hilde Windels, the legal entity that hold this board seat.

#### **Executive Officers**

*Gil Beyen* has served as our Chief Executive Officer since May 2013 and Chairman of the Board since August 2013. Prior to his appointment as Chief Executive Officer, he assisted our company in a consulting role as of 2012 and also served as Chairman of our supervisory board from August 2012 until May 2013. Between 2000 and 2013, Mr. Beyen was Chief Executive Officer and director of TiGenix, a company he co-founded. He previously served as the head of the Life Sciences division of Arthur D. Little, an international management consulting firm, in Brussels. Mr. Beyen received an M.S. in Bioengineering from the University of Leuven (Belgium) and an M.B.A. from the University of Chicago.

*Eric Soyer* has served as our Chief Financial Officer and Chief Operating Officer since September 2015. Prior to his appointment as our Chief Financial Officer, he served for eight years as Chief Financial Officer of EDAP TMS S.A., a French therapeutic ultrasound company. He also was Managing Director of the French affiliate of EDAP TMS from May 2012 to August 2015, and previously was EDAP TMS's Executive Vice President of Finance, Human Resources and Administration from December 2006 to May 2012. From 2005 to 2006, he served as Chief Financial Officer for Medica, a company operating nursing homes and post-care clinics throughout France and Italy. From 1999 to 2005, he served in various positions of increasing responsibility for April Group, an insurance services company. He has international experience as a controller and cost accountant for Michelin Group in France, the United States and Africa. Mr. Soyer graduated from the ESC Clermont School of Management (France) and holds an M.B.A. from the University of Kansas and an Executive M.B.A. from the HEC Paris School of Management (France).

*Jean-Sébastien Cleiftie* has served as our Chief Business Officer since October 2016. Prior to joining us, he served as Associate Vice-President, Global Business Development & Licensing at Sanofi in Paris, France from October 2010 to August 2016. Prior to joining Sanofi, Mr. Cleiftie served as a principal at Innoven Partners, a European venture capital firm focused on investments in the healthcare and information technology industries in Europe and the United States, from February 2004 to October 2010. From 1997 to 1999, Mr. Cleiftie was a research scientist with Aventis (now Sanofi) in the fields of immunotherapy and gene therapy for cancer. Mr. Cleiftie holds an M.S. in Biological & Medical Sciences and an M.S. in Immunology from the University of Paris V, and received his M.B.A from Cornell University.

*Iman El-Hariry, M.D., Ph.D.* has served as our Chief Medical Officer and employee of our wholly-owned U.S. subsidiary, ERYTECH Pharma, Inc., since June 2015. Prior to her appointment as Chief Medical Officer, she served as President of Azure Oncology Consulting from July 2014 to June 2015 and also assisted us in a consulting role from November 2014 to June 2015. Dr. El-Hariry served as Vice President of Clinical Research at Synta Pharmaceuticals from November 2010 to July 2014 and as Global Head of Oncology at Astellas Pharma, Inc. from June 2009 to July 2010. From 2001 to 2009, she served as Director of Clinical Development, Oncology at Glaxo Smith Kline. Dr. El-Hariry is a licensed oncologist with an M.D. from Alexandria Medical School (Egypt) and a Ph.D. in Cancer Research from Imperial College of Science and Medicine (United Kingdom).

*Alexander Scheer, Ph.D.* has served as our Chief Scientific Officer since October 2016. Prior to joining us, he served as the Head of Research at Pierre Fabre Laboratories, a pharmaceutical company, in France from 2014 to 2016, and also served as a Deputy Head of Research at Pierre Fabre from 2012 to 2014. Prior to joining Pierre Fabre, Dr. Scheer served as a Director, Global Research Informatics & Knowledge Management R&D and Project Leader, Neglected Diseases at Merck Serono in Switzerland from 2007 to 2012. From 2001 to 2007, Dr. Scheer served as Head of Molecular Screening and Cellular Pharmacology Department, Group Leader of Biochemical Pharmacology and Research Scientist at Merck Serono. Dr. Scheer holds a B.Sc. in Natural Sciences and M.Sc. in Chemistry, both from the University of Gottingen (Germany), and a Ph.D. in Chemistry and Biochemistry from the German Cancer Research Center.

*Jérôme Bailly, Pharm.D.* has served as our Qualified Person since December 2011, as our Director of Pharmaceutical Operations since 2007 and as a Vice President and *Directeur Général Délégué*, or Deputy General Manager, since 2017. Prior to 2007, he was the Director of QA/Production at Skyepharma and Laboratoire Aguettant. Dr. Bailly holds a Pharm.D. and a degree in Chemical Engineering, specializing in Biopharmaceutical Engineering and Cellular Production from École Polytechnique de Montréal (Canada).

# **Non-Employee Directors**

*Sven Andréasson* (acting as legal representative of Galenos Sprl) has served as a member of our board of directors since 2013 and has served as representative of Galenos SPRL, the legal entity that holds this board seat, since 2014. He also served as a member of our supervisory board from 2009 to May 2013. Mr. Andréasson has served as Senior Vice President, Corporate Development for Novavax, Inc. (United States), a pharmaceutical company, since June 2014. From 2012 to 2013, he served as Chief Executive Officer of Isconova AB (Uppsala, Sweden), a leading international vaccine adjuvant company acquired by Novavax in 2013, currently operating as Novavax AB. Prior to his role at Novavax AB, he served as Chief Executive Officer of Beta-Cell N.V. (Brussels, Belgium) from 2008 to 2012 and as Chief Executive Officer of Active Biotech AB (Lund, Sweden) from 1999 to 2008. Mr. Andréasson spent a number of years in roles at Pharmacia Corporation (merged with Pfizer Inc.), including President of Pharmacia SA, France, President of KabiPharmacia International and President of Pharmacia Arzneimittel GmbH. He has extensive experience in international biotechnology companies and in the pharmaceutical industry. Mr. Andréasson received his B.S. in Business Administration and Economics from the Stockholm School of Economics (Sweden).

*Philippe Archinard, Ph.D.* has served as a member of our supervisory board since 2007 and of our board of directors since 2013. Dr. Archinard was appointed General Manager, Chief Executive Officer and director of Transgene in December 2004, after spending 15 years in various senior positions with bioMérieux, a multinational biotechnology company, including directing its U.S. subsidiary. He has served as a member of bioMérieux's board of directors since 2005. He also serves as Chief Executive Officer of Innogenetics N.V., a position he has held since March 2000. Dr. Archinard is a chemical engineer, holds a Ph.D. in biochemistry from the University of Lyon (France), and completed Harvard Business School's Program of Management PMD.

*Allene Diaz* has served as a member of our board of directors since 2017. She currently serves as Senior Vice President, Global Commercial Development at TESARO, Inc. (Waltham, United States), a biopharmaceutical company, a position she has held since May 2015. Prior to joining TESARO, Ms. Diaz served as Senior Vice President, Managed Markets at EMD Serono, an affiliate of Merck KGaA, Darmstadt, Germany, from October 2013 to May 2015. Previously from June 2008 to October 2013, Ms. Diaz also held the positions of Senior Vice President, Head of Oncology Commercial, U.S. and Vice President, Oncology Marketing at EMD Serono, where she oversaw the commercial pre-launch efforts for EMD Serono's oncology products. Ms. Diaz has held executive, management and/or line positions at other companies including Amylin Pharmaceuticals, Cancervax Corporation, Biogen Idec, Pfizer Inc. and Parke-Davis Pharmaceuticals. Ms. Diaz received her B.Sc. from Florida State University. She has also attended executive education programs at the London School of Business and Finance, University of Michigan School of Business, China Europe International Business School (Shanghai, China), Stanford University School of Business and INSEAD (Fontainebleau, France).

*Luc Dochez, Pharm.D.* has served as a member of our board of directors since 2015. He serves as Chief Executive Officer of Tusk Therapeutics N.V. and Ltd., a private company focused on developing novel immuno-oncology products. Mr. Dochez has over 15 years of experience in the biotechnology industry. He served as the Chief Business Officer and Senior Vice President of Business Development of Prosensa Holding N.V., a biotechnology company, from November 2008 until its acquisition by BioMarin Pharmaceutical Inc. in January 2015. He played a key role in the execution of a more than €500 million partnership with GSK, and he was actively involved in the IPO of the company on NASDAQ. He also worked on the acquisition of the company by Biomarin for \$860 million. Before joining Prosensa, he served as Vice President of Business Development at TiGenix, Director Business Development at Methexis Genomics, and a consultant at Arthur D. Little. Mr. Dochez is a board member of Pharvaris BV, a Dutch company focused on rare diseases, as well as Bioncotech Therapeutics SL, a Spanish oncology company. He serves as an advisor to EverImmune SA, a French microbiome company, and is an expert member of the Investment Committee of QBIC II, a Belgian seed investment fund. Mr. Dochez holds a Pharm.D. degree and a postgraduate degree in business economics from the University of Leuven (Belgium) and an M.B.A. degree from Vlerick Management School (Belgium).

*Martine Ortin George, M.D.* has served as a member of our board of directors since 2014. She has extensive experience in the U.S. in clinical research, medical affairs and regulatory issues, acquired in small and large companies specialized in oncology. She currently serves as principal and senior executive consultant-life sciences for Global Development Inc. Dr. George held the position of Vice President in charge of Global Medical Affairs for Oncology at Pfizer Inc., New York from 2010 to 2015. Previously, Dr. George held the positions of Senior Vice President and Chief Medical Officer at GPC Biotech, Princeton and Senior Vice President, Head of the Oncology Department at Johnson & Johnson, New Jersey. She is a qualified gynecologist and oncologist, trained in France and in Montreal. Dr. George began her career as Chief of Service at the Institut Gustave Roussy (France), was a visiting professor at the Memorial Sloan Kettering Cancer Center, New York, and then held positions of increasing responsibility at Lederle Laboratories (a predecessor company to Pfizer Inc.), Sandoz (now a division of Novartis AG) and Rhône-Poulenc Rorer (today part of Sanofi).

*Hilde Windels* (acting as legal representative of BVBA Hilde Windels) has served as a member of our board of directors since 2014 and has served as the representative of BVBA Hilde Windels, the legal entity that holds this seat, since 2017. She has over 20 years of experience in corporate finance, capital markets and strategic initiatives. She currently serves as

Executive Chairman of the board of directors of Mycartis, an immune diagnostics company in Belgium and a spin-out of Biocartis, a molecular diagnostics company and as a member of the board of directors of MDx Health NV since November 2017. Ms. Windels served as Chief Financial Officer of Devgen from 1999 to 2008 and as a member of its board of directors from 2001 to 2008. From early 2009 to mid-2011, she worked as an independent chief financial officer for several private biotechnology companies and served as a director of MDxHealth from June 2010 until August 2011. In August 2011, she joined Biocartis as Chief Financial Officer until September 2015 when she was appointed co-Chief Executive Officer. Previously, she was in charge of the banking services for corporates at a regional level at ING. From March 2017 until September 2017, she held the position of interim Chief Executive Officer. Ms. Windels holds a Masters in Economics from the University of Leuven (Belgium).

# **Family Relationships**

There are no family relationships among any of our executive officers or directors.

## **B.** Compensation.

The aggregate compensation paid and benefits in kind granted by us to our current executive officers and directors, including share-based compensation, for the year ended December 31, 2017 was  $\in$  3.6 million. The total amount set aside or accrued to provide pension, retirement or similar benefits for our executive officers was  $\notin$  44 thousand. We did not set aside any similar pension or retirement benefits for the benefit of our directors.

## **Director Compensation**

At our combined general meetings of shareholders held on June 23, 2015, June 24, 2016 and June 27, 2017, shareholders set the total annual attendance fees (*jetons de présence*) to be distributed among non-employee directors at  $\epsilon$ 176 thousand,  $\epsilon$ 240 thousand and  $\epsilon$ 280 thousand, respectively. The following table sets forth information regarding the compensation earned by our non-employee directors for service on our board of directors during the year ended December 31, 2017. Gil Beyen, our Chief Executive Officer and Chairman of the Board, is a director but does not receive any additional compensation for his services as a director.

	FEES EARNED	WARRANTS (1)	TOTAL
NAME	(€)	(€)	(€)
Philippe Archinard	37,000	68,120	105,120
Allene Diaz	41,500(2)	111,700	153,200
Luc Dochez	32,500	68,120	100,620
Galenos SPRL	42,500	68,120	110,620
Martine Ortin George	42,000	68,120	110,120
Hilde Windels	33,000	68,120	101,120

- (1) As required by SEC rules governing disclosures in this Annual Report on Form 20-F, our equity grants (e.g., options, warrants or free shares) are required to be disclosed at their fair value on the date of grant and do not have any intrinsic value to their recipients if the strike price of the warrants is higher than the underlying share price. The assumptions we used in valuing these awards are described in Note 5.3 to our consolidated financial statements and do not necessarily correspond to the actual value recognized or that may be recognized by our directors. Any intrinsic value would only be recognized for tax purposes upon exercise of the equity grants and/or sale of the shares pursuant to applicable tax laws.
- (2) Does not include consulting fees in the amount of €8,000 paid to Ms. Diaz in 2017 for services rendered to us in 2016. Our consulting agreement with Ms. Diaz terminated in 2016.

## **Executive Committee Compensation**

Our executive committee consists of (i) our Chief Executive Officer, (ii) our Chief Financial Officer and Chief Operating Officer, (iii) our Chief Business Officer, (iv) our Chief Medical Officer, (v) our Chief Scientific Officer and (vi) our Vice President and Director of Pharmaceutical Operations and Qualified Person. The executive committee discusses and consults with the board and advises the board on our day-to-day management. The following table sets forth information regarding compensation earned by Gil Beyen, our Chairman and Chief Executive Officer, and by Jérôme Bailly, our Vice President and Director of Pharmaceutical Operations and Qualified Person, during the year ended December 31, 2017.

NAME AND PRINCIPAL POSITION Gil Beyen	SALARY (€) 276,000(1)	BONUS (€) 165,600(2)(7)	EQUITY AWARDS (€) 195,000 <sup>(3)</sup>	ALL OTHER COMPENSATION $(\varepsilon)$ 8,058(4)	TOTAL (€) 644,658
Chief Executive Officer and Chairman of the Board					
Jérôme Bailly	160,366(1)	39,999(2)	97,500(5)	22,779(6)	320,644
Vice President and Director of Pharmaceutical Operations and Qualified Person					
All other executive committee members	1,146,474	363,791	401,920	34,095	1,946,280

(1) Reflects gross remuneration before taxes.

(2) Reflects compensation received for achievement of strategic goals related to (i) the advancement of clinical trials with eryaspase, (ii) the advancement of other development programs and (iii) building the organization and securing additional financing.

(3) Reflects €195,000 for the valuation of 15,000 free shares granted during the year ended December 31, 2017.

- (4) Reflects vehicle rental, gas cards, healthcare insurance
- (5) Reflects €97,500 for the valuation of 7,500 performance shares granted during the year ended December 31, 2017.
- (6) Reflects (i) gross remuneration before taxes of €8,034.72 for exceptional compensation and vehicle lease and (ii) €2,131.85 for gas cards, health insurance and (iii) €18,546 for retirement benefits.
- (7) Subject to approval of our shareholders at the next Annual General Meeting of Shareholders.

#### **Executive Compensation Arrangements**

For a discussion of our employment arrangements with our executive officers, see "Item 7.B.—Related Party Transactions—Arrangements with Our Directors and Executive Officers." Except the arrangements described in "Item 7.B.—Related Party Transactions—Agreements with Our Directors and Executive Officers," there are no arrangements or understanding between us and any of our other executive officers providing for benefits upon termination of their employment, other than as required by applicable law.

#### Limitations on Liability and Indemnification Matters

Under French law, provisions of bylaws that limit the liability of directors are prohibited. However, French law allows *sociétés anonymes* to contract for and maintain liability insurance against civil liabilities incurred by any of their directors and officers involved in a third-party action, provided that they acted in good faith and within their capacities as directors or officers of the company. Criminal liability cannot be indemnified under French law, whether directly by the company or through liability insurance.

We have obtained directors and officers liability insurance for our directors and officers, which includes coverage against liability under the Securities Act. We have entered into agreements with our directors and executive officers to provide contractual indemnification. With certain exceptions and subject to limitations on indemnification under French law, these agreements provide for indemnification for damages and expenses including, among other things, attorneys' fees, judgments and settlement amounts incurred by any of these individuals in any action or proceeding arising out of his or her actions in that capacity.

These agreements may discourage shareholders from bringing a lawsuit against our directors and executive officers for breach of their fiduciary duty. These provisions also may have the effect of reducing the likelihood of derivative litigation against directors and executive officers, even though such an action, if successful, might otherwise benefit us and our shareholders. Furthermore, a shareholder's investment in our equity securities may be adversely affected to the extent we pay the costs of settlement and damage awards against directors and officers pursuant to these insurance agreements.

#### **Equity Incentives**

We believe our ability to grant equity incentives is a valuable and necessary compensation tool that allows us to attract and retain the best available personnel for positions of substantial responsibility, provides additional incentives to employees and promotes the success of our business. Due to French corporate law and tax considerations, we have historically granted several different equity incentive instruments to our directors, executive officers, employees and other service providers, including:

- founder's share warrants (otherwise known as bons de souscription de parts de créateurs d'entreprise, or BSPCE), which are granted to our officers and employees;
- share warrants (otherwise known as bons de souscription d'actions, or BSA), which have historically only been granted to non-employee directors;
- restricted, or free, shares (otherwise known as actions gratuites); and
- stock options (otherwise known as options de souscription et/ou d'achat d'actions).

Our board of directors' authority to grant these equity incentive instruments and the aggregate amount authorized to be granted under these instruments must be approved by a two-thirds majority of the votes held by our shareholders present, represented or voting by authorized means, at the relevant extraordinary shareholders' meeting. Once approved by our shareholders, our board of directors can grant share warrants (BSA) for up to 18 months, and restricted (free) shares and stock options for up to 38 months from the date of the applicable shareholders' approval. The authority of our board of directors to grant equity incentives may be extended or increased only by extraordinary shareholders' meetings. As a result, we typically request that our shareholders authorize new pools of equity incentive instruments at every annual shareholders' meeting.

We have four share-based compensation plans for our executive officers, non-employee directors and employees, the 2012 Plan, the 2014 Plan, the 2016 Plan and the 2017 Plan. In general, founder's share warrants and share warrants no longer continue to vest following termination of the employment, office or service of the holder and all vested shares must be exercised within post-termination exercise periods set forth in the grant documents. In the event of certain changes in our share capital structure, such as a consolidation or share split or dividend, French law and applicable grant documentation provides for appropriate adjustments of the numbers of shares issuable and/or the exercise price of the outstanding warrants.

As of December 31, 2017, employee warrants, non-employee warrants, employee stock options and free shares were outstanding allowing for the purchase of an aggregate of 858,186 ordinary shares at a weighted average exercise price of  $\leq 14.2155$  ( $\leq 17.0899$ ) per ordinary share based on the exchange rate in effect as of such date (this weighted average exercise price does not include 217,447 ordinary shares issuable upon the vesting of outstanding free shares that may be issued for free with no exercise price being paid).

#### Founder's Share Warrants (BSPCE)

Founder's share warrants have traditionally been granted to certain of our employees who were French tax residents because the warrants carry favorable tax and social security treatment for French tax residents. Similar to options, founder's share warrants entitle a holder to exercise the warrant for the underlying vested shares at an exercise price per share determined by our board of directors and at least equal to the fair market value of an ordinary share on the date of grant. However, unlike options, the exercise price per share is fixed as of the date of implementation of the plans pursuant to which the warrants may be granted, rather than as of the date of grant of the individual warrants.

We have issued two types of founder's share warrants as follows:

Meeting date	April 2, 2013	Mar 21 2012
meeting date		May 21, 2012
Dates of allocation	January 22, 2014	May 31, 2012
	June 23, 2015	July 18, 2013
	May 6, 2016	July 17, 2014
Total number of BSPCEs authorized	19,500 (1)	33,787
Total number of BSPCEs granted	18,410 (2)	33,787
ר fc	For senior management, one-third was vested in T2 2015 and two-thirds were vested in T2 2016; or other employees, immediately upon each grant except for 6,500 BSPCE <sub>2014</sub> which could not be exercised before July 1, 2017	From May to July 2012, 2013 and 2014
BSPCE expiry date	January 22, 2024	May 20, 2020
BSPCE exercise price per share	€12.250	€7.362
Number of shares subscribed as of December 31, 2017	15,000	168,110
Total number of BSPCEs granted but not exercised as of December 31, 2017	16,910	16,976
Total number of shares available for subscription as of December 31, 2017	169,100	169,760
Maximum number of new shares that can be issued	169,100	169,760

(1) 22,500 BSPCE<sub>2014</sub> were originally allocated by the board of directors on January 22, 2014. On December 4, 2014, the board of directors approved the conversion of 3,000 BSPCE<sub>2014</sub> into 3,000 BSA<sub>2014</sub>.

(2) Excludes 1,000 BSPCE initially allocated to Yann Godfrin which were forfeited following his resignation in January 2016 and 90 BSPCE allocated to a former employee which were forfeited.

Our shareholders, or pursuant to delegations granted by our shareholders, our board of directors, determines the recipients of the warrants, the dates of grant, the number and exercise price of the founder's share warrants to be granted, the number of shares issuable upon exercise and certain other terms and conditions of the founder's share warrants, including the period of their exercisability and their vesting schedule. However, notwithstanding any shareholder authorization, under applicable law, we are no longer eligible to issue any further founders' share warrants (BSPCE).

## Share Warrants (BSA)

Share warrants have historically only been granted to our non-employee directors. Similar to options, share warrants entitle a holder to exercise the warrant for the underlying vested shares at an exercise price per share determined by our board of directors and at least equal to the fair market value of an ordinary share on the date of grant. However, unlike options, the exercise price per share is fixed as of the date of implementation of the plans pursuant to which the warrants may be granted, rather than as of the date of grant of the individual warrants.

As of December 31, 2017, we have issued four types of share warrants as follows:

Plan title	BSA 2017	BSA 2016	BSA 2014	BSA 2012
Meeting date	June 27, 2017	June 24, 2016	April 2, 2013	May 21, 2012
Dates of allocation	June 27, 2017	October 3, 2016 January 8, 2017	June 23, 2015	May 31, 2012 August 3, 2012 July 18, 2013 July 17, 2014 April 29, 2015 August 31, 2015
Total number of BSAs authorized	55,000	60,000	3,000(1)	11,263
Total number of BSAs granted	55,000	60,000	3,000	10,760
Start date for the exercise of the BSAs	(5)	(2)	One-third vested in T2 2015 and two-thirds vested in T2 2016 for senior management	From May to July 2012, 2013, 2014 and 2015
BSA expiry date	June 27, 2022	(3)	January 22, 2024	May 20, 2020
BSA exercise price per share	€26.47	(4)	€12.25	€7.362
Number of shares subscribed as of December 31, 2017	0	0	1,000	67,420
Total number of BSAs granted but not exercised as of December 31, 2017	55,000	60,000	2,900	4,018
Total number of shares available for subscription as of December 31, 2017	0	0	29,000	40,180
Maximum number of new shares that can be issued	55,000	60,000	29,000	40,180

- (1) Reflects conversion of 3,000 BSPCE<sub>2014</sub> into 3,000 BSA<sub>2014</sub> pursuant to a decision of the board of directors on December 4, 2014.
- (2) For the 45,000 BSA<sub>2016</sub> granted on October 3, 2016, half can be exercised as from October 4, 2017. The remainder can be exercised as from October 4, 2018. For the 15,000 BSA<sub>2016</sub> granted on January 8, 2017, one-third can be exercised as from January 8, 2018, one-third as from January 8, 2019 and the remainder as from January 8, 2020.
- (3) October 3, 2021 for the 45,000 BSA granted on October 3, 2016. January 8, 2022 for the 15,000 BSA granted on January 8, 2017.
- (4) €18.52 for the 45,000 BSA granted on October 3, 2016. €13.60 for the 15,000 BSA granted on January 8, 2017.
- (5) Approximately one-third can be exercised as from June 27, 2018, approximately one-third can be exercised as from June 27, 2019 and the remainder can be exercised as from June 27, 2020.

Our shareholders, or pursuant to delegations granted by our shareholders, our board of directors, determines the recipients of the warrants, the dates of grant, the number and exercise price of the share warrants to be granted, the number of shares issuable upon exercise and certain other terms and conditions of the share warrants, including the period of their exercisability and their vesting schedule.

# Free Shares (AGA)

Under our 2016 Free Share Plan, which was adopted by our board of directors on October 3, 2016, we have granted free shares to certain of our employees and officers.

Free shares may be granted to any individual employed by us or by any affiliated company. Free shares may also be granted to our Chairman and our Chief Executive Officer. However, no free share may be granted to a beneficiary holding more than 10% of our share capital or to a beneficiary who would hold more than 10% of our share capital as a result of such grant. The maximum number of shares that may be granted or issued under the 2016 Free Share Plan is 250,000. In addition, under French law, the maximum number of shares that may be granted shall not exceed 10% of the share capital as at the date of grant of the free shares (30% if the allocation benefits all employees).

Our board of directors has the authority to administer the 2016 Free Share Plan. Subject to the terms of the 2016 Free Share Plan, our board of directors determines the recipients, the dates of grant, the number of free shares to be granted and the terms and conditions of the free shares, including the length of their vesting period (starting on the grant date, during which the beneficiary holds a right to acquire shares for free but has not yet acquired any shares) and holding period (starting when the shares are issued and definitively acquired but may not be transferred by the recipient) within the limits determined by the shareholders. Our shareholders have determined that the vesting period should be set by the board of directors. From the beginning of the vesting period, the cumulated vesting and holding period should not be less than two years.

The board of directors has the authority to modify awards outstanding under our 2016 Free Share Plan, subject to the consent of the beneficiary for any modification adverse to such beneficiary. For example, the board has the authority to release a beneficiary from the continued service condition during the vesting period after the termination of the employment.

The free shares granted under our 2016 Free Share Plan will be definitively acquired at the end of the vesting period as set by our board of directors subject to continued service during the vesting period, except if the board releases a given beneficiary from this condition upon termination of his or her employment contract. At the end of the vesting period, the beneficiary will be the owner of the shares. However, the shares may not be sold, transferred or pledged during the holding period. In the event of disability before the end of the vesting period, the free shares shall be definitively acquired by the beneficiary on the date of disability. In the event the beneficiary dies during the vesting period, the free shares shall be definitively acquired at the date of the request of allocation made by his or her beneficiaries in the framework of the inheritance provided that such request is made within six months from the date of death.

In 2016, the board granted an aggregate of 111,261 free shares under the 2016 Free Share Plan which will vest as follows:

			HOLDING PERIOD			
	NUMBER OF FREE SHARES	VESTING PERIOD	FOR NON- CORPORATE OFFICERS		FOR DRPORATE DFFICERS	EXERCISABLE (SUBJECT TO PERFORMANCE CONDITIONS)
AGA Tranche 1					10% of the	
		One	One	One	cumulated	October 3,
	37,087	year	year	year	free shares	2018
AGA Tranche 2					until	
		Two			termination	October 3,
	37,087	years	None		of office	2018
AGA Tranche 3		Three				October 3,
	37,087	years	None			2019

As of December 31, 2016, 111,261 free shares granted under the 2016 Free Share Plan were acquired on October 3, 2016 and are under the holding period of one year, of which 59,001 free shares are held by our directors and officers.

On January 8, 2017, our board of directors granted an additional aggregate of 15,000 free shares under the 2016 Free Share Plan to Alexander Scheer, which will vest in three tranches of 5,000 free shares, on January 8, 2018, January 8, 2019 and January 8, 2020.

On June 27, 2017, our Chief Executive Officer and Chairman granted an additional aggregate of 8,652 free shares under the 2016 Free Share Plan to certain employees.

On June 27, 2017, our board of directors adopted the 2017 Free Share Plan and granted 45,000 free shares to certain employees. On the same date, our Chief Executive Officer and Chairman granted 29,475 free shares to certain employees. The free shares will vest in three equal tranches, on June 27, 2018, June 27, 2019 and June 27, 2020.

On October 3, 2017, our Chief Executive Officer and Chairman granted an additional aggregate of 16,650 free shares under the 2016 Free Share Plan to certain employees.

On January 7, 2018, our board of directors granted an additional aggregate of 40,500 free shares under the 2016 Free Share Plan to officers and 27,000 free shares under the 2017 Free Share Plan.

On January 7, 2018, our Chief Executive Officer and Chairman granted an additional aggregate of 86,940 free shares under the 2016 Free Share Plan to certain employees.

#### Stock Options (SO)

On October 3, 2016, our board of directors adopted our 2016 Stock Option Plan which will expire on October 3, 2026. Stock options issued pursuant to the 2016 Stock Option Plan provide the holder with the right to purchase a specified number of ordinary shares from us at a fixed exercise price payable at the time the stock option is exercised, as determined by our board of directors. The 2016 Stock Option Plan generally provides that the exercise price for any stock option will be no less than 95% of the average of the closing sales prices per ordinary share during the 20 market trading days prior to the day of the board of directors' decision to grant the options. The maximum number of ordinary shares subject to stock options issued is 250,000 ordinary shares under the 2016 Stock Option Plan. Incentive stock options and non-statutory stock options may be granted under the 2016 Stock Option Plan.

Stock options may be granted to any individual employed by us or by any affiliated company. Stock options may also be granted to our Chairman, our general manager and to our deputy general managers. In addition, incentive stock options may not be granted to owners of shares possessing 10% or more of the share capital of the company.

Our board of directors has the authority to administer and interpret the 2016 Stock Option Plan. Subject to the terms and conditions of the 2016 Stock Option Plan, our board of directors determines the recipients, dates of grant, exercise price, number of stock options to be granted and the terms and conditions of the stock options, including the length of their vesting schedules. Our board of directors is not required to grant stock options with vesting and exercise terms that are the same for every participant. The term of each stock option granted under the 2016 Stock Option Plan will generally be 10 years from the date of grant. Further, stock options will generally terminate on the earlier of when the beneficiary ceases to be an employee of our company or upon certain transactions involving our company.

The board of directors has the authority to modify awards outstanding under our 2016 Stock Option Plan, subject to the written consent of the beneficiary for any modification adverse to such beneficiary. For example, the board of directors has the authority to extend a post-termination exercise period.

Stock options granted under the 2016 Stock Option Plan generally may not be sold, transferred or pledged in any manner other than by will or by the laws of descent or distribution. In the event of disability, unless otherwise resolved by our board of directors, the beneficiary's right to exercise the vested portion of his or her stock option generally terminates six months after the last day of such beneficiary's service, but in any event no later than the expiration of the maximum term of the applicable stock options. In the event the beneficiary dies during the vesting period, then, unless otherwise resolved by our board of directors, the beneficiary's setate or any recipient by inheritance or bequest may exercise any portion of the stock option vested at the time of the beneficiary's death within the six months following the date of death, but in any event no later than the expiration of the maximum term of the applicable stock options.

As of December 31, 2016, a maximum of 250,000 stock options may be issued under the 2016 Stock Option Plan. This figure includes 44,499 stock options granted under the 2016 Stock Option Plan on October 3, 2016 with an exercise price of  $\leq$ 18.520 per ordinary share, of which 21,999 were granted to certain of our directors and executive officers.

On January 8, 2017, our Chief Executive Officer and Chairman granted 3,000 stock options to certain employees with an exercise price of €15.65 per ordinary share.

On June 27, 2017, our board of directors adopted the 2017 Stock Option Plan and granted 12,000 stock options to certain employees. On the same date, our Chief Executive Officer and Chairman granted 10,200 stock options to certain employees with an exercise price of  $\leq$ 26.47 per ordinary share. On June 27, 2017, our Chief Executive Officer and Chairman granted 18,000 stock options under the 2016 Stock Option Plan to certain employees with an exercise price of  $\leq$ 26.47 per ordinary share.

On October 3, 2017, our Chief Executive Officer and Chairman granted an aggregate of 30,000 stock options to certain employees with an exercise price of €23.59 per ordinary share under the 2016 Stock Option Plan.

On January 7, 2018, our board of directors granted an aggregate of 40,500 stock options to certain employees with an exercise price of €18.00 per ordinary share under the 2016 Stock Option Plan to officers.

On January 7, 2018, our Chief Executive Officer and Chairman granted an aggregate of 56,703 stock options to certain employees with an exercise price of €18.00 per ordinary share under the 2016 Stock Option Plan

#### **C. Board Practices.**

Until May 2013, our company had a two-tier corporate governance system: an executive board was responsible for managing the company and a supervisory board oversaw and advised the executive board. We have now established a board of directors. Our board of directors currently consists of seven members, less than a majority of whom are citizens or residents of the United States. As permitted by French law, two of our directors, Galenos SPRL and BVBA Hilde Windels, are legal entities. Each of these entities has designated an individual, Sven Andréasson and Hilde Windels, respectively, to represent it and to act on its behalf at meetings of our board of directors. These representatives have the same responsibilities to us and to our shareholders as he or she would have if he or she had been elected to our board of directors in his or her individual capacity.

Under French law and our bylaws, our board of directors must be comprised of between three and 18 members, without prejudice to the derogation established by law in the event of merger. Since January 1, 2017, the number of directors of each gender may not be less than 40%. Any appointment made in violation of this limit that is not remedied within six months of this appointment will be null and void. Within these limits, the number of directors is determined by our shareholders. Directors are appointed, reappointed to their position, or removed by the company's ordinary general meeting, and in particular, any appointment which remedies a violation of the 40% limit must be ratified by our shareholders at the next ordinary general meeting. Their term of office, in accordance with our bylaws, is three years. Directors chosen or appointed to fill a vacancy must be elected by our board of directors for the remaining duration of the current term of the vacant director. The appointment must then be ratified at the next shareholders' general meeting. In the event the board of directors would be comprised of less than three directors as a result of a vacancy, the remaining directors shall immediately convene a shareholders' general meeting to elect one or several new directors so there are at least three directors serving on the board of directors, in accordance with French law.

The following table sets forth the names of our directors, the years of their initial appointment as directors of the board and the expiration dates of their current term.

	CURRENT POSITION	YEAR OF INITIAL <u>APPOINTMENT</u>	TERM EXPIRATION YEAR
Gil Beyen	Chairman	2013	2019
Galenos SPRL represented by Sven Andréasson (1)	Director	2014	2019
Philippe Archinard	Director	2013	2019
Allene Diaz (2)	Director	2017	2020
Luc Dochez	Director	2015	2019
Martine Ortin George	Director	2014	2020
BVBA Hilde Windels represented by Hilde Windels <sup>(3)</sup>	Director	2017	2020

(1) Galenos SPRL has designated an individual, Sven Andréasson, to represent it and to act on its behalf at meetings of our board of directors. Mr. Andréasson previously served as a member of our board from 2013 to 2014. Galenos SPRL is a company controlled by Mr. Andréasson.

(2) Ms. Diaz was initially appointed to our board of directors as a non-voting member (*censeur*) in September 2016 and was subsequently appointed by our board of directors as a voting board member of the board in January 2017. Her appointment was ratified by our shareholders at our combined general meeting in June 2017.

(3) BVBA Hilde Windels was appointed as a director by our shareholders at our combined general meeting in June 2017. BVBA Hilde Windels has designated an individual, Hilde Windels, to represent it and to act on its behalf at meetings of our board of directors. She served as a member of the board of directors in her individual capacity from 2014 to 2017. BVBA Hilde Windels is a company controlled by Ms. Windels.

#### **Director Independence**

As a foreign private issuer, under the listing requirements and rules of the Nasdaq Global Select Market, we are not required to have independent directors on our board of directors, except to the extent that our audit committee is required to consist of independent directors, subject to certain phase-in schedules. Nevertheless, our board of directors has undertaken a review of the independence of the directors and considered whether any director has a material relationship with us that could compromise his or her ability to exercise independent judgment in carrying out his or her responsibilities. Based upon information requested from, and provided by, each director concerning such director's background, employment and affiliations, including family relationships, our board of directors determined that all of our directors, except for Mr. Beyen, qualify as "independent directors" as defined under applicable rules of the Nasdaq Global Select Market and the independence requirements contemplated by Rule 10A-3 under the Exchange Act. In making these determinations, our board of directors considered the current and prior relationships that each non-employee director has with our company and all other facts and circumstances that our board of directors deemed relevant in determining their independence, including the beneficial ownership of our ordinary shares by each non-employee director and his or her affiliated entities (if any).

#### Role of the Board in Risk Oversight

Our board of directors is primarily responsible for the oversight of our risk management activities and has delegated to the audit committee the responsibility to assist our board in this task. The audit committee also monitors our system of disclosure controls and procedures and internal control over financial reporting and reviews contingent financial liabilities. The audit committee, among other things, examines our balance sheet commitments and risks and the relevance of risk monitoring procedures. While our board oversees our risk management, our management is responsible for day-to-day risk management processes. Our board of directors expects our management to consider risk and risk management in each business decision, to proactively develop and monitor risk management strategies and processes for day-to-day activities and to effectively implement risk management strategies adopted by the board of directors. We believe this division of responsibilities is the most effective approach for addressing the risks we face.

#### **Corporate Governance Practices**

As a French *société anonyme*, we are subject to various corporate governance requirements under French law. In addition, as a foreign private issuer listed on the Nasdaq Global Select Market, we will be subject to Nasdaq corporate governance listing standards. However, the corporate governance standards provide that foreign private issuers are permitted to follow home country corporate governance practices in lieu of Nasdaq rules, with certain exceptions. We intend to rely on these exemptions for foreign private issuers and follow French corporate governance practices in lieu of the Nasdaq corporate governance rules, which would otherwise require that (1) a majority of our board of directors consist of independent directors; (2) we establish a nominating and corporate governance committee; and (3) our remuneration committee be composed entirely of independent directors.

As a foreign private issuer, we are required to comply with Rule 10A-3 of the Exchange Act, relating to audit committee composition and responsibilities. Rule 10A-3 provides that the audit committee must have direct responsibility for the nomination, compensation and choice of our auditors, as well as control over the performance of their duties, management of complaints made, and selection of consultants. However, if the laws of a foreign private issuer's home country require that any such matter be approved by the board of directors or the shareholders, the audit committee's responsibilities or powers with respect to such matter may instead be advisory. Under French law, the audit committee may only have an advisory role and appointment of our statutory auditors, in particular, must be decided by the shareholders at our annual meeting.

In addition, Nasdaq rules require that a listed company specify that the quorum for any meeting of the holders of common stock be at least 33 1/3% of the outstanding shares of the company's voting stock. Consistent with French law, our bylaws provide that a quorum requires the presence of shareholders having at least (1) 20% of the shares entitled to vote in the case of an ordinary shareholders' general meeting or at an extraordinary shareholders' general meeting where shareholders are voting on a capital increase by capitalization of reserves, profits or share premium, or (2) 25% of the shares entitled to vote in the case of any other extraordinary shareholders' general meeting. If a quorum is not present, the meeting is adjourned. There is no quorum requirement when an ordinary general meeting is reconvened, but the reconvened meeting may consider only questions which were on the agenda of the adjourned meeting. When an extraordinary general meeting is reconvened, the quorum required is 20% of the shares entitled to vote, except where the reconvened meeting is considering capital increases through capitalization of reserves, profits or share premium. For these matters, no quorum is required at the reconvened meeting. If a quorum is not present at a reconvened meeting a quorum, then the meeting may be adjourned for a maximum of two months.

#### **Board Committees**

The board of directors has established an audit committee and a remuneration and appointments committee, which operate pursuant to rules of procedure adopted by our board of directors. The board of directors has also established a clinical strategy committee, which is responsible for analyzing and reviewing our clinical and regulatory strategy. Subject to available exemptions, the composition and functioning of all of our committees will comply with all applicable requirements of the French Commercial Code, the Exchange Act, the Nasdaq Global Select Market and SEC rules and regulations.

In accordance with French law, committees of our board of directors will only have an advisory role and can only make recommendations to our board of directors. As a result, decisions will be made by our board of directors taking into account non-binding recommendations of the relevant board committee.

*Audit Committee.* Our audit committee assists our board of directors in its oversight of our corporate accounting and financial reporting and submits the selection of our statutory auditors, their remuneration and independence for approval. Mr. Andréasson, Dr. Archinard, Ms. Windels and Mr. Dochez currently serve on our audit committee. Ms. Windels is the chairperson of our audit committee. Our board has determined that each of Mr. Andréasson, Dr. Archinard, Ms. Windels and Mr. Dochez is independent within the meaning of the applicable listing rules and the independence requirements contemplated by Rule 10A-3 under the Exchange Act. Our board of directors has further determined that Ms. Windels is an "audit committee financial expert" as defined by SEC rules and regulations and that each of the members qualifies as financially sophisticated under the applicable exchange listing rules. The principal responsibility of our audit committee is to monitor the existence and efficacy of the company's financial audit and risk control procedures on an ongoing basis.

Our board of directors has specifically assigned the following duties to the audit committee:

- examining the corporate and consolidated annual and interim financial statements;
- validating the relevance of the company's accounting methods and choices;
- verifying the relevance of financial information published by the company;
- ensuring the implementation of internal control procedures;
- verifying the correct operation of internal controls with the assistance of internal quality audits;
- examining the schedule of work for internal and external audits;
- examining any subject likely to have a significant financial and accounting impact;
- examining the state of significant disputes;
- examining off-balance sheet commitments and risks;
- examining the relevance of risk monitoring procedures;
- establishing and overseeing procedures for the treatment of complaints or submissions identifying concerns regarding accounting, internal
  accounting controls, or auditing matters;
- examining any regulated agreements;
- directing the selection of statutory auditors, their remuneration, and ensuring their independence;
- ensuring proper performance of the statutory auditors' mission; and
- establishing the rules for the use of statutory auditors for work other than auditing of the accounts and verifying the correct execution thereof.

*Remuneration and Appointments Committee*. Mr. Andréasson, Dr. Archinard and Ms. Diaz currently serve on our remuneration and appointments committee. Dr. Archinard is the chairperson of our remuneration and appointments committee.

Our board of directors has specifically assigned the following duties to the remuneration and appointments committee:

- formulating recommendations and proposals concerning (i) the various elements of the remuneration, pension and health insurance plans for
  executive officers and directors, (ii) the procedures for establishing the terms and conditions for setting the variable portion of their
  remunerations, and (iii) a general policy for awarding share warrants and founder's warrants;
- examining the amount of attendance fees and the system for distributing such fees amongst the directors, taking into account their dedication and the tasks performed within the board of directors;
- advising and assisting the board of directors as necessary in the selection of senior executives and the establishment of their remuneration;

- assessing any increases in capital reserved for employees;
- assisting the board of directors in the selection and recruitment of new directors;
- ensuring the implementation of structures and procedures to allow the application of good governance practices within the company;
- preventing conflicts of interest within the board of directors; and
- implementing the procedure for evaluating the board of directors.

## D. Employees.

As of December 31, 2017, we had 114 full-time equivalent employees. We consider our labor relations to be positive. At each date shown, we had the following full-time equivalents, broken out by department and geography:

	At December 31		- /
	<u>2015</u>	<u>2016</u>	<u>2017</u>
Function:			
Research and preclinical development	17	21	28
Clinical, medical and regulatory affairs	9	17	24
Pharmaceutical operations	14	21	29
Management and administration	16	25	28
Business development and licensing			5
Total	56	84	114
Geography:			
France	52	76	100
United States	4	8	14
Total	56	84	114

#### E. Share Ownership.

For information regarding the share ownership of our directors and executive officers, see "Item 6.B—Compensation" and "Item 7.A—Major Shareholders."

#### Item 7. Major Shareholders and Related Party Transactions

# A. Major Shareholders

The following table and accompanying footnotes set forth, as of December 31, 2017, information regarding beneficial ownership of our ordinary shares by:

- each person, or group of affiliated persons, known by us to beneficially own more than 5% of our ordinary shares;
- each of our executive officers;
- each of our directors; and
- all of our executive officers and directors as a group.

Beneficial ownership is determined according to the rules of the SEC and generally means that a person has beneficial ownership of a security if he, she or it possesses sole or shared voting or investment power of that security, including free shares that vest within 60 days of December 31, 2017 and options and warrants that are currently exercisable or exercisable within 60 days of December 31, 2017. Shares subject to free shares that vest within 60 days of December 31, 2017 and shares subject to warrants currently exercisable or exercisable or exercisable or exercisable within 60 days of December 31, 2017 are deemed to be outstanding for computing the percentage ownership of the person holding these free shares and warrants and the percentage ownership of any group of which the holder is a member, but are not deemed outstanding for computing the percentage of any other person.

Except as indicated by the footnotes below, we believe, based on the information furnished to us, that the persons named in the table below have sole voting and investment power with respect to all shares shown that they beneficially own, subject to community property laws where applicable. The information does not necessarily indicate beneficial ownership for any other purpose, including for purposes of Sections 13(d) and 13(g) of the Securities Act.

Our calculation of the percentage of beneficial ownership is based on 17,937,559 of our ordinary shares (including ordinary shares in the form of ADSs) outstanding as of December 31, 2017.Unless otherwise indicated, the address of each beneficial owner listed in the table below is c/o ERYTECH Pharma S.A., Bâtiment Adénine, 60 Avenue Rockefeller, 69008 Lyon, France.



	NUMBER OF ORDINARY SHARES BENEFICIALLY	PERCENTAGE OF ORDINARY SHARES BENEFICIALLY
NAME OF BENEFICIAL OWNER	OWNED	OWNED
5% Shareholders:		
Baker Bros. Advisors LP (1)	4,898,337	27.3%
Auriga Ventures III FCPR (2)	1,147,522	6.4
BVF Inc. (3)	930,175	5.2
Directors and Executive Officers:		
Gil Beyen <sup>(4)</sup>	140,176	*
Eric Soyer <sup>(5)</sup>	20,773	*
Jean-Sébastien Cleiftie <sup>(6)</sup>	1,054	*
Iman El-Hariry (7)	29,000	*
Alexander Scheer (8)	2,476	*
Jérôme Bailly (9)	28,053	*
Galenos SPRL (10)	11,671	*
Philippe Archinard <sup>(11)</sup>	14,800	*
Allene Diaz (7)	5,000	*
Luc Dochez (7)	13,170	*
Martine Ortin George (12)	16,671	*
BVBA Hilde Windels (12)	16,671	*
All directors and executive officers as a group (12 persons) (13)	299,515	1.6%

Represents beneficial ownership of less than 1%.

- (1) The address of Baker Bros. Advisors LP is 860 Washington Street, 3rd Floor, New York, NY 10014. Julian C. Baker and Felix J. Baker are the managing partners of Baker Bros. Advisors LP and may be deemed to be beneficial owners of securities of the company directly held by Baker Bros. Advisors LP, and may be deemed to have the power to vote or direct the vote of and the power to dispose or direct the disposition of such securities. Julian C. Baker and Felix J. Baker disclaim beneficial ownership of the securities held directly by Baker Bros. Advisors LP, except to the extent of their pecuniary interest.
- (2) Jacques Chatain, Bernard Daugeras and Patrick Bamas are managers of Auriga Ventures III FCPR, or Auriga, and exercise voting and investment power with respect to shares held by Auriga. The managers disclaim beneficial ownership of all shares held by Auriga. The address of Auriga is c/o Auriga Partners, 18 avenue Matignon 75008 Paris, France.
- (3) Based solely on information contained in the Schedule 13G filed with the SEC on January 2, 2018 reporting that (i) Biotechnology Value Fund, L.P., or BVF, beneficially owned 436,257 shares, (ii) Biotechnology Value Fund II, L.P., or BVF2, beneficially owned 289,906 shares of the company, and (iii) Biotechnology Value Trading Fund OS LP, or Trading Fund OS, beneficially owned 74,806 shares. BVF Partners OS Ltd., or Partners OS, as the general partner of Trading Fund OS, may be deemed to beneficially own the 74,806 shares beneficially owned by Trading Fund OS. BVF Partners L.P., or Partners, as the general partner of BVF, BVF2, the investment manager of Trading Fund OS, and the sole member of Partners OS, may be deemed to beneficially own the 930,175 shares beneficially owned in the aggregate by BVF, BVF2, Trading Fund OS, and certain Partners managed accounts, or the Partners Managed Accounts, including 129,206 shares, of which 63,239 are represented by ADSs, held in the Partners Managed Accounts. BVF Inc., as the general partner of BVF Inc., may be deemed to beneficially own the 930,175 shares of the company beneficially owned by BVF Inc. Partners, BVF Inc. and Mr. Lampert share voting and dispositive power over the shares of the company beneficially owned by BVF, BVF2, Trading Fund OS, and the Partners Managed Accounts. Partners OS disclaims beneficial ownership of the shares beneficially owned by BVF, BVF2, Trading Fund OS, and the Partners Managed Accounts. Partners, BVF Inc. and Mr. Lampert disclaims beneficial ownership of the shares beneficially owned by BVF, BVF2, Trading Fund OS, and the Partners, BVF Inc. and Mr. Lampert disclaims beneficial ownership of the shares beneficially owned by BVF, BVF2, Trading Fund OS, and the Partners Managed Accounts. Partners OS disclaims beneficial ownership of the shares beneficially owned by BVF, BVF2, Trading Fund OS, and the Partners Managed Accounts. The address of BVF Inc. is 1 Sansome Street, 30th Floor, San Francisco, California 94104.
- (4) Consists of 1,546 ordinary shares issued upon the vesting of free shares that had no exercise price (however, these shares may not be sold, transferred or pledged prior to October 3, 2018), and 138,630 ordinary shares issuable upon exercise of warrants that are exercisable within 60 days of December 31, 2017.
- 5) Consists of 773 ordinary shares issued upon the vesting of free shares that had no exercise price (however, these shares may not be sold, transferred or pledged prior to October 3, 2018), and 20,000 ordinary shares issuable upon exercise of warrants that are exercisable within 60 days of December 31, 2017.
- (6) Consists of 1,054 ordinary shares issued upon the vesting of free shares that had no exercise price (however, these shares may not be sold, transferred or pledged prior to October 3, 2018).
- (7) Consists of ordinary shares issuable upon exercise of warrants that are exercisable within 60 days of December 31, 2017.

- (8) Consists of 2,476 ordinary shares issuable for free upon the vesting of free shares with no exercise price paid within 60 days of December 31, 2017(however, these shares may not be sold, transferred or pledged prior to January 8, 2019).
- (9) Consists of 280 ordinary shares, 773 ordinary shares issued upon the vesting of outstanding free shares that had no exercise price (however, these shares may not be sold, transferred or pledged prior to October 3, 2018), and 27,000 ordinary shares issuable upon exercise of warrants that are exercisable within 60 days of December 31, 2017.
- (10) Consists of one ordinary share and 11,670 ordinary shares issuable upon exercise of warrants that are exercisable within 60 days of December 31, 2017.
- (11) Consists of 10,300 ordinary shares and 4,500 ordinary shares issuable upon exercise of warrants that are exercisable within 60 days of December 31, 2017.
- (12) Consists of one ordinary share and 16,670 ordinary shares issuable upon exercise of warrants that are exercisable within 60 days of December 31, 2017.
- (13) Consists of 10,583 ordinary shares, 4,146 ordinary shares issued upon the vesting of free shares that had no exercise price (however, these shares may not be sold, transferred or pledged prior to October 3, 2018), 2,476 ordinary shares issuable upon the vesting of free shares that are issuable for free with no exercise price paid within 60 days of December 31, 2017 and 282,310 ordinary shares issuable upon exercise of warrants that are exercisable within 60 days of December 31, 2017.

The significant changes in the percentage ownership held by some of our principal shareholders since January 1, 2015 are largely as a result of the transactions described in our prospectus dated November 9, 2017, filed with the SEC pursuant to Rule 424(b), under the heading "Related Party Transactions —November 2017 Global Offering" and the dilution resulting from our underwritten global offering in November 2017. None of our principal shareholders have voting rights different than our other shareholders.

As of December 31, 2017, we estimate that approximately 46% of our outstanding ordinary shares (including ordinary shares in the form of ADSs) were held in the United States by approximately 30 holders of record. The actual number of holders is greater than these numbers of record holders, and includes beneficial owners whose ordinary shares or ADSs are held in street name by brokers and other nominees. This number of holders of record also does not include holders whose shares may be held in trust by other entities.

# **B. Related Party Transactions.**

Since January 1, 2017, we have engaged in the following transactions with our directors, executive officers and holders of more than five percent (5%) of our outstanding voting securities and their affiliates, which we refer to as our related parties.

# April 2017 Offering

In April 2017, we issued an aggregate of 3,000,000 ordinary shares in an offering to institutional investors in the United States and Europe at an issue price of  $\notin$ 23.50 per share for a total aggregate purchase price of  $\notin$ 70.5 million. Baker Brothers Advisors LP, a holder of more than 5% of our outstanding voting securities, purchased 462,000 ordinary shares in the offering for an aggregate purchase price of  $\notin$ 10.9 million. No other securities were purchased in the offering by our executive officers, directors or a holder of more than 5% of our outstanding voting securities.

## November 2017 Global Offering

In November 2017, we completed a global public offering of an aggregate of 6,180,137 ordinary shares, including the full exercise of the underwriters' options to purchase additional shares, for gross proceeds of \$143.7 million. The global offering consisted of a U.S. initial public offering of 5,389,021 American Depositary Shares, each representing one ordinary share and a concurrent private placement in Europe and other countries outside of the U.S. and Canada of 791,116 ordinary shares. Baker Brothers Advisors LP, a holder of more than 5% of our outstanding voting securities, purchased approximately 3,090,096 ordinary shares in the offering for an aggregate purchase price approximately \$61.8 million. No other securities were purchased in the offering by our executive officers, directors or a holder of more than 5% of our outstanding voting securities.

## Agreements with Our Directors and Executive Officers

## Severance Pay

On May 24, 2013, the board of directors approved terms for severance pay to be awarded under certain conditions to our then-executive officers: Gil Beyen, Pierre-Olivier Goineau and Yann Godfrin. Mr. Goineau resigned effective January 11, 2015 and Dr. Godfrin resigned effective January 18, 2016. The agreement provided that, in the event of expiration of the executive's term of office (except where renewal is rejected by the executive) or in the event of revocation (unless the executive has been revoked for gross negligence or willful misconduct as that term is defined by the labor chamber of the French Supreme Court), the executive is entitled to severance equal to 12 times the average of monthly remuneration (bonuses included) received during the 12 months preceding the revocation decision or the expiration of the executive's term of office. The payment of the compensation shall be subject to the performance of the following conditions: (i) respect of our company's budget and expenditures and (ii) at least one of the following conditions: (a) an agreement of collaboration or a current license, and (b) one product in an active phase of clinical development by the company. No related expense has been recorded to date.

#### **Profit-Sharing Agreement**

On November 29, 2013, we implemented a profit-sharing agreement covering the period from January 1, 2014 to December 31, 2016 for the benefit of certain employees and for the benefit of Messrs. Beyen and Goineau and Dr. Godfrin. Mr. Goineau resigned effective January 11, 2015 and Dr. Godfrin resigned effective January 18, 2016. They are no longer participants in such plan. Under the terms of the agreement, a percentage of each executive's gross annual remuneration at December 31 of each year is distributed (i) to the executive's beneficiaries (subject to certain ceilings) and (ii) upon completion of certain performance objectives. The profit-sharing percentage of the gross annual remuneration was set at 2.5% for 2014 and was subsequently increased to 4% in 2015 and to 5% in 2016. It has remained at 5% for 2017.

#### Employment Agreements with Eric Soyer, Jean-Sebastien Cleiftie and Alexander Scheer

In September 2015, October 2016, and November 2016, respectively, we entered into employment agreements with Messrs. Soyer, Cleiftie and Scheer. Each employment agreement provides for an annual base salary and variable compensation in amounts ranging from 30% to 35% of the executive's current base salaries, based upon achievement of specified performance objectives. These employment agreements also provide for severance pay in specified situations. In the event of the executive's termination in the absence of gross negligence or willful misconduct, the executive will be entitled to an amount equal to six months' base salary, plus an additional three months' base salary for each full year such executive has worked for us, up to a maximum of 12 months' base salary in total, including any additional indemnity as provided for by French law. In connection with a change of control of our company, if the executive is terminated in the absence of gross negligence or willful misconduct or resigns pursuant to suffering a diminution of the executive's job duties, or in the event of a mutually agreed termination (*rupture conventionnelle*) under French law, such executive will be entitled to an amount equal to 12 times the average of monthly remuneration, including bonuses, received during the 12 months preceding the termination. If a change of control of our company occurs within 24 months of the granting of bonus shares, such executive will be entitled to an amount intended to compensate for the potential loss of compensation in the event of cancellation of bonus shares granted or for the potential loss of favorable tax treatment in the event of the sale of such shares, in the context of this change of control. These agreements also provide for a 12-month non-compete clause (18 months in the case of Mr. Soyer), whereby the executive is entitled to an amount equal to 33% of his average monthly remuneration over the last three months (12 months in the case of Mr. Soyer).

#### **Employment Agreement with Iman El-Hariry**

In June 2015, our U.S. subsidiary, ERYTECH Pharma, Inc., entered into an employment agreement with Dr. El-Hariry that provides for an annual base salary and variable compensation in an amount up to 35% of her base salary, based upon achievement of specified performance objectives. The agreement also provides for severance pay in specified situations. In the event of Dr. El-Hariry's termination without cause (as defined in Dr. El-Hariry's employment agreement), she will be entitled to an amount equal to six months' base salary, plus an additional three months' base salary for each full year she has worked for us, up to a maximum of 12 months' base salary in total. If Dr. El-Hariry resigns as a result of (i) a diminution of her job duties, (ii) a change in reporting or (iii) a relocation, she will be entitled to an amount up to 12 months' base salary compensation depending upon the length of her employment with us. In connection with a change of control, if Dr. El-Hariry is terminated within 12 months (a) by us, (b) by mutual agreement or (c) by her decision to resign after receiving an offer that is not at least equivalent to her position prior to the change in control, she will be entitled to a lump sum payment equal to one year's salary plus bonus (under the condition that she would not be eligible for the other severance benefits described above). Upon termination for any reason, our company may request Dr. El-Hariry to execute a non-competition agreement for a period of 12 months, whereby Dr. El-Hariry will be entitled to severance pay.

#### Employment Agreement with Jérôme Bailly

In January 2007, we entered into an employment agreement with Dr. Bailly, which was amended as of January 2017. He is entitled to an annual base salary set at  $\leq 159,996$ , and variable compensation, in an amount up to 25% of his base salary, upon achievement of specified performance objectives. If a change of control of our company occurs within 24 months of the granting of bonus shares, Dr. Bailly will be entitled to an amount intended to compensate for the potential loss of compensation in the event of cancellation of bonus shares granted or for the potential loss of favorable tax treatment in the event of the sale of such shares.

## **Other Arrangements**

We have entered into other compensatory arrangements with our executive officers, which have been ratified by our board of directors. The primary arrangements are summarized in the table below.

NAME Gil Beyen	SAVINGS PLAN (PEE) V	RETIREMENT SAVINGS PLAN (PERCO)	FINANCIAL ASSISTANCE FOR THE MANAGEMENT OF SECURITIES	TAX ASSISTANCE V	TRAINING
-	Λ	Λ	Λ	А	
Eric Soyer	Х	Х	Х		
Jean-Sébastien Cleiftie	Х	Х	Х		
Iman El-Hariry			Х		
Alexander Scheer	Х	Х	Х		
Jérôme Bailly	Х	Х	Х		Х

# Director and Executive Officer Compensation

See "Item 6.B—Compensation" for information regarding compensation of directors and executive officers.

## **Equity Awards**

Since December 31, 2017, we allocated on January 7, 2018:

- 97,203 SOP<sub>2017</sub> options under the 2017 Plan to certain employees;
- 40,500 AGA<sub>2016</sub> free shares under the 2016 Plan to certain of our officers;
- 113,940 AGA<sub>2017</sub> free shares under the 2017 Plan to certain of our officers and employees;
- 40,500 BSA<sub>2017</sub> warrants under the 2017 Plan to our directors.

See "Item. 7A—Major Shareholders" for information regarding equity awards to our executive officers.

## **Bonus Plans**

All our executive officers are entitled to a bonus ranging between 25% and 50% based on yearly objectives determined by our board of directors upon recommendation of our remuneration and appointments committee.

# **Indemnification Agreements**

We have entered into indemnification agreements with each of our directors and executive officers. See "Item. 6B—Limitations on Liability and Indemnification Matters."

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers or persons controlling us pursuant to the foregoing provisions, we have been informed that in the opinion of the SEC such indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable.

# **Related-Party Transactions Policy**

We comply with French law regarding approval of transactions with related parties. We have adopted a related person transaction policy that sets forth our procedures for the identification, review, consideration and approval or ratification of related person transactions. The policy became effective immediately upon the closing of the global offering. For purposes of our policy only, a related person transaction is defined as (i) any transaction, arrangement or relationship (or any series of similar transactions, arrangements or relationships) in which we and any related person are, were or will be participants in and the amount involved exceeds \$120,000, or (ii) any agreement or similar transaction under French law which falls within the scope of Article L. 225-38 of the French Commercial Code. A related person is any executive officer, director or beneficial owner of more than 5% of any class of our voting securities, including any of their immediate family members and any entity owned or controlled by such persons.

Under the policy, if a transaction has been identified as a related person transaction, including any transaction that was not a related person transaction when originally consummated or any transaction that was not initially identified as a related person transaction prior to consummation, our management must present information regarding the related person transaction to our board of directors for review, consideration and approval or ratification. The presentation must include a description of, among other things, the material facts, the interests, direct and indirect, of the related persons, the benefits to us of the transaction and whether the transaction is on terms that are comparable to the terms available to or from, as the case may be,

an unrelated third party or to or from employees generally. Under the policy, we will collect information that we deem reasonably necessary from each director, executive officer and, to the extent feasible, significant shareholder to enable us to identify any existing or potential related-person transactions and to effectuate the terms of the policy.

In addition, under our Code of Business Conduct and Ethics, our employees and directors have an affirmative responsibility to disclose any transaction or relationship that reasonably could be expected to give rise to a conflict of interest.

In considering related person transactions, our board of directors will take into account the relevant available facts and circumstances including, but not limited to:

- the risks, costs and benefits to us;
- the impact on a director's independence in the event that the related person is a director, immediate family member of a director or an entity with which a director is affiliated;
- the availability of other sources for comparable services or products; and
- the terms available to or from, as the case may be, unrelated third parties or to or from employees generally.

The policy requires that, in determining whether to approve, ratify or reject a related person transaction, our board of directors must consider, in light of known circumstances, whether the transaction is in, or is not inconsistent with, our best interests and those of our shareholders, as our board of directors determines in the good faith exercise of its discretion.

All of the transactions described above were entered into prior to the adoption of the written policy, but all were approved by our board of directors to the extent required by, and in compliance with, French law.

#### C. Interests of Experts and Counsel.

Not applicable.

## Item 8. Financial Information

# A. Consolidated Statements and Other Financial Information.

# **Consolidated Financial Statements**

Our consolidated financial statements are included as part of this Annual Report, starting at page F-1.

## **Dividend Distribution Policy**

We have never declared or paid any cash dividends on our ordinary shares. We do not anticipate paying cash dividends on our equity securities in the foreseeable future and intend to retain all available funds and any future earnings for use in the operation and expansion of our business, given our state of development.

Subject to the requirements of French law and our bylaws, dividends may only be distributed from our distributable profits, plus any amounts held in our available reserves which are reserves other than legal and statutory and revaluation surplus. See "Item 10. B—Memorandum and Articles of Association" for further details on the limitations on our ability to declare and pay dividends. Dividend distributions, if any in the future, will be made in euros and converted into U.S. dollars with respect to the ADSs, as provided in the amended and restated deposit agreement.

# Legal Proceedings

From time to time we may become involved in legal proceedings or be subject to claims arising in the ordinary course of our business. We are not presently a party to any legal proceedings that, if determined adversely to us, would individually or taken together have a material adverse effect on our business, results of operations, financial condition or cash flows. Regardless of the outcome, litigation can have an adverse impact on us because of defense and settlement costs, diversion of management resources and other factors.

#### **B.** Significant Changes.

Not applicable.

# Item 9. The Offer and Listing.

# A. Offer and Listing Details.

Our ADSs have been listed on the Nasdaq Global Select Market under the symbol "ERYP" since November 10, 2017. Our global offering in November 2017 was priced at \$23.26 per ADS or €20.00 per ordinary share on November 9, 2017. Our ordinary shares have been trading on Euronext Paris under the symbol "ERYP" since May 7, 2013. Prior to that date, there was no public trading market for our ADSs or our ordinary shares.

The following tables set forth for the periods indicated the reported high and low sale prices per ADS on the Nasdaq Global Select Market in U.S. dollars and per ordinary share on Euronext Paris in euros.

# Nasdaq Global Select Market

		ADS
Period	High	Low
Annual		
2017 (beginning November 10, 2017)	\$30.56	\$17.50
Quarterly		
Fourth Quarter 2017 (beginning November 10, 2017)	30.56	17.50
First Quarter 2018	23.46	20.00
Second Quarter 2018 (through April 9, 2018)	21.07	20.25
Month Ended:		
November 2017 (beginning November 10, 2017)	28.70	24.59
December 2017	30.56	17.50
January 2018	23.46	20.00
February 2018	23.03	21.16
March 2018	21.04	20.16
April 2018 (through April 9, 2018)	21.07	20.25

# **Euronext Paris**

2014       34.97       10.16         2015       40.20       23.04         2016       28.18       11.50         2017       30.20       12.10         Quarterly	Period	High	Low
2014       34.97       10.16         2015       40.20       23.04         2016       28.18       11.50         2017       30.20       12.10         Quarterly	Annual		
2015       40.20       23.04         2016       28.18       11.50         2017       30.20       12.10         Quarterly	2013 (beginning May 7, 2013)	€12.07	€ 8.58
2016       28.18       11.50         2017       30.20       12.10         Quarterly       26.90       17.62         Second Quarter 2016       28.18       15.44         Third Quarter 2016       24.42       18.51         Fourth Quarter 2016       18.56       11.50         First Quarter 2016       24.42       18.51         Fourth Quarter 2016       18.56       11.50         First Quarter 2017       29.82       12.10         Second Quarter 2017       29.82       12.10         Second Quarter 2017       30.20       23.81         Third Quarter 2017       30.20       23.81         Third Quarter 2017       29.70       15.60         First Quarter 2018 (through April 9, 2018)       19.57       16.01         Second Quarter 2018 (through April 9, 2018)       19.57       16.01         Second Puarter 2017       25.30       21.29         December 2017       25.30       21.29         December 2017       26.25       15.60         January 2018       19.57       17.64         February 2018       18.83       16.01         March 2018       17.48       16.14	2014	34.97	10.16
2017       30.20       12.10         Quarterly       5       17.62         First Quarter 2016       28.18       15.44         Third Quarter 2016       24.42       18.51         Fourth Quarter 2016       18.56       11.50         First Quarter 2017       29.82       12.10         Second Quarter 2017       15.60       15.60         First Quarter 2018       19.57       16.01         Second Quarter 2018 (through April 9, 2018)       17.26       16.85         Month Ended       29.70       23.05         November 2017       25.30       21.29         December 2017       25.30       21.29         December 2017       26.25       15.60         January 2018       19.57       17.64         February 2018       19.57       17.64         March 2018       19.57       17.64	2015	40.20	23.04
QuarterlyFirst Quarter 201626.9017.62Second Quarter 201628.1815.44Third Quarter 201624.4218.51Fourth Quarter 201729.8212.10Second Quarter 201729.8212.10Second Quarter 201730.2023.81Third Quarter 201730.2023.81Third Quarter 201729.7015.60First Quarter 201819.5716.01Second Quarter 2018 (through April 9, 2018)17.2616.85Month Ended29.7023.05November 201725.3021.29December 201726.2515.60January 201819.5717.64February 201818.8316.01March 201817.4816.14	2016	28.18	11.50
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Second Quarter 2016       28.18       15.44         Third Quarter 2016       24.42       18.51         Fourth Quarter 2016       18.56       11.50         First Quarter 2017       29.82       12.10         Second Quarter 2017       30.20       23.81         Third Quarter 2017       27.96       22.44         Fourth Quarter 2017       29.70       15.60         First Quarter 2018       19.57       16.01         Second Quarter 2018 (through April 9, 2018)       17.26       16.85         Month Ended       29.70       23.05         November 2017       25.30       21.29         December 2017       26.25       15.60         January 2018       19.57       17.64         February 2018       18.83       16.01         March 2018       17.48       16.14	Quarterly		
Third Quarter 2016       24.42       18.51         Fourth Quarter 2016       18.56       11.50         First Quarter 2017       29.82       12.10         Second Quarter 2017       30.20       23.81         Third Quarter 2017       27.96       22.44         Fourth Quarter 2017       29.70       15.60         First Quarter 2018       19.57       16.01         Second Quarter 2018 (through April 9, 2018)       17.26       16.85         Month Ended       29.70       23.05         November 2017       29.30       21.29         December 2017       25.30       21.29         December 2017       26.25       15.60         January 2018       19.57       17.64         February 2018       18.83       16.01         March 2018       17.48       16.14	First Quarter 2016	26.90	17.62
Fourth Quarter 201618.5611.50First Quarter 201729.8212.10Second Quarter 201730.2023.81Third Quarter 201727.9622.44Fourth Quarter 201729.7015.60First Quarter 201819.5716.01Second Quarter 2018 (through April 9, 2018)17.2616.85Month Ended29.7023.05November 201725.3021.29December 201726.2515.60January 201819.5717.64February 201818.8316.01March 201817.4816.14	Second Quarter 2016	28.18	15.44
First Quarter 2017       29.82       12.10         Second Quarter 2017       30.20       23.81         Third Quarter 2017       27.96       22.44         Fourth Quarter 2017       29.70       15.60         First Quarter 2018       19.57       16.01         Second Quarter 2018 (through April 9, 2018)       17.26       16.85         Month Ended       29.70       23.05         October 2017       29.70       23.05         November 2017       25.30       21.29         December 2017       26.25       15.60         January 2018       19.57       17.64         February 2018       18.83       16.01         March 2018       17.48       16.14	Third Quarter 2016	24.42	18.51
Second Quarter 2017       30.20       23.81         Third Quarter 2017       27.96       22.44         Fourth Quarter 2017       29.70       15.60         First Quarter 2018 (through April 9, 2018)       19.57       16.01         Second Quarter 2018 (through April 9, 2018)       17.26       16.85         Month Ended       29.70       23.05         November 2017       29.70       23.05         November 2017       25.30       21.29         December 2017       26.25       15.60         January 2018       19.57       17.64         February 2018       18.83       16.01         March 2018       17.48       16.14	Fourth Quarter 2016	18.56	11.50
Third Quarter 2017       27.96       22.44         Fourth Quarter 2017       29.70       15.60         First Quarter 2018       19.57       16.01         Second Quarter 2018 (through April 9, 2018)       17.26       16.85         Month Ended       29.70       23.05         November 2017       25.30       21.29         December 2017       26.25       15.60         January 2018       19.57       17.64         February 2018       18.83       16.01         March 2018       17.48       16.14	First Quarter 2017	29.82	12.10
Fourth Quarter 201729.7015.60First Quarter 201819.5716.01Second Quarter 2018 (through April 9, 2018)17.2616.85Month Ended29.7023.05October 201725.3021.29December 201726.2515.60January 201819.5717.64February 201818.8316.01March 201817.4816.14	Second Quarter 2017	30.20	23.81
First Quarter 2018       19.57       16.01         Second Quarter 2018 (through April 9, 2018)       17.26       16.85         Month Ended       29.70       23.05         October 2017       25.30       21.29         December 2017       26.25       15.60         January 2018       19.57       17.64         February 2018       18.83       16.01         March 2018       17.48       16.14	Third Quarter 2017	27.96	22.44
Second Quarter 2018 (through April 9, 2018)       17.26       16.85         Month Ended       29.70       23.05         October 2017       25.30       21.29         December 2017       26.25       15.60         January 2018       19.57       17.64         February 2018       18.83       16.01         March 2018       17.48       16.14	Fourth Quarter 2017	29.70	15.60
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November 2017         25.30         21.29           December 2017         26.25         15.60           January 2018         19.57         17.64           February 2018         18.83         16.01           March 2018         17.48         16.14	Month Ended		
December 2017       26.25       15.60         January 2018       19.57       17.64         February 2018       18.83       16.01         March 2018       17.48       16.14	October 2017	29.70	23.05
January 2018     19.57     17.64       February 2018     18.83     16.01       March 2018     17.48     16.14	November 2017	25.30	21.29
February 2018         18.83         16.01           March 2018         17.48         16.14	December 2017	26.25	15.60
March 2018 17.48 16.14	January 2018	19.57	17.64
	February 2018	18.83	16.01
April 2018 (through April 9, 2018)17.2616.85	March 2018	17.48	16.14
	April 2018 (through April 9, 2018)	17.26	16.85

On April 9, 2018, the last reported closing price of our ADSs on Nasdaq was \$20.44 per ADS, and the last reported closing price of our ordinary shares on Euronext Paris was €17.20 per share.

#### **B.** Plan of Distribution.

Not applicable.

#### C. Markets.

Our ADSs have been listed on Nasdaq under the symbol "ERYP" since November 10, 2017. Our ordinary shares have been trading on Euronext Paris under the symbol "ERYP" since May 7, 2013.

## **D. Selling Shareholders.**

Not applicable.

# E. Dilution.

Not applicable.

# F. Expenses of the Issue.

Not applicable.

## Item 10. Additional Information.

# A. Share Capital.

Not applicable.

# B. Memorandum and Articles of Association.

The information set forth in our prospectus dated November 9, 2017, filed with the SEC pursuant to Rule 424(b), under the headings "Description of Share Capital—Key Provisions of Our Bylaws and French Law Affecting Our Ordinary Shares," "Description of Share Capital—Differences in Corporate Law" and "Limitations Affecting Shareholders of a French Company" is incorporated herein by reference.

# C. Material Contracts.

## **Underwriting Agreement**

We entered into an underwriting agreement by and among Jefferies LLC, Jefferies International Limited, Cowen and Company LLC and Oddo BHF SCA, as representatives of the underwriters, on November 9, 2017, with respect to the ADSs and ordinary shares sold in our November 2017 global offering. We agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act, and to contribute to payments the underwriters may be required to make in respect of such liabilities.

For additional information on our material contracts, please see "Item 4. Information on the Company," "Item 6. Directors, Senior Management and Employees," and "Item 7.B. Related Party Transactions" of this Annual Report on 20-F.

# **D. Exchange Controls.**

Under current French foreign exchange control regulations there are no limitations on the amount of cash payments that we may remit to residents of foreign countries. Laws and regulations concerning foreign exchange controls do, however, require that all payments or transfers of funds made by a French resident to a non-resident such as dividend payments be handled by an accredited intermediary. All registered banks and substantially all credit institutions in France are accredited intermediaries.

## E. Taxation.

The following describes material U.S. federal income tax and French tax considerations relating to the acquisition, ownership and disposition of ADSs by a U.S. holder (as defined below). This summary does not address all U.S. federal income tax and French tax matters that may be relevant to a particular U.S. holder. This summary does not address tax considerations applicable to a holder of ADSs that may be subject to special tax rules including, without limitation, the following:

- banks, financial institutions or insurance companies;
- brokers, dealers or traders in securities, currencies, commodities, or notional principal contracts;
- tax-exempt entities or organizations, including an "individual retirement account" or "Roth IRA" as defined in Section 408 or 408A of the Code (as defined below), respectively;
- real estate investment trusts, regulated investment companies or grantor trusts;
- persons that hold the ADSs as part of a "hedging," "integrated," "wash sale" or "conversion" transaction or as a position in a "straddle" for U.S. federal income tax purposes;

- S corporations;
- certain former citizens or long-term residents of the United States;
- persons that received ADSs as compensation for the performance of services;
- persons acquiring ADSs in connection with a trade or business conducted outside of the United States, including a permanent establishment in France;
- persons subject to Section 451(b) of the Code;
- holders that own directly, indirectly, or through attribution 10% or more of the voting power or value of our ADSs and shares or, in the case of the
  discussion of French tax consequences, 5% or more of the voting stock or our share capital; and
- holders that have a "functional currency" other than the U.S. dollar.

For the purposes of this description, a "U.S. holder" is a beneficial owner of ADSs that is (or is treated as), for U.S. federal income tax purposes:

- an individual who is a citizen or resident of the United States;
- a domestic corporation;
- · an estate, the income of which is subject to U.S. federal income taxation regardless of its source; or
- a trust, if a court within the United States is able to exercise primary supervision over its administration and one or more U.S. persons have the authority to control all of the substantial decisions of such trust, or if such trust has a valid election in effect under applicable U.S. Treasury Regulations to be treated as a U.S. person.

If a partnership (or any other entity treated as a partnership for U.S. federal income tax purposes) holds ADSs, the U.S. federal income tax consequences relating to an investment in the ADSs will depend in part upon the status of the partner and the activities of the partnership. Such a partner or partnership should consult its tax advisor regarding the U.S. federal income tax considerations of acquiring, owning and disposing of the ADSs in its particular circumstances.

The discussion in this section is based in part upon the representations of the depositary and the assumption that each obligation in the amended and restated deposit agreement and any related agreement will be performed in accordance with its terms.

Persons considering an investment in the ADSs should consult their own tax advisors as to the particular tax consequences applicable to them relating to the acquisition, ownership and disposition of the ADSs, including the applicability of U.S. federal, state and local tax laws, French tax laws and other non-U.S. tax laws.

### **Material French Tax Considerations**

The following describes the material French income tax consequences to U.S. holders of purchasing, owning and disposing of our ADSs and, unless otherwise noted, this discussion is the opinion of Gide Loyrette Nouel A.A.R.P.I, our French tax counsel, insofar as it relates to matters of French tax law and legal conclusions with respect to those matters.

This discussion does not purport to be a complete analysis or listing of all potential tax effects of the acquisition, ownership or disposition of our ADSs to any particular investor, and does not discuss tax considerations that arise from rules of general application or that are generally assumed to be known by investors. All of the following is subject to change. Such changes could apply retroactively and could affect the consequences described below.

The description of the French income tax and wealth tax consequences set forth below is based on the Convention Between the Government of the United States of America and the Government of the French Republic for the Avoidance of Double Taxation and the Prevention of Fiscal Evasion with Respect to Taxes on Income and Capital of August 31, 1994, or the Treaty, which came into force on December 30, 1995 (as amended by any subsequent protocols, including the protocol of January 13, 2009), and the tax guidelines issued by the French tax authorities in force as of the date of this Annual Report.



This discussion applies only to investors that are entitled to Treaty benefits under the "Limitation on Benefits" provision contained in the Treaty.

France has recently introduced a comprehensive set of new tax rules applicable to French assets that are held by or in foreign trusts. These rules provide inter alia for the inclusion of trust assets in the settlor's net assets for the purpose of applying the French wealth tax, for the application of French gift and death duties to French assets held in trust, for a specific tax on capital on the French assets of foreign trusts not already subject to the French wealth tax and for a number of French tax reporting and disclosure obligations. The following discussion does not address the French tax consequences applicable to securities (including ADSs) held in trusts. If ADSs are held in trust, the grantor, trustee and beneficiary are urged to consult their own tax advisor regarding the specific tax consequences of acquiring, owning and disposing of securities (including ADSs).

U.S. holders are urged to consult their own tax advisors regarding the tax consequences of the purchase, ownership and disposition of securities in light of their particular circumstances, especially with regard to the "Limitations on Benefits" provision.

### Estate and Gift Taxes and Transfer Taxes

In general, a transfer of securities by gift or by reason of death of a U.S. holder that would otherwise be subject to French gift or inheritance tax, respectively, will not be subject to such French tax by reason of the Convention between the Government of the United States of America and the Government of the French Republic for the Avoidance of Double Taxation and the Prevention of Fiscal Evasion with Respect to Taxes on Estates, Inheritances and Gifts, dated November 24, 1978 (as amended by the protocol of December 8, 2014), unless (i) the donor or the transferor is domiciled in France at the time of making the gift or at the time of his or her death, or (ii) the securities were used in, or held for use in, the conduct of a business through a permanent establishment or a fixed base in France.

Pursuant to Article 235 ter ZD of the Code général des impôts (French Tax Code, or FTC), purchases of shares or ADSs of a French company listed on a regulated market of the European Union or on a foreign regulated market formally acknowledged by the French Financial Market Authority (AMF) are subject to a 0.3% French tax on financial transactions provided that the issuer's market capitalization exceeds 1 billion euros as of December 1 of the year preceding the taxation year. The Nasdaq Global Select Market is not currently acknowledged by the French AMF but this may change in the future. A list of French relevant companies whose market capitalization exceeds 1 billion euros as of December 1 of the year preceding the taxation year is published annually and at least once a year, by the French State. As at December 1, 2017, our market capitalization did not exceed 1 billion euros.

Following the global offering, purchases of our securities may be subject to such tax provided that its market capitalization exceeds 1 billion euros and that the Nasdaq Global Select Market is acknowledged by the French AMF.

In the case where Article 235 ter ZD of the FTC is not applicable, transfers of shares issued by a listed French company are subject to uncapped registration duties at the rate of 0.1% if the transfer is evidenced by a written statement ("acte") executed either in France or outside France. Although there is no case law or official guidelines published by the French tax authorities on this point, transfers of ADSs should remain outside of the scope of the aforementioned 0.1% registration duties.

#### Tax on Sale or Other Disposition

As a matter of principle, under French tax law, a U.S. holder should not be subject to any French tax on any capital gain from the sale, exchange, repurchase or redemption by us of ordinary shares or ADSs, provided such U.S. holder is not a French tax resident for French tax purposes and has not held more than 25% of our dividend rights, known as "*droits aux benefices sociaux*," at any time during the preceding five years, either directly or indirectly, and, as relates to individuals, alone or with relatives (as an exception, a U.S holder resident, established or incorporated in a non-cooperative State or territory as defined in Article 238-0 A of the FTC should be subject to a 75% withholding tax in France on any such capital gain, regardless of the fraction of the dividend rights it holds).

Under application of the Treaty, a U.S. holder who is a U.S. resident for purposes of the Treaty and entitled to Treaty benefit will not be subject to French tax on any such capital gain unless the ordinary shares or the ADSs form part of the business property of a permanent establishment or fixed base that the U.S. holder has in France. U.S. holders who own ordinary shares or ADSs through U.S. partnerships that are not resident for Treaty purposes are advised to consult their own tax advisors regarding their French tax treatment and their eligibility for Treaty benefits in light of their own particular circumstances. A U.S. holder that is not a U.S. resident for Treaty purposes or is not entitled to Treaty benefit (and in both cases is not resident, established or incorporated in a non-cooperative State or territory as defined in Article 238-0 A of the FTC) and has held more than 25% of our dividend rights, known as "*droits aux benefices sociaux*," at any time during the preceding five years, either directly or indirectly, and, as relates to individuals, alone or with relatives will be subject to a levy in France at the rate of 12.8% for individuals or 33 1/3% for corporate bodies or other legal entities. Special rules apply to U.S. holders who are residents of more than one country.

### Taxation of Dividends

Dividends paid by a French corporation to non-residents of France are generally subject to French withholding tax at a rate of 12.8% when the recipient is an individual and 30% otherwise. Dividends paid by a French corporation in a non-cooperative State or territory, as defined in Article 238-0 A of the FTC, will generally be subject to French withholding tax at a rate of 75%. However, eligible U.S. holders, other than individuals subject to the French withholding tax at a rate of 12.8%, entitled to Treaty benefits under the "Limitation on Benefits" provision contained in the Treaty who are U.S. residents, as defined pursuant to the provisions of the Treaty, will not be subject to this 30% or 75% withholding tax rate, but may be subject to the withholding tax at a reduced rate (as described below).

Under the Treaty, the rate of French withholding tax on dividends paid to an eligible U.S. holder who is a U.S. resident as defined pursuant to the provisions of the Treaty and whose ownership of the ordinary shares or ADSs is not effectively connected with a permanent establishment or fixed base that such U.S. holder has in France, may be reduced to 15%, or to 5% if such U.S. holder is a corporation and owns directly or indirectly at least 10% of the share capital of the issuer; such U.S. holder may claim a refund from the French tax authorities of the amount withheld in excess of the Treaty rates of 15% or 5%, if any.

For U.S. holders that are not individuals but are U.S. residents, as defined pursuant to the provisions of the Treaty, the requirements for eligibility for Treaty benefits, including the reduced 5% or 15% withholding tax rates contained in the "Limitation on Benefits" provision of the Treaty, are complex, and certain technical changes were made to these requirements by the protocol of January 13, 2009. U.S. holders are advised to consult their own tax advisors regarding their eligibility for Treaty benefits in light of their own particular circumstances. Dividends paid to an eligible U.S. holder may immediately be subject to the reduced rates of 5% or 15% provided that:

- such holder establishes before the date of payment that it is a U.S. resident under the Treaty by completing and providing the depositary with a treaty form (Form 5000); or
- the depositary or other financial institution managing the securities account in the U.S. of such holder provides the French paying agent with a
  document listing certain information about the U.S. holder and its ordinary shares or ADSs and a certificate whereby the financial institution
  managing the U.S. holder's securities account in the United States takes full responsibility for the accuracy of the information provided in the
  document.

Otherwise, dividends paid to a U.S. holder, other than individuals subject to the French withholding tax at a rate of 12.8%, will be subject to French withholding tax at the rate of 30%, or 75% if paid in a non-cooperative State or territory (as defined in Article 238-0 A of the FTC), and then reduced at a later date to 5% or 15%, provided that such holder duly completes and provides the French tax authorities with the treaty forms Form 5000 and Form 5001 before December 31 of the second calendar year following the year during which the dividend is paid.

Certain qualifying pension funds and certain other tax-exempt entities are subject to the same general filing requirements as other U.S. holders except that they may have to supply additional documentation evidencing their entitlement to these benefits.

Form 5000 and Form 5001, together with instructions, will be provided by the depositary to all U.S. holders registered with the depositary. The depositary will arrange for the filing with the French tax authorities of all such forms properly completed and executed by U.S. holders of ordinary shares or ADSs and returned to the depositary in sufficient time so that they may be filed with the French tax authorities before the distribution in order to immediately obtain a reduced withholding tax rate. Otherwise, the depositary must withhold tax at the full rate of 30% or 75% as applicable. In that case, the U.S. holders may claim a refund from the French tax authorities of the excess withholding tax.

Since the withholding tax rate applicable under French domestic law to U.S. holders who are individuals does not exceed the cap provided in the Treaty (i.e. 15%), the 12.8% rate shall apply, without any reduction provided under the Treaty.

### Wealth Tax

The French real estate wealth tax ("*impôt sur la fortune immobilière*") which applies only to individuals who own directly or indirectly through one or more legal entities, real estate property in France (subject to certain exemptions) and whose net taxable assets amount to at least €1,300,000.



French real estate wealth tax may only apply to U.S. holders to the extent the company holds real estate assets that are not allocated to its operational activity, for the fraction of the value of the financial rights representing such assets. In any case, pursuant to Article 965 2° of the FTC, shares of an operating entity holding French real estate assets in which the taxpayer holds, directly and indirectly, less than 10% of the share capital or voting rights are exempt from real estate wealth tax.

### Material U.S. Federal Income Tax Considerations

This section discusses the material U.S. federal income tax considerations relating to the acquisition, ownership and disposition of ADSs by a U.S. holder. This description does not address the U.S. federal estate, gift, or alternative minimum tax considerations, or any U.S. state, local, or non-U.S. tax considerations of the acquisition, ownership and disposition of the ADSs.

This description is based on the U.S. Internal Revenue Code of 1986, as amended, or the Code, existing, proposed and temporary U.S. Treasury Regulations promulgated thereunder and administrative and judicial interpretations thereof, in each case as in effect and available on the date hereof. All the foregoing is subject to change, which change could apply retroactively, and to differing interpretations, all of which could affect the tax considerations described below. There can be no assurances that the U.S. Internal Revenue Service, or the IRS, will not take a position concerning the tax consequences of the acquisition, ownership and disposition of the ADSs or that such a position would not be sustained by a court. Holders should consult their own tax advisers concerning the U.S. federal, state, local and non-U.S. tax consequences of acquiring, owning and disposing of the ADSs in their particular circumstances.

As indicated below, this discussion is subject to U.S. federal income tax rules applicable to a "passive foreign investment company," or a PFIC.

In general, and taking into account the earlier assumptions, for U.S. federal income and French tax purposes, a U.S. holder holding ADRs evidencing ADSs will be treated as the owner of the shares presented by the ADRs. Exchanges of shares for ADRs, and ADRs for shares, generally will not be subject to U.S. federal income or to French tax.

Distributions. Subject to the discussion under "-Passive Foreign Investment Company Considerations," below, the gross amount of any distribution (including any amounts withheld in respect of foreign tax) actually or constructively received by a U.S. holder with respect to ADSs will be taxable to the U.S. holder as a dividend to the extent of the U.S. holder's pro rata share of our current and accumulated earnings and profits as determined under U.S. federal income tax principles. Distributions in excess of earnings and profits will be non-taxable to the U.S. holder to the extent of, and will be applied against and reduce, the U.S. holder's adjusted tax basis in the ADSs. Distributions in excess of earnings and profits and such adjusted tax basis will generally be taxable to the U.S. holder as either long-term or short-term capital gain depending upon whether the U.S. holder has held the ADSs for more than one year as of the time such distribution is received. However, since we do not calculate our earnings and profits under U.S. federal income tax principles, it is expected that any distribution will be reported as a dividend, even if that distribution would otherwise be treated as a non-taxable return of capital or as capital gain under the rules described above. Non-corporate U.S. holders may qualify for the preferential rates of taxation with respect to dividends on ADSs applicable to long-term capital gains (i.e., gains from the sale of capital assets held for more than one year) applicable to qualified dividend income (as discussed below) if we are a "qualified foreign corporation" and certain other requirements (discussed below) are met. A non-U.S. corporation (other than a corporation that is classified as a PFIC for the taxable year in which the dividend is paid or the preceding taxable year) generally will be considered to be a qualified foreign corporation (a) if it is eligible for the benefits of a comprehensive tax treaty with the United States which the Secretary of Treasury of the United States determines is satisfactory for purposes of this provision and which includes an exchange of information provision, or (b) with respect to any dividend it pays on ADSs which are readily tradable on an established securities market in the United States. Our ADSs have been approved for listing on the Nasdaq Global Select Market, which is an established securities market in the United States, and we expect the ADSs to be readily tradable on the Nasdaq Global Select Market. There can be no assurance that the ADSs will be considered readily tradable on an established securities market in the United States in later years. The Company, which is incorporated under the laws of France, believes that it qualifies as a resident of France for purposes of, and is eligible for the benefits of, the Convention between the Government of the United States of America and the Government of the French Republic for the Avoidance of Double Taxation and the Prevention of Fiscal Evasion with Respect to Taxes on Income and Capital, signed on August 31, 1994, as amended and currently in force, or the U.S.-France Tax Treaty, although there can be no assurance in this regard. Further, the IRS has determined that the U.S.-France Tax Treaty is satisfactory for purposes of the qualified dividend rules and that it includes an exchange-of-information program. Therefore, subject to the discussion under "-Passive Foreign Investment Company Considerations," below, such dividends will generally be "qualified dividend income" in the hands of individual U.S. holders, provided that a holding period requirement (more than 60 days of ownership, without protection from the risk of loss, during the 121-day period beginning 60 days before the ex-dividend date) and certain other requirements are met. The dividends will not be eligible for the dividends-received deduction generally allowed to corporate U.S. holders.

A U.S. holder generally may claim the amount of any French withholding tax as either a deduction from gross income or a credit against its U.S. federal income tax liability. However, the foreign tax credit is subject to numerous complex limitations that must be determined and applied on an individual basis. Generally, the credit cannot exceed the proportionate share of a U.S. holder's U.S. federal income tax liability that such U.S. holder's taxable income bears to such U.S. holder's worldwide taxable income. In applying this limitation, a U.S. holder's various items of income and deduction must be classified, under complex rules, as either "foreign source" or "U.S. source." In addition, this limitation is calculated separately with respect to specific categories of income. The amount of a distribution with respect to the ADSs that is treated as a "dividend" may be lower for U.S. holder should consult its own tax advisors regarding the foreign tax credit rules.

In general, the amount of a distribution paid to a U.S. holder in a foreign currency will be the dollar value of the foreign currency calculated by reference to the spot exchange rate on the day the Depositary receives the distribution, regardless of whether the foreign currency is converted into U.S. dollars at that time. Any foreign currency gain or loss a U.S. holder realizes on a subsequent conversion of foreign currency into U.S. dollars will be U.S. source ordinary income or loss. If dividends received in a foreign currency are converted into U.S. dollars on the day they are received, a U.S. holder should not be required to recognize foreign currency gain or loss in respect of the dividend.

*Sale, Exchange or Other Taxable Disposition of the ADSs.* A U.S. holder will generally recognize gain or loss for U.S. federal income tax purposes upon the sale, exchange or other taxable disposition of ADSs in an amount equal to the difference between the U.S. dollar value of the amount realized from such sale or exchange and the U.S. holder's tax basis in those ADSs, determined in U.S. dollars. Subject to the discussion under "—*Passive Foreign Investment Company Considerations*" below, this gain or loss will generally be a capital gain or loss. The adjusted tax basis in the ADSs generally will be equal to the cost of such ADSs. Capital gain from the sale, exchange or other taxable disposition of ADSs of a non-corporate U.S. holder is generally eligible for a preferential rate of taxation applicable to capital gains, if the non-corporate U.S. holder's holding period determined at the time of such sale, exchange or other taxable disposition for such ADSs exceeds one year (i.e., such gain is long-term taxable gain). The deductibility of capital losses for U.S. federal income tax purposes is subject to limitations. Any such gain or loss that a U.S. holder recognizes generally will be treated as U.S. source gain or loss for foreign tax credit limitation purposes.

For a cash basis taxpayer, units of foreign currency paid or received are translated into U.S. dollars at the spot rate on the settlement date of the purchase or sale. In that case, no foreign currency exchange gain or loss will result from currency fluctuations between the trade date and the settlement date of such a purchase or sale. An accrual basis taxpayer, however, may elect the same treatment required of cash basis taxpayers with respect to purchases and sales of the ADSs that are traded on an established securities market, provided the election is applied consistently from year to year. Such election may not be changed without the consent of the IRS. For an accrual basis taxpayer who does not make such election, units of foreign currency paid or received are translated into U.S. dollars at the spot rate on the trade date of the purchase or sale. Such an accrual basis taxpayer may recognize exchange gain or loss based on currency fluctuations between the trade date and the settlement date. Any foreign currency gain or loss a U.S. Holder realizes will be U.S. source ordinary income or loss.

*Medicare Tax.* Certain U.S. holders that are individuals, estates or trusts are subject to a 3.8% tax on all or a portion of their "net investment income," which may include all or a portion of their dividend income and net gains from the disposition of ADSs. Each U.S. holder that is an individual, estate or trust is urged to consult its tax advisors regarding the applicability of the Medicare tax to its income and gains in respect of its investment in the ADSs.

**Passive Foreign Investment Company Considerations.** If we are classified as a PFIC in any taxable year, a U.S. holder will be subject to special rules generally intended to reduce or eliminate any benefits from the deferral of U.S. federal income tax that a U.S. holder could derive from investing in a non-U.S. company that does not distribute all of its earnings on a current basis.

We will be classified as a PFIC for U.S. federal income tax purposes in any taxable year in which, after applying certain look-through rules with respect to the income and assets of our subsidiaries, either: (i) at least 75% of the gross income is "passive income" or (ii) at least 50% of the average quarterly value of our total gross assets (which would generally be measured by fair market value of our assets, and for which purpose the total value of our assets may be determined in part by the market value of the ADSs and our ordinary shares, which are subject to change) is attributable to assets that produce "passive income" or are held for the production of "passive income."

Passive income for this purpose generally includes dividends, interest, royalties, rents, gains from commodities and securities transactions, the excess of gains over losses from the disposition of assets which produce passive income, and includes amounts derived by reason of the temporary investment of funds raised in offerings of the ADSs. If a non-U.S. corporation

owns directly or indirectly at least 25% by value of the stock of another corporation, the non-U.S. corporation is treated for purposes of the PFIC tests as owning its proportionate share of the assets of the other corporation and as receiving directly its proportionate share of the other corporation's income. If we are classified as a PFIC in any year with respect to which a U.S. holder owns the ADSs, we will continue to be treated as a PFIC with respect to such U.S. holder in all succeeding years during which the U.S. holder owns the ADSs, regardless of whether we continue to meet the tests described above.

The market value of our assets may be determined in large part by reference to the market price of the ADSs and our ordinary shares, which is likely to fluctuate after the global offering. In addition, the composition of our income and assets will be affected by how, and how quickly, we use the cash proceeds from the global offering in our business. Whether we are a PFIC for any taxable year will depend on our assets and income (including whether we receive certain non-refundable grants or subsidies and whether such amounts and reimbursements of certain refundable research tax credits will constitute gross income for purposes of the PFIC income test) in each year, and because this is a factual determination made annually after the end of each taxable year, there can be no assurance that we will not be considered a PFIC in any taxable year. Based on the composition of our gross income and assets in 2017, certain estimates of our gross income and assets for 2018, and the nature of our business, we do not believe that we were characterized as a PFIC in our 2017 taxable year and do not expect to be characterized as a PFIC for our taxable year ending December 31, 2018; however, there can be no assurance that we will not be considered a PFIC for any future taxable year. Our U.S. counsel expresses no opinion regarding our conclusions or our expectations regarding our PFIC status.

If we are a PFIC, and you are a U.S. holder that does not make one of the elections described below, a special tax regime will apply to both (a) any "excess distribution" by us to you (generally, your ratable portion of distributions in any year which are greater than 125% of the average annual distribution received by you in the shorter of the three preceding years or your holding period for the ADSs) and (b) any gain realized on the sale or other disposition of the ADSs. Under this regime, any excess distribution and realized gain will be treated as ordinary income and will be subject to tax as if (a) the excess distribution or gain had been realized ratably over your holding period, (b) the amount deemed realized in each year had been subject to tax in each year of that holding period at the highest marginal rate for such year (other than income allocated to the current period or any taxable period before we became a PFIC, which would be subject to tax at the U.S. holder's regular ordinary income rate for the current year and would not be subject to the interest charge discussed below), and (c) the interest charge generally applicable to underpayments of tax had been imposed on the taxes deemed to have been payable in those years. In addition, dividend distributions made to you will not qualify for the lower rates of taxation applicable to qualified dividends discussed above under "Distributions."

Certain elections may alleviate some of the adverse consequences of PFIC status and would result in an alternative treatment of the ADSs. If a U.S. holder makes a mark-to-market election, the U.S. holder generally will recognize as ordinary income any excess of the fair market value of the ADSs at the end of each taxable year over their adjusted tax basis, and will recognize an ordinary loss in respect of any excess of the adjusted tax basis of the ADSs over their fair market value at the end of the taxable year (but only to the extent of the net amount of income previously included as a result of the mark-to-market election). If a U.S. holder makes the election, the U.S. holder's tax basis in the ADSs will be adjusted to reflect these income or loss amounts. Any gain recognized on the sale or other disposition of ADSs in a year when we are a PFIC will be treated as ordinary income and any loss will be treated as an ordinary loss (but only to the extent of the net amount of income previously included as a result of the mark-to-market election is available only if we are a PFIC and the ADSs are "regularly traded" on a "qualified exchange." The ADSs will be treated as "regularly traded" in any calendar year in which more than a de minimis quantity of the ADSs are traded on a qualified exchange on at least 15 days during each calendar quarter (subject to the rule that trades that have as one of their principal purposes the meeting of the trading requirement as disregarded). The Nasdaq Global Select Market is a qualified exchange for this purpose and, consequently, if the ADSs are regularly traded, the mark-to-market election will be available to a U.S. holder.

We do not currently intend to provide the information necessary for U.S. holders to make qualified electing fund elections if we were treated as a PFIC for any taxable year. U.S. Holders should consult their tax advisors to determine whether any of these elections would be available and if so, what the consequences of the alternative treatments would be in their particular circumstances.

If we are determined to be a PFIC, the general tax treatment for U.S. Holders described in this section would apply to indirect distributions and gains deemed to be realized by U.S. Holders in respect of any of our subsidiaries that also may be determined to be PFICs.

If a U.S. holder owns ADSs during any taxable year in which we are a PFIC, the U.S. holder generally will be required to file an IRS Form 8621 (Information Return by a Shareholder of a Passive Foreign Investment Company or Qualified Electing Fund) with respect to the company, generally with the U.S. holder's federal income tax return for that year. If our company were a PFIC for a given taxable year, then you should consult your tax advisor concerning your annual filing requirements.

The U.S. federal income tax rules relating to PFICs are complex. Prospective U.S. investors are urged to consult their own tax advisers with respect to the acquisition, ownership and disposition of the ADSs, the consequences to them of an investment in a PFIC, any elections available with respect to the ADSs and the IRS information reporting obligations with respect to the acquisition, ownership and disposition of the ADSs.

**Backup Withholding and Information Reporting.** U.S. holders generally will be subject to information reporting requirements with respect to dividends on ADSs and on the proceeds from the sale, exchange or disposition of ADSs that are paid within the United States or through U.S.-related financial intermediaries, unless the U.S. holder is an "exempt recipient." In addition, U.S. holders may be subject to backup withholding on such payments, unless the U.S. holder provides a taxpayer identification number and a duly executed IRS Form W-9 or otherwise establishes an exemption. Backup withholding is not an additional tax, and the amount of any backup withholding will be allowed as a credit against a U.S. holder's U.S. federal income tax liability and may entitle such holder to a refund, provided that the required information is timely furnished to the IRS.

*Certain Reporting Requirements With Respect to Payments of Offer Price.* U.S. holders paying more than U.S. \$100,000 for the ADSs generally may be required to file IRS Form 926 reporting the payment of the Offer Price for the ADSs to us. Substantial penalties may be imposed upon a U.S. holder that fails to comply. Each U.S. holder should consult its own tax advisor as to the possible obligation to file IRS Form 926.

*Foreign Asset Reporting.* Certain individual U.S. holders are required to report information relating to an interest in the ADSs, subject to certain exceptions (including an exception for shares held in accounts maintained by U.S. financial institutions) by filing IRS Form 8938 (Statement of Specified Foreign Financial Assets) with their federal income tax return. U.S. holders are urged to consult their tax advisors regarding their information reporting obligations, if any, with respect to their ownership and disposition of the ADSs.

THE DISCUSSION ABOVE IS A SUMMARY OF THE MATERIAL FRENCH AND U.S. FEDERAL INCOME TAX CONSEQUENCES OF AN INVESTMENT IN OUR ADSS OR ORDINARY SHARES AND IS BASED UPON LAWS AND RELEVANT INTERPRETATIONS THEREOF IN EFFECT AS OF THE DATE OF THIS ANNUAL REPORT ON FORM 20-F, ALL OF WHICH ARE SUBJECT TO CHANGE, POSSIBLY WITH RETROACTIVE EFFECT. EACH PROSPECTIVE INVESTOR IS URGED TO CONSULT ITS OWN TAX ADVISOR ABOUT THE TAX CONSEQUENCES TO IT OF AN INVESTMENT IN ADSS OR ORDINARY SHARES IN LIGHT OF THE INVESTOR'S OWN CIRCUMSTANCES.

# F. Dividends and Paying Agents.

Not applicable.

### G. Statement by Experts.

Not applicable.

## H. Documents on Display.

We are subject to the information reporting requirements of the Exchange Act applicable to foreign private issuers and under those requirements will file reports with the SEC. Those reports may be inspected without charge at the locations described below. As a foreign private issuer, we are exempt from the rules under the Exchange Act related to the furnishing and content of proxy statements, and our officers, directors and principal shareholders are exempt from the reporting and short-swing profit recovery provisions contained in Section 16 of the Exchange Act. In addition, we are not required under the Exchange Act to file periodic reports and financial statements with the SEC as frequently or as promptly as United States companies whose securities are registered under the Exchange Act. Nevertheless, we will file with the SEC an Annual Report on Form 20-F containing financial statements that have been examined and reported on, with and opinion expressed by an independent registered public accounting firm.

We maintain a corporate website at *www.erytech.com*. We intend to post our Annual Report on Form 20-F on our website promptly following it being filed with the SEC. Information contained on, or that can be accessed through, our website does not constitute a part of this Annual Report on Form 20-F. We have included our website address in this Annual Report on Form 20-F solely as an inactive textual reference.

You may also review a copy of this Annual Report on Form 20-F, including exhibits and any schedule filed herewith, and obtain copies of such materials at prescribed rates, at the SEC's Public Reference Room in Room 1580, 100 F Street, NE, Washington, D.C. 20549-0102. You may obtain information on the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330. The Securities and Exchange Commission maintains a website (*www.sec.gov*) that contains reports, proxy and information statements and other information regarding registrants, such as ERYTECH Pharma S.A., that file electronically with the SEC.

With respect to references made in this Annual Report on Form 20-F to any contract or other document of our company, such references are not necessarily complete and you should refer to the exhibits attached or incorporated by reference to this Annual Report on Form 20-F for copies of the actual contract or document.

## I. Subsidiary Information.

Not required.

### Item 11. Quantitative and Qualitative Disclosures About Market Risk.

### Liquidity Risk

We do not believe that we are exposed to short-term liquidity risk, considering the cash and cash equivalents that we had available as of December 31, 2017, amounting to  $\in$ 185.5 million, which was primarily cash and term deposits that are convertible into cash in approximately 30 days without penalty. Management believes that the amount of cash and cash equivalents available at December 31, 2017 is sufficient to fund our planned operations through at least the next 24 months.

Historically, we have financed our growth by strengthening our shareholders' equity in the form of capital increases and the issuance of convertible bonds. We believe that the capital increase associated with our initial public offering on Euronext Paris in May 2013, as well as the capital increases we completed in 2014, 2015, 2016 and 2017, including the November 2017 global offering, will enable us to continue as a going concern.

### Foreign Currency Exchange Risk

We use the euro as our functional currency for our financial communications. Our operating results and our bank account held in U.S dollars are exposed to changes in foreign currency exchange rates between the euro and various foreign currencies, including the U.S. dollar. However, a portion of our operating expenses is denominated in U.S. dollars as a result of our clinical trials performed in the United States at our office based in Cambridge, Massachusetts and our production facility in Philadelphia, Pennsylvania in conjunction with the American Red Cross. For the years ended December 31, 2015, 2016 and 2017, these expenses in U.S. dollars totaled \$3,149 thousand, \$6,242 thousand and \$11,620 thousand, respectively, based on the exchange rate in effect at December 31, 2015, 2016 and 2017, respectively, or 16%, 23% and 30%, respectively, of our operating expenses for the periods presented. As a result, we are exposed to foreign currency exchange risk inherent in operating expenses incurred. Part of this exposure to foreign currency exchange risk relates to our cash and cash equivalents being denominated in U.S. dollars and converted into euros for financial communications and reporting purposes in our consolidated accounts.

We do not currently engage in hedging transactions or the use of forward contracts but may in the future in order to minimize the impact of uncertainty in future exchange rates on cash flows.

Our results of operations and cash flows are subject to fluctuations as a result of changes in foreign currency exchange rates, and we believe our exposure to foreign currency exchange risk is likely to have a material adverse impact on our results of operations or financial position. In addition, we do not currently have revenues in euros, dollars or any other currency. As we advance our clinical development in the United States and potentially commercialize our product candidates in that market, we expect to face greater exposure to exchange rate risk and would then consider using exchange rate derivative or hedging techniques at that time. Based on our overall foreign currency exchange rate exposures at December 31, 2017, we believe that a near-term 10% fluctuation of the U.S. dollar exchange rate could result in a potential change in the fair value of our foreign currency sensitive assets, excluding our investments by approximately \$11.3 million. We expect to continue to enter into transactions based in foreign currencies that could be impacted by changes in exchange rates.

# Interest Rate Risk

We believe we have very low exposure to interest rate risk. Such exposure primarily involves our money market funds and time deposit accounts. Changes in interest rates have a direct impact on the rate of return on these investments and the cash flows generated.

Other than the unsecured bank loan that we entered into in 2016 with Société Générale (of which the outstanding amount drawn at December 31, 2017 was €1.4 million), we have no other credit facilities. The repayment flows of the conditional advances from BPI France are not subject to interest rate risk.

# Credit Risk

We believe that the credit risk related to our cash and cash equivalents is not significant in light of the quality of the financial institutions at which such funds are held.

### Inflation Risk

We do not believe that inflation has had a material effect on our business, financial condition or results of operations. If our costs were to become subject to significant inflationary pressures, we may not be able to fully offset such higher costs through price increases. Our inability or failure to do so could harm our business, financial condition and results of operations.

### Item 12. Description of Securities Other than Equity Securities.

## A. Debt Securities.

Not applicable.

## **B.** Warrants and Rights.

Not applicable.

## C. Other Securities.

Not applicable.

# **D.** American Depositary Shares.

The Bank of New York Mellon acts as the depositary for the American Depositary Shares. The Bank of New York Mellon's depositary offices are located at 101 Barclay Street, New York, N.Y. 10286. American Depositary Shares are frequently referred to as ADSs and represent ownership interests in securities that are on deposit with the depositary. Each ADS represents one ordinary share, nominal value  $\in 0.10$  per share (or a right to receives one ordinary share). ADSs may be represented by certificates that are commonly known as American Depositary Receipts, or ADRs. The depositary typically appoints a custodian to safekeep the securities on deposit. In this case, the custodian is Société Générale.

We have appointed The Bank of New York Mellon as depositary pursuant to an amended and restated deposit agreement, which sets out the ADS holder rights as well as the rights and obligations of the depositary. A copy of the amended and restated deposit agreement is on file with the SEC under cover of a Registration Statement on Form F-6. You may obtain a copy of the amended and restated deposit agreement from the SEC's Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549 and from the SEC's website (www.sec.gov). Please refer to Registration Number 333-201279 when retrieving such copy.

You may hold ADSs either (1) directly (a) by having an ADR, which is a certificate evidencing a specific number of ADSs, registered in your name, or (b) by having uncertificated ADSs registered in your name in the Direct Registration System, or DRS, or (2) indirectly by holding a security entitlement in ADSs through your broker or other financial institution that is a direct or indirect participant in the Depository Trust Company, or DTC. If you hold ADSs directly, you are a registered ADS holder, also referred to as an ADS holder. This description assumes you are an ADS holder. If you hold the ADSs indirectly, you must rely on the procedures of your broker or other financial institution to assert the rights of ADS holders described in this section. You should consult with your broker or financial institution to find out what those procedures are.

DRS is a system administered by DTC pursuant to which the depositary may register the ownership of uncertificated ADSs, which ownership is confirmed by periodic statements sent by the depositary to the registered holders of uncertificated ADSs.

As an ADS holder, you will not be treated as one of our shareholders and you will not have shareholder rights. French law governs shareholder rights. The depositary will be the holder of the ordinary shares underlying your ADSs. As a holder of ADSs, you will have ADS holder rights. An amended and restated deposit agreement among us, the depositary and you, as an ADS holder, and all other persons directly and indirectly holding ADSs sets out ADS holder rights as well as the rights and obligations of the depositary. New York law governs the amended and restated deposit agreement and the ADRs. In the event of any discrepancy between the ADRs and the amended and restated deposit agreement, the amended and restated deposit agreement governs.

#### Fees and Expenses

Pursuant to the terms of the amended and restated deposit agreement, the holders of our ADSs will be required to pay the following fees:

Persons depositing or withdrawing ordinary shares or ADSs must pay:

\$5.00 (or less) per 100 ADSs (or portion of 100 ADSs)

\$0.05 (or less) per ADS

A fee equivalent to the fee that would be payable if securities distributed to you had been ordinary shares and the shares had been deposited for issue of ADSs

\$0.05 (or less) per ADS per calendar year

Registration or transfer fees

Expenses of the depositary

Taxes and other governmental charges the depositary or the custodian have to pay on any ADS or share underlying an ADS, for example, share transfer taxes, stamp duty or withholding taxes

Any charges payable by the depositary, custodian or their agents in connection with the servicing of deposited securities

For:

- Issue of ADSs, including issues resulting from a distribution of ordinary shares or rights
- Cancellation of ADSs for the purpose of withdrawal, including if the amended and restated deposit agreement terminates
- Any cash distribution to you
- Distribution of securities distributed to holders of deposited securities which are distributed by the depositary to you
- · Depositary services
- Transfer and registration of ordinary shares on our share register to or from the name of the depositary or its agent when you deposit or withdraw shares
- Cable (including SWIFT) and facsimile transmissions as expressly provided in the amended and restated deposit agreement
- · Converting foreign currency to U.S. dollars
- As necessary
- As necessary

The depositary collects its fees for delivery and surrender of ADSs directly from investors depositing ordinary shares or surrendering ADSs for the purpose of withdrawal or from intermediaries acting for them. The depositary collects fees for making distributions to investors by deducting those fees from the amounts distributed or by selling a portion of distributable property to pay the fees. The depositary may collect its annual fee for depositary services by deduction from cash distributions or by directly billing investors or by charging the book-entry system accounts of participants acting for them. The depositary may collect any of its fees by deduction from any cash distribution payable to ADS holders that are obligated to pay those fees. The depositary may generally refuse to provide for-fee services until its fees for those services are paid.

From time to time, the depositary may make payments to us to reimburse or share revenue from the fees collected from ADS holders, or waive fees and expenses for services provided, generally relating to costs and expenses arising out of establishment and maintenance of the ADS program. In performing its duties under the amended and restated deposit agreement, the depositary may use brokers, dealers, foreign currency or other service providers that are affiliates of the depositary and that may earn or share fees, spreads or commissions.

The depositary may convert foreign currency itself or through any of its affiliates and, in those cases, acts as principal for its own account and not as agent, advisor, broker or fiduciary on behalf of any other person and earns revenue, including, without limitation, transaction spreads, that it will retain for its own account. The revenue is based on, among other things, the difference between the exchange rate assigned to the currency conversion made under the amended and restated deposit agreement and the rate that the depositary or its affiliate receives when buying or selling foreign currency for its own account. The depositary makes no representation that the exchange rate used or obtained in any currency conversion under the amended and restated deposit agreement will be the most favorable rate that could be obtained at the time or that the method by which that rate will be determined will be the most favorable to holders of our ADSs, subject to the depositary's obligations under the amended and restated deposit agreement. The methodology used to determine exchange rates used in currency conversions is available upon request.

We may agree with the depositary to amend the amended and restated deposit agreement and the ADRs without your consent for any reason. If an amendment adds or increases fees or charges, except for taxes and other governmental charges, registration fees, facsimile costs, delivery costs or other such expenses, or that would otherwise prejudice a substantial right of ADS holders, it will not become effective for outstanding ADSs until 30 days after the depositary notifies ADS holders of the amendment. *At the time an amendment becomes effective, ADS holders are considered, by continuing to hold their ADSs, to agree to the amendment and to be bound by the ADRs and the amended and restated deposit agreement as further amended.* 

From time to time, the depositary may make payments to us to reimburse us for costs and expenses generally arising out of establishment and maintenance of the American Depositary Shares program, waive fees and expenses for services provided by the depositary or share revenue from the fees collected from owners or holders of our ADSs.

### **Payment of Taxes**

ADS holders are responsible for any taxes or other governmental charges payable on your ADSs or on the deposited securities represented by any of their ADSs. The depositary may refuse to register any transfer of an ADS holder's ADSs or allow an ADS holder to withdraw the deposited securities represented by an ADS holder's ADSs until such taxes or other charges are paid. It may apply payments owed to an ADS holder or sell deposited securities represented by an ADS holder's ADSs to pay any taxes owed and the ADS holder will remain liable for any deficiency. If the depositary sells deposited securities, it will, if appropriate, reduce the number of ADSs registered in such ADS holder's name to reflect the sale and pay such ADS holder any net proceeds, or send such ADS holder any property, remaining after it has paid the taxes. Such ADS holder's obligation to pay taxes and indemnify us and the depositary against any tax claims will survive the transfer or surrender of such ADS holder's ADSs, the withdrawal of the deposited ordinary shares as well as the termination of the amended and restated deposit agreement.

#### PART II

### Item 13. Defaults, Dividend Arrearages and Delinquencies.

Not applicable.

# Item 14. Material Modifications to the Rights of Security Holders and Use of Proceeds.

# **Global Offering**

In November 2017, we completed a global offering of an aggregate of 6,180,137 ordinary shares, including the full exercise of the underwriters' option to purchase 806,104 additional ordinary shares. The global offering consisted of a U.S. initial public offering of 5,389,021 ordinary shares in the form of American Depositary Shares, each representing one ordinary share, at an offering price of \$23.26 per ADS and a concurrent private placement in Europe and other countries outside of the United States and Canada of 791,116 ordinary shares at an offering price of  $\leq 20.00$  per ordinary share for aggregate gross proceeds to us of approximately \$143.7 million. The net offering proceeds to us, after deducting underwriting discounts and commissions and offering expenses, were approximately  $\leq 112.1$  million (\$130.4 million). The offering commenced on November 6, 2017 and did not terminate before all of the securities registered in the registration statement were sold. The effective date of the registration statement, File No. 333-220867, for our global offering was November 9, 2017.

Jefferies LLC acted as global coordinator and joint book-runner for the global offering. Cowen and Company, LLC acted as joint book-runner and JMP Securities LLC acted as lead manager for the offering of ADSs in the United States. Oddo BHF SCA acted as joint book-runner for the private placement of ordinary shares in Europe.

The net proceeds from our global offering have been used, and are expected to continue to be used, as described in the final prospectus for the global offering filed with the U.S. Securities and Exchange Commission on November 13, 2017.

None of the net proceeds of our global offering were paid directly or indirectly to any director, officer, general partner of ours or to their associates, persons owning ten percent or more of any class of our equity securities, or to any of our affiliates.

#### Item 15. Controls and Procedures.

#### **Disclosure Controls and Procedures**

Our management, with the participation of our chief executive officer (*principal executive officer*) and our chief financial officer and chief operating officer (*principal financial officer*), has evaluated the effectiveness of our disclosure controls and procedures, as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, as of the end of the period covered by this Annual Report on Form 20-F. Based on such evaluation, our principal executive officer and principal financial officer have concluded that our disclosure controls and procedures were not effective at the reasonable assurance level as of December 31, 2017 as a result of the material weakness described below. Notwithstanding this material weakness, our management has concluded that the financial statements included elsewhere in this Annual Report present fairly, in all material respects, our financial position, results of operations and cash flows in conformity with IFRS.

In connection with the preparation of our financial results for the years ended December 31, 2016 and 2017, our management concluded that, as of December 31, 2017, our internal control over financial reporting was not effective as a result of a material weakness in our internal control over financial reporting discussed below. The material weakness remained unremediated as of December 31, 2017. A material weakness is a deficiency, or a combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of our financial statements will not be prevented or detected on a timely basis.

The material weakness identified in our internal control over financial reporting related to our having not designed and maintained controls over the operating effectiveness of information technology, or IT, general controls for information systems that are relevant to the preparation of our financial statements. Specifically, we did not design and maintain effective controls over program change management; user access, including segregation of duties; or computer operations.

We plan to initiate the following remediation efforts focused on improving our internal control over financial reporting and to specifically address the control deficiencies that led to our material weakness. These efforts include the following:

- hiring of finance and accounting personnel with experience in accounting operations, financial controls and SEC reporting;
- completing the implementation of a new enterprise resource planning, or ERP system;
- initiating design and implementation of our financial control environment, including policies and procedures, controls, reporting and analysis, and segregation of duties; and
- implementation of formal disclosure controls and procedures.

We believe that these activities will further support the remediation of this material weakness.

### Management's Annual Report on Internal Control over Financial Reporting

This Annual Report on Form 20-F does not include a report of management's assessment regarding internal control over financial reporting due to a transition period established by rules of the Securities and Exchange Commission for newly public companies.

### Attestation Report of the Registered Public Accounting Firm

This Annual Report on Form 20-F does not include an attestation report of our registered public accounting firm due to a transition period established by rules of the Securities and Exchange Commission for newly public companies.

### Changes in Internal Control over Financial Reporting

Except as described above, there has been no change in our internal control over financial reporting during the year ended December 31, 2017 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

#### Item 16. Reserved.

Not applicable.

# Item 16A. Audit Committees Financial Expert.

Our board of directors has determined that Ms. Windels is an audit committee financial expert as defined by SEC rules and regulations and each of the members of our board of directors has the requisite financial sophistication under the applicable rules and regulations of the Nasdaq Stock Market. Ms. Windels is independent as such term is defined in Rule 10A-3 under the Exchange Act and under the listing standards of the Nasdaq Stock Market.

### Item 16B. Code of Business Conduct and Ethics.

We have adopted a Code of Business Conduct and Ethics, or the Code of Conduct, that is applicable to all of our employees, executive officers and directors. A copy of the Code of Conduct is available on our website at *www.erytech.com*. The audit committee of our board of directors is responsible for overseeing the Code of Conduct and must approve any waivers of the Code of Conduct for employees, executive officers and directors. We expect that any amendments to the Code of Conduct, or any waivers of its requirements, will be disclosed on our website.

### Item 16C. Principal Accountant Fees and Services.

KPMG S.A., or KPMG, has served as our independent registered public accounting firm for 2016 and 2017. Our accountants billed the following fees to us for professional services in each of those fiscal years, all of which were approved by our audit committee:

		Year Ended December 31,		
		2016	2017	
		(Amount in thou	isands of Euros)	
Audit Fees	€	165	211	
Audit-Related Fees		3	30	
All Other Fees		232	254	
Total	€	400	495	

"<u>Audit Fees</u>" are the aggregate fees billed for the audit of our annual financial statements. This category also includes services that KPMG provides, such as consents and assistance with and review of documents filed with the SEC.

"<u>Audit-Related Fees</u>" are the aggregate fees billed for assurance and related services that are reasonably related to the performance of the audit and are not reported under Audit Fees.

"All <u>Other Fees</u>" are additional amounts billed for products and services provided by KPMG in particular fees billed for assurance and related services regarding our November 2017 global offering.

There were no "Tax Fees" or billed or paid during 2016 or 2017.

### Audit and Non-Audit Services Pre-Approval Policy

The audit committee has responsibility for appointing, setting compensation of and overseeing the work of the independent registered public accounting firm. In recognition of this responsibility, the audit committee has adopted a policy governing the pre-approval of all audit and permitted non-audit services performed by our independent registered public accounting firm to ensure that the provision of such services does not impair the independent registered public accounting firm has received general pre-approval from the audit committee, it requires specific pre-approval by the audit committee. The payment for any proposed services in excess of pre-approved cost levels requires specific pre-approval by the audit committee.

Pursuant to its pre-approval policy, the audit committee may delegate its authority to pre-approve services to the chairperson of the audit committee. The decisions of the chairperson to grant pre-approvals must be presented to the full audit committee at its next scheduled meeting. The audit committee may not delegate its responsibilities to pre-approve services to the management.

The audit committee has considered the non-audit services provided by KPMG as described above and believes that they are compatible with maintaining KPMG's independence as our independent registered public accounting firm.

## Item 16D. Exemptions from the Listing Standards for Audit Committees.

Not applicable.

# Item 16E. Purchases of Equity Securities by the Issuer and Affiliated Purchasers.

Not applicable.

# Item 16F. Change in Registrant's Certifying Accountant.

Not applicable.

### Item 16G. Corporate Governance.

As a French *société anonyme*, we are subject to various corporate governance requirements under French law. In addition, as a foreign private issuer listed on the Nasdaq Global Select Market, we will be subject to Nasdaq corporate governance listing standards. However, the corporate governance standards provide that foreign private issuers are permitted to follow home

country corporate governance practices in lieu of Nasdaq rules, with certain exceptions. We intend to rely on these exemptions for foreign private issuers and follow French corporate governance practices in lieu of the Nasdaq corporate governance rules, which would otherwise require that (1) a majority of our board of directors consist of independent directors; (2) we establish a nominating and corporate governance committee; and (3) our remuneration committee be composed entirely of independent directors.

The following are the significant ways in which our corporate governance practices differ from those required for U.S. companies listed on Nasdaq:

As a foreign private issuer, we are required to comply with Rule 10A-3 of the Exchange Act, relating to audit committee composition and responsibilities. Rule 10A-3 provides that the audit committee must have direct responsibility for the nomination, compensation and choice of our auditors, as well as control over the performance of their duties, management of complaints made, and selection of consultants. However, if the laws of a foreign private issuer's home country require that any such matter be approved by the board of directors or the shareholders, the audit committee's responsibilities or powers with respect to such matter may instead be advisory. Under French law, the audit committee may only have an advisory role and appointment of our statutory auditors, in particular, must be decided by the shareholders at our annual meeting.

In addition, Nasdaq rules require that a listed company specify that the quorum for any meeting of the holders of common stock be at least 33 1/3% of the outstanding shares of the company's voting stock. Consistent with French law, our bylaws provide that a quorum requires the presence of shareholders having at least (1) 20% of the shares entitled to vote in the case of an ordinary shareholders' general meeting or at an extraordinary shareholders' general meeting where shareholders are voting on a capital increase by capitalization of reserves, profits or share premium, or (2) 25% of the shares entitled to vote in the case of any other extraordinary shareholders' general meeting is adjourned. There is no quorum requirement when an ordinary general meeting is reconvened, but the reconvened meeting may consider only questions which were on the agenda of the adjourned meeting. When an extraordinary general meeting is reconvened, the quorum required is 20% of the shares entitled to vote, except where the reconvened meeting is considering capital increases through capitalization of reserves, profits or share premium. For these matters, no quorum is required at the reconvened meeting. If a quorum is not present at a reconvened meeting requiring a quorum, then the meeting may be adjourned for a maximum of two months.

# Item 16H. Mine Safety Disclosure.

Not applicable.

# PART III

# Item 17. Financial Statements.

See pages F-1 through F-7 of this Annual Report on Form 20-F.

# Item 18. Financial Statements.

Not applicable.

# Item 19. Exhibits.

The Exhibits listed below are filed as Exhibits to this Annual Report on Form 20-F.

# EXHIBIT INDEX

			Incorporated	oy Referer	ice
Exhibit	Description	Schedule/ Form	File Number	Exhibit	File Date
1.1*	Bylaws (statuts) of the registrant (English translation)				
2.1*	Amended and Restated Deposit Agreement				
2.2*	Form of American Depositary Receipt (included in Exhibit 2.1)				
4.1	<u>Lease Agreement by and between the registrant and PFO2 SCPI (represented by PERIAL Asset</u> <u>Management SASU), dated June 9, 2015 (English translation)</u>	F-1	333-220867	10.1	October 6, 2017
4.2	Addendum #1 to the Lease Agreement by and between the registrant and PF02 SCPI (represented by PERIAL Asset Management SASU), dated December 30, 2016 (English translation)	F-1	333-220867	10.2	October 6, 2017
4.3*	<u>Lease Agreement by and between the registrant and EUROGAL, dated December 6, 2017 (English</u> <u>Translation)</u>				
4.4#	Exclusive License and Distribution Agreement by and between the registrant and Orphan Europe, dated as of November 22, 2012, First Amendment to the Exclusive License and Distribution Agreement, dated as of February 22, 2013 and Second Amendment to the Exclusive License and Distribution Agreement, dated as of August 4, 2014	F-1	333-220867	10.3	October 6, 2017
4.5#	<u>Addendum #3 to the Exclusive License and Distribution Agreement by and between the registrant</u> and Orphan Europe, dated July 21, 2016	F-1	333-220867	10.4	October 6, 2017
4.6#	Exclusive Distribution Agreement by and between the registrant and Abic Marketing Limited, dated as of March 28, 2011	F-1	333-220867	10.5	October 6, 2017
4.7#	Exclusive Supply Agreement for L-asparaginase by and between the registrant and medac GmbH, dated as of December 12, 2008 and Addendum #1 to the Exclusive Supply Agreement for L-Asparaginase, dated August 19, 2009	F-1	333-220867	10.6	October 6, 2017

4.8#	Exclusive Supply Agreement for recombinant L-asparaginase by and between the registrant and medac GmbH, dated as of May 3, 2011 and Addendum #1 to the Exclusive Supply Agreement for recombinant L-asparaginase, dated April 4, 2014	F-1	333-220867	10.7	October 6, 2017
4.9	Addendum #2 to the Exclusive Supply Agreement for L-asparaginase by and between the registrant and medac GmbH, dated July 25, 2016	F-1	333-220867	10.8	October 6, 2017
4.10#	Addendum #2 to the Exclusive Supply Agreement for recombinant L-asparaginase by and between the registrant and medac GmbH, dated July 25, 2016	F-1	333-220867	10.9	October 6, 2017
4.11#	Patent License Agreement by and between the registrant and the Public Health Service, dated as of June 19, 2012	F-1	333-220867	10.10	October 6, 2017
4.12†	Form of indemnification agreement between the registrant and each of its executive officers and directors	F-1	333-220867	10.11	October 6, 2017
4.13†	Summary of BSA Plans	F-1	333-220867	10.12	October 6, 2017
4.14†	Summary of BSPCE Plans	F-1	333-220867	10.13	October 6, 2017
4.15†	2016 Share Option Plan (English translation)	F-1	333-220867	10.14	October 6, 2017
4.16†	2016 Free Share Plan (English translation)	F-1	333-220867	10.15	October 6, 2017
4.17†	2017 Share Option Plan (English translation)	S-8	333-222673	99.5	January 24, 2018
4.18†	2017 Free Share Plan (English translation)	S-8	333-222673	99.6	January 24, 2018
8.1	List of subsidiaries of the registrant	F-1	333-220867	21.1	October 6, 2017
12.1*	<u>Certification by the Principal Executive Officer pursuant to Securities Exchange Act Rules</u> <u>13a-14(a) and 15d-14(a) as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002</u>				
12.2*	<u>Certification by the Principal Financial Officer pursuant to Securities Exchange Act Rules</u> <u>13a-14(a) and 15d-14(a) as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002</u>				

13.1\*\*Certification by the Principal Executive Officer and Principal Financial Officer pursuant to 18<br/>U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002

15.1*	Consent of KPMG S.A.
101.SCH***	XBRL Taxonomy Extension Schema Document
101.CAL***	XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF***	XBRL Taxonomy Extension Definition Linkbase Document
101.LAB***	XBRL Taxonomy Extension Label Linkbase Document
101.PRE***	XBRL Taxonomy Extension Presentation Linkbase Document

\* Filed herewith.

\*\* Furnished herewith.

\*\*\*

To be filed by amendment. Indicates a management contract or any compensatory plan, contract or arrangement. Confidential treatment has been granted from the Securities and Exchange Commission as to certain portions of this document. † #

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# INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

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## **Report of Independent Registered Public Accounting Firm**

To the Stockholders and Board of Directors ERYTECH Pharma S.A.

# Opinion on the Consolidated Financial Statements

We have audited the accompanying consolidated statements of financial position of Erytech Pharma S.A. and subsidiaries (the Company) as of December 31, 2017, 2016 and 2015, the related consolidated statements of income (loss), comprehensive income (loss), changes in shareholders' equity, and cash flows for each of the years in the three year period ended December 31, 2017, and the related notes (collectively, the consolidated financial statements). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2017, 2016 and 2015, and the results of its operations and its cash flows for each of the years in the three year period ended December 31, 2017, in conformity with International Financial Reporting Standards ("IFRS") as issued by the International Accounting Standards Board.

### Basis for Opinion

These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these consolidated financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud. Our audits included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. We believe that our audits provide a reasonable basis for our opinion.

We have served as the Company's auditor since 2004.

Lyon, April 23, 2018

KPMG Audit A division of KPMG S.A.

/s/ Sara Righenzi de Villers

Sara Righenzi de Villers Partner

KPMG S.A., a French limited liability entity and a member firm of the KPMG Network of Independent member firms artilisted with KPMG International Cooperative, a Swiss entity. Société anonyme d'expertise comptable et de commissariat aux comptes à directoire et conseil de surveillance. Insorte au Tableau de l'Ordre à Paris sous en 1 43-0000101 et à la Compagnie Réglonale des Commissaries aux Comptes de Versalies. Hesdouarters: KPMG 8.A. Tour Egno 2 avenue Gambetts 32066 Paris Is Défense Dedex Capital : 5 457 100 € Code APE 62022 775 726 417 R.C.8. Nanterre TVA Union Européerne FR 77 775 726 417

# CONSOLIDATED STATEMENTS OF INCOME (LOSS)

(Amounts in thousands of euros, except loss per share)		Very ended	December 31,	
	Notes	2015 €	2016 €	<u>2017</u> €
Operating income		£	£	£
Revenues				
Other income	5.1	2,929	4,138	3,364
Total operating income	5.1	2,929	4,138	3,364
Operating expenses				
Research and development expenses	5.2, 5.3	(10,776)	(19,720)	(25,463)
General and administrative expenses	5.2, 5.3	(7,736)	(6,808)	(8,791)
Total operating expenses		(18,512)	(26,528)	(34,254)
Operating loss		(15,583)	(22,390)	(30,889)
Financial income	5.5	631	558	539
Financial expenses	5.5	(64)	(70)	(3,183)
Financial income		567	488	(2,644)
Income tax	5.6	3	(10)	3
Net loss		(15,013)	(21,913)	(33,530)
Basic / Diluted loss per share (€/share)	6.7	(2.16)	(2.74)	(2.95)

# CONSOLIDATED STATEMENTS OF COMPREHENSIVE INCOME (LOSS)

(Amounts in thousands of euros)	Year e	nded Decembe	r 31,
	2015 £	2016 £	2017 £
Net loss	(15,013)	(21,913)	(33,530)
Elements that may be reclassified subsequently to income (loss)			
Foreign subsidiary – Currency translation adjustment	(9)	21	(38)
Elements that may not be reclassified subsequently to income (loss)			
Actuarial gains or losses on defined benefits liability	8	(30)	8
Tax effect	(3)	10	(3)
Other comprehensive income (loss)	(3)	1	(33)
Total comprehensive loss	(15,017)	(21,912)	(33,563)

# CONSOLIDATED STATEMENTS OF FINANCIAL POSITION

(Amounts in thousands of euros)	<u>Notes</u>	December 31, 2015 €	As of December 31, 2016 €	December 31, 2017 €
ASSETS				
Non-current assets				
Intangible assets	6.1	61	57	53
Property, plant and equipment, net	6.2	918	2,245	3,406
Other non-current financial assets	6.3	97	132	234
Total non-current assets		1,076	2,434	3,693
Current assets				
Inventories	6.4	166	145	176
Trade and other receivables	6.5	424	218	76
Other current assets	6.6	5,705	4,524	5,791
Cash and cash equivalents	6.7	45,634	37,646	185,525
Total current assets		51,929	42,533	191,568
TOTAL ASSETS		53,004	44,967	195,261
		As of	As	of December

		As of	As	of
	<u>Notes</u>	December 31, 2015 €	December 31, 2016 €	December 31, 2017 €
LIABILITIES AND SHAREHOLDERS' EQUITY				
Shareholders' equity				
Share capital		792	873	1,794
Premiums related to share capital		95,931	105,090	281,745
Reserves		(34,578)	(48,247)	(68,386)
Translation reserve			(165)	(203)
Net loss for the period		(15,013)	(21,913)	(33,530)
Total shareholders' equity	6.8	47,132	35,638	181,419
Non-current liabilities				
Long-term provisions	6.9	100	163	214
Financial liabilities – non-current portion	6.10	151	2,816	2,019
Deferred tax		—	3	3
Total Non-current liabilities		251	2,982	2,236
Current liabilities				
Provisions – current portion	6.9	81		
Financial liabilities – current portion	6.10	557	50	824
Trade and other payables	6.11	3,672	4,832	8,076
Other current liabilities	6.12	1,311	1,465	2,706
Total current liabilities		5,621	6,347	11,606
TOTAL LIABILITIES AND SHAREHOLDERS' EQUITY		53,004	44,967	195,261

# CONSOLIDATED STATEMENTS OF CASH FLOW

Mount in thousands of euros)Year ended December 31, 2015Notes $2015$ $2016$ $2017$ $\epsilon$ <
$\epsilon$ $\epsilon$ $\epsilon$ $\epsilon$ ash flows from operating activities(15,013)(21,913)(33,530)ectonciliation of net loss and the cash used for operating activities(15,013)(21,913)(33,530)oss on exchange—3,159mortization and depreciation288425532rovision – non-current portion203157xpense related to share-based payments5.32,7161,1781,769interest expense301323acome tax expense5.6(3)10(3)hange in trade and payables in foreign currency——(38)
iet loss       (15,013)       (21,913)       (33,530)         econciliation of net loss and the cash used for operating activities       -       3,159         oss on exchange       -       288       425       532         mortization and depreciation       20       31       57         rovision – non-current portion       5.3       2,716       1,178       1,769         interest expense       30       13       23         income tax expense       5.6       (3)       10       (3)         hange in trade and payables in foreign currency
econciliation of net loss and the cash used for operating activities       —       3,159         oss on exchange       —       288       425       532         mortization and depreciation       20       31       57         rovision – non-current portion       20       31       1,769         xpense related to share-based payments       30       13       23         interest expense       30       13       23         income tax expense       5.6       (3)       10       (3)         hange in trade and payables in foreign currency       —       —       (38)
oss on exchange       —       3,159         mortization and depreciation       288       425       532         rovision – non-current portion       20       31       57         xpense related to share-based payments       5.3       2,716       1,178       1,769         interest expense       30       13       23         income tax expense       5.6       (3)       10       (3)         hange in trade and payables in foreign currency
mortization and depreciation $288$ $425$ $532$ rovision – non-current portion $20$ $31$ $57$ xpense related to share-based payments $5.3$ $2,716$ $1,178$ $1,769$ interest expense $30$ $13$ $23$ income tax expense $5.6$ $(3)$ $10$ $(3)$ hange in trade and payables in foreign currency $\_$ $\_$ $\_$ $\_$
rovision – non-current portion       20       31       57         xpense related to share-based payments <b>5.3</b> 2,716       1,178       1,769         interest expense       30       13       23         income tax expense <b>5.6</b> (3)       10       (3)         hange in trade and payables in foreign currency
xpense related to share-based payments       5.3       2,716       1,178       1,769         interest expense       30       13       23         income tax expense       5.6       (3)       10       (3)         hange in trade and payables in foreign currency
atterest expense301323accome tax expense5.6(3)10(3)hange in trade and payables in foreign currency(38)
acome tax expense5.6(3)10(3)hange in trade and payables in foreign currency———(38)
hange in trade and payables in foreign currency (38)
newsting each flow before change in weating conital (11,000) (20,005) (20,004)
perating cash flow before change in working capital (11,962) (20,255) (28,031)
ncrease in inventories <b>6.4</b> 32 21 (31)
icrease in trade and other receivables (319) 206 142
increase in other current assets 6.5 (3,470) 1,181 (1,266)
icrease in trade and other payables <b>6.11</b> 1,588 1,160 3,243
ncrease in other current liabilities <b>6.12</b> (528) 154 1,241
ncrease in provision – current portion 81 (81) —
hange in working capital (2,616) 2,641 3,329
Tet cash flow used in operating activities         (14,578)         (17,614)         (24,702)
ash flows from investing activities
cquisition of property, plant and equipment <b>6.2</b> (220) (1,726) (1,664)
cquisitions of intangible assets <b>6.1</b> (49) (25) (25)
cquisition of other non-current financial assets <b>6.3</b> (15) (40) (102)
isposal of property, plant and equipment 6.2 — — —
isposal of non-current financial assets 6.3 — 5 —
tet cash flow used in investing activities (284) (1,786) (1,791)
ash flows from financing activities
apital increases, net of transaction costs 23,544 9,239 177,576
roceeds from borrowings — 2,717 421
epayment of borrowings (85) (563) (452)
reasury shares 64 — —
tet cash flow from financing activities         23,524         11,393         177,545
hange rate effect on cash in foreign currency (16) 19 (3,183)
ncrease / Decrease in cash and cash equivalents 8,646 (7,988) 147,869
et Cash and cash equivalents at the beginning of the period <b>6.7</b> 36,988 45,634 37,646
ank overdraft 6.7 — — 11
et Cash and cash equivalents at the closing of the period <b>6.7</b> 45,634 37,646 185,525
upplemental disclosure of cash flows information
ash paid for interest 34 72 115
ash paid for income tax — — —

### NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS

The notes are an integral part of the accompanying consolidated financial statements. The Consolidated Financial Statements were approved and authorized for issuance by the Board of Directors of the Company on March 9, 2018.

### **1. DESCRIPTION OF THE BUSINESS**

ERYTECH Pharma S.A. ("ERYTECH" together with its subsidiary the "Company") is incorporated in Lyon, France, and was founded in 2004 to develop and market innovative therapies for acute leukemia and other orphan diseases. The Company's most advanced product candidates are being developed for the treatment of pancreatic cancer, acute lymphoblastic leukemia, or ALL, and acute myeloid leukemia, or AML.

The Company completed its initial public offering on Euronext Paris in May 2013, raising  $\notin 17.7$  million and a follow-on offering of  $\notin 30.0$  million (on a gross basis before deducting offering expenses), in October 2014. The initial public offering triggered the conversion of the totality of the convertible bonds previously issued. Two private placements of respectively 940,000 ordinary and 793,877 ordinary shares for  $\notin 25.4$  million and  $\notin 9.9$  million (on a gross basis before deducting offering expenses) were completed in December 2015 and 2016 with institutional investors in the United States and in Europe. In April 2017, the Company completed a follow-on offering of  $\notin 70.5$  million (on a gross basis before deducting offering expenses). The Company completed an initial public offering on the Nasdaq Global Select Market raising  $\notin 124$  million (\$144 million on a gross basis before deducting offering expenses) (see below "Major events of 2017").

The Company has incurred losses and negative cash flows from operations since its inception and had shareholders' equity of €181,419 thousand as at December 31, 2017 as a result of several financing rounds, including an initial public offering.

The Company anticipates incurring additional losses until such time, if ever, that it can generate significant revenue from its product candidates in development. Substantial additional financing will be needed by the Company to fund its operations and to commercially develop its product candidates.

The Company's future operations are highly dependent on a combination of factors, including: (i) the success of its research and development; (ii) regulatory approval and market acceptance of the Company's proposed future products; (iii) the timely and successful completion of additional financing; and (iv) the development of competitive therapies by other biotechnology and pharmaceutical companies. As a result, the Company is and should continue, in the short to mid-term, to be financed through partnership agreements for the development and commercialization of its drug candidates and through the issuance of new equity instruments.

The accompanying consolidated financial statements and related notes (the "**Consolidated Financial Statements**") present the operations of ERYTECH Pharma S.A. and its subsidiary, ERYTECH Pharma, Inc., incorporated in April 2014, which headquarters are in Cambridge, Massachusetts – United States of America. The activity of this subsidiary had no material impact on any of the years presented.

## Major events of 2017

Eryaspase

The Company announced positive topline results from its Phase 2b clinical study evaluating its product candidate, eryaspase (GRASPA®), in combination with chemotherapy for the treatment of second-line metastatic pancreatic cancer.

The multicenter, randomized Phase 2b study met its prespecified co-primary endpoints, and showed improvement in both progression-free survival (PFS) and overall survival (OS) in patients treated with eryaspase combined with chemotherapy compared to chemotherapy alone.

The Phase 2b study evaluated eryaspase, L-asparaginase encapsulated in red blood cells, as a second-line treatment in combination with chemotherapy in patients with metastatic pancreatic cancer. In this 141patient study, conducted in France, eryaspase was added to the standard of care (gemcitabine or FOLFOX) and compared to the standard of care alone in a 2-to-1 randomization.

The Company has resubmitted to the European Medicine Agency (EMA) its Marketing Authorization Application (MAA) for eryaspase (GRASPA®) for the treatment of patients with relapsed or refractory (R/R) acute lymphoblastic leukemia (ALL). The MAA resubmission includes the data from ERYTECH's GRASPALL 2009-06 Phase 2/3 clinical trial in children and adults with R/R ALL as well as additional data to address the outstanding questions of the Committee for Medicinal Products for Human Use (CHMP) of the EMA.

An investigator-initiated clinical trial has been launched to evaluate eryaspase, also known by the trade name GRASPA<sup>®</sup>, in patients with acute lymphoblastic leukemia (ALL). The study takes place in seven Nordic countries and is being conducted in collaboration with the Nordic Society of Pediatric Hematology and Oncology (NOPHO). This clinical trial is co-financed by ERYTECH Pharma and Orphan Europe.

The open-label, randomized, multi-center clinical study, evaluated eryaspase in newly diagnosed AML patients over the age of 65 and unfit for intensive chemotherapy. The study enrolled a total of 123 patients at 30 European sites. The median age of the patients was 78 years. Patients were randomized two-to-one to receive eryaspase in combination with low-dose cytarabine (LDAC) versus LDAC alone. The primary endpoint in this proof-of concept study was overall survival (OS). The key secondary endpoints included progression free survival, overall response and toxicity. The study was performed in collaboration with Orphan Europe (Recordati Group), ERYTECH's partner for the anticipated commercialization of GRASPA® for the treatment of ALL and AML in Europe. The study did not meet its primary endpoint of overall survival (OS).

The recommended pivotal Phase 3 dosing from its U.S. Phase 1 dose escalation study with eryaspase (GRASPA®) has been determined in first line treatment of adult ALL patients.

### Erymethionase

The Company pursues the development of its second product-candidate erymethionase also based on the ERYCAPS technology and with methioninase as the active drug substance.

The Company presented preclinical data on its erymethionase product candidate at the American Society of Clinical Oncology's Gastrointestinal Cancers Symposium in January 2017 and at the American Association for Cancer Research's Annual Meeting in April 2017. Based on these preclinical studies, we believe that erymethionase represents a promising new treatment approach against a broad range of cancers that rely on methionine metabolism. We expect to commence a Phase 1 clinical trial in Europe by the end of 2018.

The development of this product-candidate is part of the TEDAC research program and reached the milestone n°4 in 2016 which allowed the payment of subsidies and conditional advances.

The Company has initiated a project of change in manufacturing process. The project has reached the milestone  $n^{\circ}3$  of the development and capitalized  $\notin$ 766 thousand which amounted to a cumulated total asset of  $\notin$ 1,596 thousand as of December 31, 2017.

### Funds raised and Global Offering

In April 2017, the Company issued an aggregate of 3,000,000 ordinary shares in an offering to institutional investors in the United States and in Europe, at an issue price of &23.50 per share, including share premium, for a total amount subscribed of &70.5 million (gross amount before deducting offering expenses), representing approximately 25.55% of the share capital of the Company. The issue price of the new shares represented a discount of 5.62% from the closing price on April 12, 2017 and 6.37% from the weighted average share price of the Company's shares on the regulated market of Euronext Paris during the 20 trading days preceding the determination of the issue price on April 12, 2017.

The Company completed an offering in November 2017 on the Nasdaq Global Select Market and Euronext Paris for an aggregate gross proceeds of 144 million ( $\pounds$ 124 million), in the context of an initial public and a follow-on offering to specified categories of investors of an aggregate of 5,374,033 new ordinary shares, comprising an offer of 4,686,106 ordinary shares in the form of American Depositary Shares, each representing one ordinary share ("ADSs"), in the United States at an offering price of \$23.26 ( $\pounds$ 20) per ADS and a concurrent private placement in Europe (including France) and other countries outside of the United States and Canada of 687,927 ordinary shares at the corresponding offering price of \$23.26 ( $\pounds$ 20) per ordinary share (together, the "Global Offering"), for aggregate gross proceeds of \$124 million ( $\pounds$ 108 million) before deducting underwriting commissions and estimated expenses payable by the Company. By virtue of the delegation of authority granted by the Company's annual general meeting of June 27, 2017, the Board at a meeting held on November 6, 2017 approved the offering which was executed by the CEO on November 9, 2017. In addition, ERYTECH had granted the underwriters a 30-day option to purchase up to 806,104 additional ADSs and/or ordinary shares on the same terms and conditions, representing 15% of the ADSs and/or ordinary shares to be issued by the Company in the Global Offering. The gross proceeds of the additional offering amounted to \$19 million ( $\pounds$ 16 million).

The offering price per ADS in the U.S. offering corresponds to the offering price of &20 per ordinary share (based on the November 9, 2017 exchange rate of &1.00 = \$1.163). The offering price represented a discount of 9.79% from the volume-weighted average price of the Company's ordinary shares on the regulated market of Euronext Paris during the three trading days preceding the date of determination of the offering price on November 9, 2017 (i.e. November 7, 8 and 9, 2017).

Following the additional closing, aggregate net proceeds to ERYTECH, after deducting underwriting commissions and estimated offering expenses payable by ERYTECH, were \$130 million (€112 million).

### Management

The Board of Directors held on January 8, 2017 and the Chief Executive Officer granted share-based payments as follows:

- 15,000 AGA<sub>2016</sub> to Alexander Scheer;
- 15,000 BSA<sub>2016</sub> (share warrants) to Allene Diaz; and
- 3,000 SO<sub>2016</sub> to an ERYTECH Pharma, Inc. employee.

The Board of Directors held on June 27, 2017 and the Chief Executive Officer granted share-based payments as follows:

- 8,652 AGA<sub>2016</sub> to ERYTECH Pharma S.A employees; and
- 18,000 SO<sub>2016</sub> to ERYTECH Pharma, Inc. employees.

By virtue of the delegation of authority granted by the Company's annual general meeting of June 27, 2017, the Board at a meeting held on June 27, 2017 approved the following share-based payments:

- 55,000 BSA2017 to independent members of the Board of Directors
- 74,475 AGA<sub>2017</sub> to ERYTECH Pharma S.A employees; and
- 22,200 SO<sub>2017</sub> to ERYTECH Pharma, Inc. employees.

By virtue of the delegation of authority granted by the Company's annual general meeting of June 27, 2017, the Chief Executive Officer on October 3, 2017 approved the following share-based payments:

- 16,650 AGA<sub>2016</sub> to ERYTECH Pharma S.A employees; and
- 30,000 SO<sub>2016</sub> to ERYTECH Pharma, Inc. employees.

# 2. BASIS OF PREPARATION

The Consolidated Financial Statements as of December 31, 2015, 2016 and 2017 have been prepared under the responsibility of the management of the Company in accordance with the underlying assumptions of going concern as the Company's loss-making situation is explained by the innovative nature of the products developed, therefore involving a multi-year research and development phase.

The general accounting conventions were applied in compliance with the principle of prudence, in accordance with the underlying assumptions namely (i) going concern, (ii) permanence of accounting methods from one year to the next and (iii) independence of financial years, and in conformity with the general rules for the preparation and presentation of consolidated financial statements in accordance with IFRS, as defined below.

All amounts are expressed in thousands of euros, unless stated otherwise.

## 3. STATEMENT OF COMPLIANCE

The Consolidated Financial Statements have been prepared in accordance with International Financial Reporting Standards ("**IFRS**") as issued by the International Accounting Standard Board ("**IASB**") and were approved and authorized for issuance by the Board of Directors of the Company on March 9, 2018.

Due to the listing of ordinary shares of the Company on Euronext Paris and in accordance with the European Union's regulation No. 1606/2002 of July 19, 2002, the Consolidated Financial Statements of the Company are also prepared in accordance with IFRS, as adopted by the European Union (EU).

As of December 31, 2017, all IFRS that the IASB had published and that are mandatory are the same as those endorsed by the EU and mandatory in the EU, with the exception of IAS 39 *Financial Instruments: Recognition and Measurement* (revised December 2003), which the EU only partially adopted. The part not adopted by the EU has no impact on the Consolidated Financial Statements of the Company. As a result, the Consolidated Financial Statements comply with International Financial Reporting Standards as published by the IASB and as adopted by the EU.

IFRS include International Financial Reporting Standards (IFRS), International Accounting Standards ("**IAS**"), as well as the interpretations issued by the Standing Interpretations Committee ("**SIC**"), and the International Financial Reporting Interpretations Committee ("**IFRIC**"). The main accounting methods used to prepare the Financial Statements are described below. These methods were used for all periods presented.

The Group adopted the following standards, amendments and interpretations that are applicable as at January 1, 2017:

- Amendments to IAS 7 Disclosure initiative;
- Amendments to IAS 12 Income taxes; and
- Amendments to IFRSs 2014-2016 Cycle, for amendments effective for annual periods beginning on or after January 1, 2017.

These new texts did not have any significant impact on the Group's results or financial position.

The standards and interpretations that are optionally applicable as at December 31, 2017 were not applied in advance.

Recently issued accounting pronouncements that may be relevant to the Company's operations but have not yet been adopted are as follows:

- IFRS 2 Classification and measurement of share-based payment transactions et Amendments to IFRSs 2014-2016 Cycle, effective for annual periods beginning on or after January 1, 2018 (IAS 28).
- IFRS 9 Financial Instruments will be effective for the Group on January 1, 2018, with early adoption permitted. The Group does not expect its adoption to have a material impact on its consolidated financial statements.
- IFRS 15—Revenue from Contracts with Customers will be effective for the Group on January 1, 2018 with early adoption permitted. The Group does not expect its adoption to have a material impact on its consolidated financial statements. Revenue is generated mainly by the Research Tax Credit.
- IFRS 16—Leases will be effective for the Group on January 1, 2019, with early adoption permitted if applied at the same time as IFRS 15. The Group does not plan to early adopt this standard and does not expect its adoption to have a material impact on its consolidated financial statements.

- IAS 40 Transfers of investment property.
- IFRIC 22 Foreign currency transactions and advance consideration.
- IFRIC 23 Uncertainty over income tax treatments.
- Amendments to IFRSs 2014-2016 Cycle, for amendments effective for annual periods beginning on or after January 1, 2018.

These new texts are not expected to have any significant impact on the Group's results or financial position.

## 4. SIGNIFICANT ACCOUNTING POLICIES

# 4.1 Basis of consolidation

In accordance with IFRS 10 *Consolidated Financial Statements*, an entity is consolidated when it is controlled by the Company. The Company controls an entity when it is exposed or has rights to variable returns from its involvement with the entity and has the ability to affect those returns through its power over the entity. All intra-company balances, transactions, unrealized gains and losses resulting from intra-group transactions and dividends are eliminated in full. As of December 31, 2017, the Company has one subsidiary for which no non-controlling interest is recognized.

Details of the Company's subsidiary as of December 31, 2017 are as follows:

	Date of	Percent of	Accounting
	Incorporation	Ownership Interest	Method
ERYTECH Pharma, Inc.	April 2014	100%	Fully consolidated

### 4.2 Intercompany transactions

Transactions involving reciprocal assets and liabilities, as well as income and expense, between ERYTECH and ERYTECH Pharma, Inc. are eliminated in the Consolidated Financial Statements.

### 4.3 Foreign currencies

# Functional Currency and Translation of Financial Statements in Presentation Currency

The Consolidated Financial Statements are presented in euros, which is also the functional currency of the parent company, ERYTECH Pharma S.A. (the "**Parent Company**"). The statements of financial position of the consolidated entity having a functional currency different from the euro are translated into euros at the closing exchange rate (spot exchange rate at the statement of financial position date) and the statements of income (loss), statements of comprehensive income (loss) and statements of such consolidated entity are translated at the average exchange rate for the period, except if exchanges rates fluctuate significantly. The resulting translation adjustment is included in other comprehensive income (loss) as a cumulative translation adjustment.

## **Conversion of Foreign Currency Transactions**

Foreign currency transactions are converted to functional currency (euros) at the rate of exchange applicable on the transaction date. At period-end, foreign currency monetary assets and liabilities are converted at the rate of exchange prevailing on that date. The resulting exchange gains or losses are recorded in the Consolidated Statements of Income in "Financial income (loss)".

The loan in U.S. dollars from ERYTECH Pharma S.A. to ERYTECH Pharma, Inc. is considered as part of the net investment in a foreign operation. Exchange differences on this loan are recognized in other comprehensive income.

## 4.4 Consolidated statements of cash flows

The consolidated statements of cash flows are prepared using the indirect method and separately present the cash flows associated with operating, investment, and financing activities.

Operating activities correspond to the Company primary income-generating activities and all the other activities that do not meet the investment or financing criteria. The Company has decided to classify grants received such as the Research Tax Credit (*Credit d'Impôt Recherche*) as an operating activity in the consolidated statement of cash flows.

Cash flows associated with investment activities correspond to cash flows associated with the purchase of property, plant and equipment, net of asset supplier payables, and with the disposal of assets and other investments.

Financing activities are operations that result in changes in the amount and composition of the share capital and borrowings of the entity. Capital increases and the obtaining or repayment of loans are classified under this category. The Company has chosen to classify the conditional advances under this category.

The increases in assets and liabilities with non-cash effects are eliminated. As such, the assets financed through a finance lease are not included in the investments for the period presented. The decrease in financial liability associated with leases is therefore included under the caption 'repayment of borrowings' for the period.

## 4.5 Use of estimates and judgments

Preparation of the financial statements in accordance with the rules prescribed by the IFRS requires the use of estimates and the formulation of assumptions having an impact on the financial statements. These estimates can be revised where the circumstances on which they are based change. The actual results may therefore differ from the estimates initially formulated. The use of estimates and judgment relate primarily to the measurement of share-based payments (Note 4.15 and Note 5.3) and accruals of hospital costs. Hospital costs are estimated using revised budgets of clinical studies currently being completed, and also using information collected from hospital centers included in the clinical study.

### 4.6 Intangible assets

## Internally generated intangible assets - Research and development costs

In accordance with IAS 38 Intangible Assets ("IAS 38"), research expenditures are expensed in the period during which they are incurred.

An internally generated intangible asset relating to a development project is recorded as an asset if, and only if, the following criteria are met:

- (a) it is technically feasible to complete the development project;
- (b) intention on the part of the Company to complete the project and to utilize it;
- (c) capacity to utilize the intangible asset;
- (d) proof of the probability of future economic benefits associated with the asset;
- (e) availability of the technical, financial, and other resources for completing the project; and
- (f) reliable evaluation of the development expenses.

The initial measurement of the asset is the sum of expenses incurred starting on the date on which the development project meets the above criteria.

Because of the risks and uncertainties related to regulatory authorizations and to the research and development process, the Company believes that the six criteria stipulated by IAS 38 have not been fulfilled to date and the application of this principle has resulted in all development costs being expensed as incurred in all periods presented.

# Other intangible assets

The costs related to the acquisition of software licenses are recognized as assets on the basis of the costs incurred to acquire and to implement the software.

They are amortized using the straight-line method over a period of one to five years depending on the anticipated period of use.

An impairment is recorded when the asset's carrying amount is greater than its recoverable value (see Note 4.8).

## 4.7 Property, plant and equipment

Property, plant and equipment are recorded at their acquisition cost, comprised of their purchase price and all the direct costs incurred to bring the asset to the location and working condition for its use as intended by the company's management.

Property, plant, and equipment are depreciated on the basis of the straight-line method over the estimated useful life of the property. The fixtures of property rented are depreciated over the term of their own lifetime or of the term of the rental agreement, whichever is shorter.

The depreciation periods used are the following:

PROPERTY, PLANT, AND EQUIPMENT ITEM	<b>D</b> EPRECIATION PERIOD
Industrial equipment	1 to 5 years
Fixtures and improvements in structures	3 to 10 years
Office equipment	3 years
Furniture	3 to 5 years

The useful lives of property, plant and equipment as well as any residual values are reviewed at each year end and, in the event of a significant change, result in a prospective revision of the depreciation pattern.

### 4.8 Impairment tests

According to IAS 36 *Impairment of Assets* ("**IAS 36**"), a loss in value must be recognized where the carrying value of an asset, or the cash generating unit to which the asset belongs (if it is not possible to estimate the recoverable amount of the individual asset), is lower than its recoverable value.

The property, plant, and equipment and intangible assets that have a finite life are subject to an impairment test when the recoverability of their carrying value is called into question by the existence of indications of impairment. An impairment is recognized in the Consolidated Financial Statements up to the amount of the excess of the value over the recoverable value of the asset. The recoverable value of an asset corresponds to its fair value less costs to sell or its value in use, whichever is higher.

#### 4.9 Financial assets and liabilities - Measurement and Presentation

The valuation and the accounting treatment of the financial assets and liabilities are defined by IAS 39 *Financial Instruments: Recognition and Measurement* ("**IAS 39**"). The Company does not use derivative instruments to hedge its currency exposure.

### Loans and receivables

These instruments are initially recognized in the Consolidated Financial Statements at their fair value and then at the amortized cost calculated with the effective interest rate ("**EIR**") method. The short-term receivables without an interest rate are valued at the amount of the original invoice, unless the application of an implicit interest rate has a material effect.

The loans and receivables are monitored for any objective indication of impairment. A financial asset is impaired if its carrying value is greater than its recoverable amount. The impairment is recognized in the statement of income (loss).

## Financial liabilities at the amortized cost

Loans and other financial liabilities are initially measured at their fair value less transaction costs directly attributable, and then at the amortized cost, calculated using the EIR method.

### Presentation of financial assets and financial liabilities measured at fair value

In accordance with IFRS 13 *Fair Value Measurement*, financial instruments are presented in three categories based on a hierarchical method used to determine their fair value:

• level 1: fair value calculated using quoted prices in an active market for identical assets and liabilities;

- level 2: fair value calculated using valuation techniques based on observable market data such as prices of similar assets and liabilities or parameters quoted in an active market;
- level 3: fair value calculated using valuation techniques based wholly or partly on unobservable inputs such as prices in an inactive market or a valuation based on multiples for unlisted securities.

# 4.10 Inventories

In compliance with the IAS 2 *Inventories*, inventories are recognized at their cost or at their net realizable value, whichever is lower. Cost is determined on a *First-In First-Out* (FIFO) cost basis. Management periodically reviews the inventory for obsolescence and adjusts as necessary.

## 4.11 Cash and cash equivalents

The item "cash and cash equivalents" in the consolidated statement of financial position includes bank accounts and highly liquid securities. They are readily convertible into a known amount of cash and are subject to a negligible risk of change in value.

They are recorded as assets in Cash equivalents, measured at their fair value, and the changes in value are recognized through financial income or loss.

The cash equivalents classification is made if the following criteria are fulfilled:

- held for the purpose of meeting short term cash commitments rather than for investment or other purposes.
- exit options exist:
  - exercisable at any time at least every three months
  - initially included in the contract and this exit option is always provided in the initial contract
  - exercisable without exit penalty and without significant risk of change in the amount received as cash reimbursement
- there is no value risk related to the level of minimum compensation acquired (i.e. that obtained in the event of early exit) because over the entire duration and at each moment this remuneration will be identical to that obtained from an investment of no more than three months that meets the definition of a cash equivalent. This can be the case when the rate is variable or revisable.

### 4.12 Provisions

A provision is recognized where the Company has a current or implicit legal obligation resulting from a past event, where the obligation can be reliably estimated, and where it is probable that an outflow of resources representing economic benefits will be necessary to settle the obligation. The portion of a provision that become due in less than one year is recorded under current liabilities, and the balance under non-current liabilities. The provisions are discounted when the impact is material.

Provisions recognized in the consolidated statement of financial position mainly include obligations pertaining to retirement indemnities and provisions for risks.

Disclosure is made in the detailed notes on any contingent assets and liabilities where the impact is expected to be material, except where the probability of occurrence is low.

### Provisions for retirement indemnities-defined benefit plans

The employees of the Company receive the retirement benefits stipulated by law in France:

- a compensation paid by the Company to employees upon their retirement (defined-benefit plan) and;
- a payment of retirement pensions by the social security agencies, which are financed by the contributions made by companies and employees (defined contribution plans in France).

For the defined-benefit plans, the costs of the retirement benefits are estimated by using the projected credit unit method. According to this method, the cost of the retirement benefit is recognized in the statement of income (loss) so that it is distributed uniformly over the term of the services of the employees. The retirement benefit commitments are valued at the current value of the future payments estimated using, for discounting, the market rate for high quality corporate bonds with a term that corresponds to the estimated term for the payment of the benefits.

The Company appoints external actuaries to conduct an annual review of the valuation of these plans.

The difference between the amount of the provision at the beginning of a period and at the close of that period is recognized through profit or loss for the portion representing the costs of services rendered and the net interest costs, and through other comprehensive income for the portion representing the actuarial gains and losses.

The Company's payments for the defined-contribution plans are recognized as expenses on the statement of income (loss) of the period in which they become payable.

### **Provisions for risks**

The provisions for risks correspond to the commitments resulting from litigations and various risks whose due dates and amounts are uncertain.

The amount recognized in the Consolidated Financial Statements as a provision is the best estimate of the expenses necessary to extinguish the obligation.

## 4.13 Lease agreements

The leases involving property, plant, and equipment are classified as finance lease agreements when the Company bears substantially all the benefits and risks inherent in the ownership of the property. The assets that are covered under finance lease agreements are capitalized as of the beginning date of the rental agreement on the basis of the fair value of the rented asset or the discounted values of the future minimum payments, whichever is lower. Each rental payment is distributed between the debt and the financial cost in such a manner to determine a constant interest rate on the principal that remains due. The corresponding rental obligations, net of the financial expenses, are classified as financial liabilities. The property, plant, or equipment acquired within the framework of a finance lease agreement is amortized over the useful life or the term of the lease agreement, whichever is shorter.

The rental agreements for which a significant portion of the risks and advantages is preserved by the lessor are classified as operating leases. The payments made for these operating leases, net of any incentive measures, are recognized as expenses on the consolidated statement of income (loss) on a straight-line basis over the term of the agreement.

## 4.14 Share capital

Common shares are classified under shareholders' equity. The costs of share capital transactions that are directly attributable to the issue of new shares or options are recognized in shareholders' equity as a deduction from the proceeds from the issue, net of tax.

## 4.15 Share-based payment

The Company has applied IFRS 2 *Share-based payment* ("**IFRS 2**") to all equity instruments e.g. free shares ("AGAP"), stock options ("SO"), share subscription warrants ("BSA") and founder subscription warrants ("BSPCE") granted since inception to its employees, members of the Board of Directors or other individuals. Pursuant to IFRS 2, the cost of the remuneration paid with equity instruments is recognized as an expense in exchange for an increase in the shareholders' equity for the vesting period during which the rights to be enjoyed from the equity instruments are acquired. As such, changes in value subsequent to the grant date have no effect on this initial measurement.

Fair value is estimated using the Black & Scholes valuation model (for BSA, SO and BSPCE valuation), Monte-Carlo valuation model (for AGAP valuation) and Cox-Ross-Rubinstein valuation model (for 2016 and 2017 BSA valuation). These models allow the Company to take into account the characteristics of the plan (vesting price, vesting period), the market data at the grant date (volatility, expected dividends, repo margin), possible performance conditions attached to warrants and recipient behavior assumptions.

### 4.16 Other income

### Research tax credit

The research tax credit (*Crédit d'Impôt Recherche* or "**CIR**") (the "**Research Tax Credit**") is granted to companies by the French tax authorities in order to encourage them to conduct technical and scientific research. Companies that prove that they have expenditures that meet the required criteria (research expenditures located in France or, since January 1, 2005, within the European Union or in another State that is a party to the Agreement on the European Economic Area that has concluded a tax treaty with France that contains an administrative assistance clause) receive a tax credit that can be used for the payment of the corporate tax due for the fiscal year in which the expenditures were made and the next three fiscal years, or, as applicable, can be reimbursed in cash. The expenses taken into account for the calculation of the Research Tax Credit involve only research expenses.

The Company has received the Research Tax Credit since its inception.

The receivable in the consolidated statement of financial position as at December 31, 2017 includes the CIR for 2017 (see Note 6.6).

The CIR is presented under other income in the consolidated statement of income (loss) as it meets the definition of government grant as defined in IAS 20 *Accounting for Government Grants and Disclosure of Government Assistance*.

## Subsidies and conditional advances

Due to the innovative nature of its product candidate development programs, the Company has benefited from certain sources of financial assistance from *Banque Publique d'Investissement* ("**BPI France**"). BPI France provides financial assistance and support to emerging French enterprises to facilitate the development and commercialization of innovative technologies.

The funds received by the Company are intended to finance its research and development efforts and the recruitment of specific personnel. The Company has received such funding in the form of non-refundable subsidies and conditional advances.

### **Subsidies**

Subsidies received are grants that are not repayable by the Company and are recognized in the financial statements as operating income where there exists reasonable assurance that the Company will comply with the conditions attached to the subsidies and the subsidies will be received.

Subsidies that are upfront payments are presented as deferred revenue and recognized ratably through income over the duration of the research program to which the subsidy relates.

A public subsidy that is to be received either as compensation for expenses or for losses already incurred, or for immediate financial support of the Company without associated future costs, is recognized in the Consolidated Financial Statements as other income when there exists reasonable assurance that the subsidies will be received.

### Conditional advances

Funds received from BPI France in the form of conditional advances are recognized as financial liabilities, as the Company has a contractual obligation to reimburse BPI France for such conditional advances in cash based on a repayment schedule provided the conditions are complied with. Each award of an advance is made to help fund a specific development milestone. The details concerning the conditional advances are provided in Note 6.10.

Receipts or reimbursements of conditional advances are reflected as financing transactions in the statement of cash flows.

The amount resulting from the benefit of conditional advances that do not bear interest at market rates is considered a subsidy. This benefit is determined by applying a discount rate equal to the rate the Company would have to pay for a bank borrowing over a similar maturity.

The implicit interest rate resulting from taking into account all the repayments plus the additional payments due in case of commercial success as described in Note 6.10 is used to determine the amount recognized annually as a finance cost.

In the event of a change in payment schedule of the stipulated repayments of the conditional advances, the Company recalculates the net book value of the debt resulting from the discounting of the anticipated new future cash flows at the initial effective interest rate. The adjustment that results therefrom is recognized in the consolidated statement of income (loss) for the period during which the modification is recognized.

The conditional advances that can be subject to this type of modification are the advances received from BPI France, presented in Note 6.10.

# Partnership with Orphan Europe AML clinical trial

As a result of its partnership agreement with Orphan Europe related to the development of Acute Myeloid Leukemia ("AML"), the Company re-invoices, with no margin, certain clinical costs incurred and invoiced to the Company by external providers.

In application of IAS 18 *Revenue*, the Company considers that, within the context of this partnership, it acts as agent regarding these reinvoiced external costs, as:

- The Company does not have primary responsibility for provision of the goods or service, the majority of services being provided by third parties, the most significant of which, the Contract Research Organization ("CRO"), directly invoices Orphan Europe. The Company is directly invoiced only for the secondary services.
- The Company bears no inventory risk,
- The Company has no capacity to determine prices, all of the external costs being reinvoiced for the exact amount of the initial invoice, with no margin, and it is not affected by any price changes applied by the suppliers.
- The Company bears a credit risk considered to be not significant.

Within the context of this same agreement, the Company also invoiced certain internal clinical costs, such as personnel costs associated with the management of clinical trials, or personnel involved in the production of batches necessary for the AML clinical trial together with internal costs related to the AML clinical trial.

Consequently, the re-invoicing of these external costs to Orphan Europe is presented as a decrease in corresponding research and development expenses incurred by the Company. For the year ended December 31, 2017 there was no re-invoicing in the context of the AML clinical trial.

## Partnership with Orphan Europe NOPHO clinical trial

These invoiced external costs are classified by the Company as "other income" in the consolidated statement of income (loss) and within the context of this agreement, amounted to  $\notin$ 177.5 thousand for the year ended December 31, 2017.

#### 4.17 Financial income and expense

Financial results relate to loans, gains and losses on exchange rate variations and other financial debts (notably overdrafts and finance leases) and includes interest expenses incurred on financial liabilities and the related amortization of debt issuance costs, and income received from cash and cash equivalents. For the year ended December 31, 2017 financial expenses are mainly composed of currency exchange losses.

#### 4.18 Income taxes

#### Current taxes

Considering the level of tax loss carryforwards not recognized, no current tax expense is recognized.

#### Deferred taxes

Except in specific cases, deferred taxes are calculated for the temporary differences between the carrying value of an asset or a liability and its tax value. Changes in the tax rates are recorded in the results of the financial year during which the rate change is decided. Deferred tax assets resulting from temporary differences or tax losses carried forward are limited to the deferred tax liabilities with the same maturity, except where their allocation on future taxable income is probable. Deferred taxes are calculated based on the most recent tax rates adopted at the date of each financial year-end.

Deferred tax assets and liabilities are not discounted and are classified in the consolidated statement of financial position under non-current assets and liabilities.

In addition, the Parent Company, as an entity incorporated in France, is subject to the territorial economic contribution (*Contribution Economique Territoriale* —*CET*), which combines the corporate real estate contribution (*cotisation foncière des entreprises*—*CFE*) and the corporate value-added contribution (*cotisation sur la valeur ajoutée des entreprises*—*CVAE*):

- the corporate real estate contribution, the amount of which depends on property rental values and which can, where applicable, have a ceiling at a
  percentage of the value added, presents significant similarities to the former business tax and is recognized under operating expenses;
- the corporate value-added contribution meets, based on the Company's analysis, the definition of an income tax as established under IAS 12 *Income Taxes* ("IAS 12") paragraph 2 ("taxes owing based on taxable income"). To enter within the scope of IAS 12, a tax must be calculated based on a net amount of income and expenses, and this net amount can be different from the net book results. The Company has judged that the corporate value-added contribution satisfies the characteristics outlined in this conclusion, insofar as the value added constitutes the intermediate level of income that systematically serves as the basis, according to French tax law, for determining the amount owing in relation to the corporate value-added contribution.

In conformity with the provisions of IAS 12, qualification of the corporate value-added contribution as an income tax leads to the recognition of deferred taxes relative to temporary differences existing at year end, with a contra-entry of a net expense in that year's statement of net income (loss). Where applicable, this deferred tax expense is presented on the line income tax. For the moment, the Company does not pay the CVAE.

#### 4.19 Earnings per share

The basic earnings per share are calculated by dividing the Company's net income (loss) by the weighted average number of shares in circulation during the corresponding period.

The diluted earnings per share are calculated by dividing the results by the weighted average number of common shares in circulation, increased by all dilutive potential common shares. The dilutive potential common shares include, in particular, the share subscription warrants, stock options, free shares and founder subscription warrants as detailed in note 5.3 and 6.8.

Dilution is defined as a reduction of earnings per share or an increase of loss per share. When the exercise of outstanding share options and warrants decreases loss per share, they are considered to be anti-dilutive and excluded from the calculation of loss per share. Thus, basic and diluted loss per share are equal as all equity instruments issued, representing 865,760 potential additional ordinary shares, have been considered anti-dilutive.

#### 4.20 Segment reporting

In accordance with IFRS 8 *Operating Segments,* reporting by operating segment is derived from the internal organization of the Company's activities; it reflects management's viewpoint and is established based on internal reporting used by the chief operating decision maker (the Chief Executive Officer and Chairman of the Board of Directors) to allocate resources and to assess performance.

The Company operates in a single operating segment: the conducting of research and development in the area of treatment of acute leukemia and other orphan diseases in order to market them in the future. The assets, liabilities, and operating loss realized are primarily located in France.

#### 4.21 Off-balance sheet commitments

The Company has defined and implemented monitoring for its off-balance sheet commitments so as to know their nature and object. Off-balance sheet items identified mainly relate to:

- future costs relate to clinical trials for which recruitment has begun,
- operating leases, purchase and investment commitments.

#### 4.22 Events After the Close of the Reporting Period

The consolidated statement of financial position and the consolidated statement of income (loss) of the Company are adjusted to reflect the subsequent events that alter the amounts related to the situations that exist as of the closing date. Modifications can be made until the date the Consolidated Financial Statements are approved and authorized for issuance by the Board of Directors.

By virtue of the delegation of authority granted by the Company's annual general meeting of June 27, 2017, the Board at a meeting held on January 7, 2018 approved the following share-based payments:

- 40,500 AGA<sub>2016</sub> to ERYTECH Pharma S.A. executive officers;
- 40,500 BSA<sub>2017</sub> to independent members of the Board of Directors;
- 27,000 AGA<sub>2017</sub> to ERYTECH Pharma S.A. employees; and
- 40,500 SO<sub>2017</sub> to ERYTECH Pharma, Inc. employees.

By virtue of the delegation of authority granted by Board of Directors held on June 27, 2017, the Chief Executive Officer at a meeting held on January 7, 2018 approved the following share-based payments:

- 86,940 AGA<sub>2017</sub> to ERYTECH Pharma S.A. executive officers; and
- 56,703 SO<sub>2017</sub> to ERYTECH Pharma, Inc. employees.

This event after the close of the reporting period did not lead to an adjustment of the consolidated financial statements.

ERYTECH conducted a comprehensive evaluation to determine other potential solid-tumor indications for developing eryaspase. Metastatic Triple-Negative Breast Cancer (TNBC) has now been selected as the next indication to expand the potential use of eryaspase in solid tumors. TNBC is an aggressive and metabolically active form of breast cancer with high rates of symptomatic metastases. This event after the close of the reporting period did not lead to an adjustment of the consolidated financial statements.

The Company evaluated subsequent events that occurred after December 31, 2017 through the date of approval and authorization of issuance of the Consolidated Financial Statements and determined that there are no significant events that require adjustments in such Consolidated Financial Statements.

### 5. NOTES RELATED TO THE CONSOLIDATED STATEMENT OF INCOME (LOSS)

### 5.1 Operating income

Operating income consists of the following:

		For the year ended December 31,		
	2015	2016	2017	
	(in th	ousands of et	ıros)	
Research Tax Credit	2,219	3,347	3,187	
Subsidies	368	463	—	
Other income	341	327	178	
Total	2,929	4,138	3,364	

The operating income was primarily generated by the CIR (research tax credit), and the subsidies associated with the pre-clinical research programs in partnership with BPI France.

Other income totaled &341 thousand, &327 thousand and &178 thousand in 2015, 2016 and 2017, respectively, representing the re-invoicing of the internal costs incurred by the Company within the context of the AML study in 2015 and 2016 and within the context of the NOPHO study in 2017. The global amount financed by Orphan Europe is &600 thousand for the NOPHO study.

The Research Tax Credit and the subsidies decreased in 2017 as compared to 2016. Clinical study expenses increased in 2017, but this increase is mainly related to vendors that are not eligible for the research tax credit, and therefore the increase in clinical study expenses does not result in an increase in the research tax credit in 2017.

The increase in the research tax credit between 2015 and 2016 is related to the increase in clinical study expenses.

The Company receives subsidies through the TEDAC project financed by BPI France; the decrease in subsidies is related to the technical milestone of the TEDAC program which is not reached as at December 31, 2017 and therefore the Company is not eligible to receive the subsidy for the 5<sup>th</sup> milestone of the project.

## 5.2 Operating expenses by nature

For the year ended December 31, 2015 (amounts in thousands of euros)	Research and development expenses	of which other R&D expenses	of which clinical studies	of which intellectual property	General and administrative expenses	Total
Consumables	1,040	244	796		36	1,076
Rental and maintenance	462	204	259	—	304	767
Services, subcontracting and fees	4,475	1,539	2,570	366	3,022	7,497
Personnel expenses	3,977	1,506	2,384	87	1,627	5,603
Other	572	56	513	3	2,627	3,200
Depreciation and amortization	250	26	224		120	369
Total général	10,776	3,575	6,745	456	7,736	18,512

For the year ended December 31, 2016 (amounts in thousands of euros)	Research and development <u>expenses</u>	of which other R&D expenses	of which clinical studies	of which intellectual property	General and administrative <u>expenses</u>	Total
Consumables	2,071	917	1,153		66	2,136
Rental and maintenance	645	161	484	—	511	1,156
Services, subcontracting and fees	11,409	2,547	8,410	453	2,793	14,203
Personnel expenses	5,282	1,173	4,070	39	2,713	7,995
Other	35	8	27		577	613
Depreciation and amortization	277	25	252	—	148	425
Total	19,720	4,831	14,397	491	6,808	26,528

For the year ended December 31, 2017 (amounts in thousands of euros)	Research and development expenses	of which other R&D expenses	of which clinical studies	of which intellectual property	General and administrative expenses	Total
Consumables	2,391	1,859	532		148	2,539
Rental and maintenance	636	140	496		894	1,531
Services, subcontracting and fees	14,175	1,423	12,407	345	2,867	17,042
Personnel expenses	7,916	2,023	5,828	66	3,688	11,604
Other	81	20	44	17	927	1,008
Depreciation and amortization	263	94	169	—	266	530
Total	25,463	5,559	19,476	428	8,791	34,254

The increase in research and development expenses in 2017 for €5,743 thousand is primarily related to:

- the increase of external services by €2,766 thousand related to the MAA re-submission, the phase 2 of the AML study and the phase 2 of the pancreatic cancer clinical trial.
- the increase of personnel expenses for €2,634 thousand (see below note 5.3)

The increase in general and administrative expenses by €1,983 thousand is due to:

- The increase in personnel expenses for an amount of €975 thousand, +36% following the staff hiring plan (see below note 5.3)
- The increase of rental and maintenance costs for €383 thousand, +75%, the Company has a new building lease related to its development; the Company's development required new office space in Lyon and IT service costs as well.
- The increase of "Other" costs including an increase of €325 thousand related to warrants allocated to Directors and Board fees.

The increase in research and development expenses from 2015 to 2016 of €8,944 thousand is primarily related to

- The increase in external services amounting to €6,934 thousand for the development of the TEDAC program and costs incurred in relation with the MAA submission; and
- The increase of personnel expenses by €1,305 thousand.

The decrease in General and Administrative expenses for an amount of  $\pounds$ 928 thousand between 2015 and 2016 is mainly due to a decrease in "Other" of  $\pounds$ 2,050 thousand, which is mainly related to warrants (BSA<sub>2014</sub>) granted to the Board of Directors, which amounted to  $\pounds$ 1,593 thousand in 2015.

#### 5.3 Personnel expenses

The personnel expenses are detailed as follows:

For the year ended December 31, 2015 (amounts in thousands of euros)	Research and development expenses	of which other R&D expenses	of which clinical studies	of which intellectual property	General and administrative expenses	Total
Wages and salaries	2,235	953	1,238	43	896	3,131
Share-based payments	822	126	678	19	302	1,124
Social security expenses	920	427	468	25	429	1,348
Total personnel expenses	3,977	1,506	2,384	87	1,627	5,604
			<i>c</i>	<i>.</i>	<b>a</b>	

For the year ended	Research and	of which	of which	of which	General and	
December 31, 2016	development	other R&D	clinical	intellectual	administrati	
(amounts in thousands of euros)	expenses	expenses	studies	property	ve expenses	Total
Wages and salaries	3,371	688	2,670	13	1,486	4,857
Share-based payments	688	136	532	6	490	1,178
Social security expenses	1,224	350	868	19	736	1,960
Total personnel expenses	5,282	1,173	4,070	39	2,713	7,995

	Research and development expenses	of which other R&D expenses	of which clinical studies	of which intellectual _property	General and administrative <u>expenses</u>	Total
Wages and salaries	5,229	1,166	4,028	34	1,990	7,218
Share-based payments	833	279	541	13	642	1,475
Social security expenses	1,854	578	1,259	18	1,057	2,911
Total personnel expenses	7,916	2,023	5,828	66	3,688	11,604

The increase in personnel expenses of €3,609 thousand between 2016 and 2017 is mainly due to:

- the increase in share-based compensation expenses for an amount of €297 thousand
- the increase in personnel expenses (wages and salaries) of research and development for €2,488 thousand following the staffing for the launching of the new phase 2 and 3 clinical trials
- the increase in wages and salaries of general and administrative for an amount of €824 thousand to support the increase in operating research and development activities

The increase in personnel expenses of  $\pounds$ 2,392 thousand between 2015 and 2016 is mainly due to the increase in wages and salaries of the subsidiary ERYTECH Pharma Inc. in the amount of  $\pounds$ 1,194 thousand and the Parent Company in the amount of  $\pounds$ 1,198 thousand following the increase in headcount (73 employees in 2016 and 49 employees in 2015).

The employee staff increased from 44 (weighted average full-time employees for the year) in 2015 to 66 into 2016 and to 98 into 2017.

## Share-based payments (IFRS 2)

Share-based awards have been granted to the directors, to certain employees, as well as to members of the Board of Directors in the form of share subscription warrants ("**BSA**"), stock options ("**SO**"), free shares ("**AGAP**") or founder subscription warrants ("**BSPCE**"). The Board of Directors has been authorized by the general meeting of the shareholders to grant warrants in the form of AGAP, SO, BSA and BSPCE through the following plans:

#### <u>"2012 Plan"</u>

Within the scope of the BSA<sub>2012</sub> plan, the Board of Directors meeting of April 29, 2015 and August 3, 2015 allocated respectively 2,150 and 3,585 BSA<sub>2012</sub> to the directors without acquisition conditions.

#### Allocation of 2,150 BSA on April 29, 2015

The main assumptions used to determine the fair value are:

- Price of the underlying share: €31.19 (based on the quoted market price of the ordinary shares of the Company as of the date of the Board of Directors that granted the BSA)
- Risk-free rate: between (0.07) % (in line with the zero-coupon government bond rates curve);
- Expected dividends: 0%;
- Volatility: 20.5% based on the historical volatility observed on the NextBiotech index;
- Expected maturity: 2.5 years.

The fair value of warrants allocated in April 2015 in relation to the 2012 plan was valued at €512 thousand and was fully recognized in the consolidated statement of income (loss) for 2015 (G&A expenses) in the absence of vesting conditions.

#### Allocation of 3,585 BSA on August 31, 2015.

The main assumptions used to determine the fair value are:

- Price of the underlying share: €37.52 (based on the quoted market price of the ordinary shares of the Company as of the date of the Board of Directors that granted the BSA)
- Risk-free rate: between (0.08) % (in line with the zero-coupon government bond rates curve);
- Expected dividends: 0%;
- Volatility: 22.5% based on the historical volatility observed on the NextBiotech index;
- Expected maturity: 2.36 years.

The fair value of warrants allocated in April 2015 in relation to the 2012 plan was valued at  $\leq$ 1,081 thousand and was fully recognized in the consolidated statement of income (loss) for 2015 (G&A expenses) in the absence of vesting conditions.

At the end of 2015, the subscription warrants for the 2012 plan are as follows:

Types of securities	BSPCE2012	<b>BSA2012</b>
Number of warrants that the company is		
authorized to issue, for all types of warrants	45	5,500
Number of warrants granted	33,788	10,760
Number of warrants exercised	16,352	5,525
Date of General Meeting	May 2	21, 2012
Exercise price per new share subscribed (in €)	€7	7,362
Final date for exercising warrants	May 2	20, 2020
Parity	1 warrant for 10 shares	1 warrant for 10 shares
General conditions of exercise	The warrants are exercisable	as of their acquisition date
Maximum number of new shares that can be		
issued	23	1,730

## <u>"2014 Plan"</u>

On January 22, 2014, the Board of Directors used the delegation granted by the mixed general shareholders meeting of April 2, 2013, to grant a free allocation of 22,500 founder share subscription warrants (hereinafter entitled BSPCE<sub>2014</sub>) to ERYTECH senior management (12,000) and to certain employees (10,500). 3,000 BSPCE<sub>2014</sub> were converted to BSA<sub>2014</sub>.

Within the scope of the BSPCE<sub>2014</sub> / BSA<sub>2014</sub> plan, the Board of Directors meeting of May 6, 2016 allocated 5,000 BSPCE<sub>2014</sub> to the employees.

At the end of 2017, the subscription warrants for the 2014 plan are as follows:

Types of securities	BSPCE2014	<b>BSA2014</b>
Number of warrants that the company is authorized		
to issue, for all types of warrants	22	2,500
Number of warrants granted	19,500	3,000
Number of warrants exercised	1,500	100
Number of obsolete warrants	1,090	0
Date of General Meeting	Januar	y 22, 2014
Exercise price per new share subscribed (in €)	€1	2,250
Final date for exercising warrants	Januar	y 22, 2024
Parity	1 warrant for 10 shares	1 warrant for 10 shares
General conditions of exercise	The warrants are exercisabl	e as of their acquisition date
Maximum number of new shares that can be issued	19	8,100

In the event of a beneficiary departure from the Company for any reason whatsoever, this beneficiary shall retain the BSPCE<sub>2014</sub> to which he subscribed prior to his departure. However, in the event of a beneficiary departure from the Company, for any reason whatsoever, prior to subscription of the BSPCE<sub>2014</sub> to which the beneficiary has a right, the BSPCE<sub>2014</sub> will be forfeited. In this situation, the BSPCE<sub>2014</sub> not subscribed may be re-allocated to other beneficiaries within the same category and/or replacing the person who left the Company.

Following the resignation of Yann Godfrin in January 2016, 1,000 BSPCE of the 3,000 BSPCE initially allocated have been forfeited and will not be granted.

The main assumptions used to determine the fair value of the 5,000 BSPCE<sub>2014</sub> allocated to employees are:

- Price of the underlying share: €24.75 (based on the quoted market price of the ordinary shares of the Company as of the date of the Board of Directors that granted the BSPCE)
- Risk-free rate: between -0.18% and -0.11% according to the tranches (according to the zero-coupon government bond rates curve);
- Expected dividends: 0%;
- Volatility: 21.25% to 22.27% based on the historical volatility observed on the NextBiotech index;
- Expected maturity: between 5 and 5.51 years in function of the tranches allocated.

The residual fair value of the plan was estimated at &636 thousand. This expense will be recorded gradually over the duration of the 2-year plan in accordance with IFRS 2 (graded vesting method). A personnel expense of &245 thousand was recognized in the consolidated statement of income (loss) (R&D for &165 thousand and G&A for &161 thousand), for the year ended December 31, 2017, &498 thousand for the year ended December 31, 2016. &1,133 thousand were recognized for the year ended December 31, 2015 for the previous allocation.

#### <u>"2016 Plan"</u>

On October 3, 2016, the Board of Directors used the delegation granted by the mixed general shareholders meeting of June 24, 2016, to grant a free allocation including on a service condition of 111,261 free shares (hereinafter entitled AGAP<sub>2016</sub>) to ERYTECH Pharma S.A senior management and employees, 44,499 stock options (hereinafter entitled SO<sub>2016</sub>) to ERYTECH Pharma, Inc. and 45,000 share subscription warrants (hereinafter entitled BSA<sub>2016</sub>) to members of the Board of Directors.

At the end of 2017, the subscription warrants for the 2016 plan are as follows:

<b>20 000</b>
aa aaa
~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~
~~ ~~~
60,000
3-oct-16
8-jan-17
? <b>7-jun-1</b> 7
3-oct-17
2
che 1: 1 year
che 2: 2 years
NA
60,000

#### Allocation of 111,261 free shares (AGAP2016) on October 3, 2016

The assumptions used to determine the fair value of these instruments are:

- Price of the underlying share: €18.52 (based on the quoted market price of the ordinary shares of the Company as of the date of the Board of Directors that granted the AGAP)
- Attrition rate: 0%;
- Expected dividends: 0%;
- Volatility: 45% based on the historical volatility observed on the ERYP index;
- Repo margin: 5%
- Maturity: 3 years
- Performance criteria: progression of the quoted market share price between the allocation date and the tranche acquisition date
  - ERYP2017: average price of the 40-quoted market share price days before the allocation date, which was €24.48
  - ERYPi : average price of the 40-quoted market share price days before the acquisition date,
  - Tri: ERYPi / (ERYP2017-1)
    - If TRi <=0 % no shares granted are acquired If Tri>100% all the shares granted are acquired
    - If 0%<TRi<100% shares granted are acquired following the TRi percentage

The fair value of the plan was estimated at  $\notin$ 974 thousand. This expense will be recorded gradually over the duration of the 1-year, 2-year and 3-year plan in accordance with IFRS 2 (graded vesting method). An expense of  $\notin$ 533 thousand was recognized in the consolidated statement of income (loss) under R&D personnel expenses for  $\notin$ 217 thousand and under G&A personnel expenses for  $\notin$ 316 thousand, for the year ended December 31, 2017. For 2016 an expense of  $\notin$ 151 thousand was recognized in the consolidated statement of income (loss) under R&D personnel expenses for  $\notin$ 61 thousand and under G&A personnel expense for  $\notin$ 90 thousand.

### Allocation of 44,499 stock options (SO<sub>2016</sub>) on October 3, 2016

The assumptions used to determine the fair value of these instruments are:

- Exercise price: €18.52
- Price of the underlying share: €18.52 (based on the quoted market price of the ordinary shares of the Company as of the date of the Board of Directors that granted the SO)
- Attrition rate: 0%;
- Expected dividends: 0%;
- Volatility: 45% based on the historical volatility observed on the ERYP index;
- Repo margin: 5%
- Maturity: 3 years

The fair value of the plan was estimated at &202 thousand. This expense will be recorded gradually over the duration of the 2-year and 3-year plan in accordance with IFRS 2 (graded vesting method). An expense of &90 thousand was recognized in the consolidated statement of income (loss) under R&D personnel expenses for the year ended December 31, 2017. An expense of &22 thousand was recognized in the consolidated statement of income (loss) under R&D personnel expenses for the year ended December 31, 2016.

## Allocation of 45,000 share subscription warrants (BSA2016) on October 3, 2016

The assumptions used to determine the fair value of these instruments are:

- Exercise price: €18.52
- Price of the underlying share: €18.52 (based on the quoted market price of the ordinary shares of the Company as of the date of the Board of Directors that granted the BSA)
- Attrition rate: 0%;
- Expected dividends: 0%;
- Volatility: 45% based on the historical volatility observed on the ERYP index;
- Repo margin: 5%
- Maturity: 3 years

The fair value of the plan was estimated at  $\leq$ 198 thousand. This expense will be recorded gradually over the duration of the 2-year plan in accordance with IFRS 2 (graded vesting method). An expense of  $\leq$ 126 thousand was recognized in the consolidated statement of income (loss) under G&A expenses for the year ended December 31, 2017. An expense of  $\leq$ 37 thousand was recognized in the consolidated statement of income (loss) under G&A expenses for the year ended December 31, 2016.

## Allocation of 16,650 free shares (AGAP2016) on October 3, 2017

The assumptions used to determine the fair value of these instruments are:

- Price of the underlying share: €24.48 (based on the quoted market price of the ordinary shares of the Company as of the date of the Board of Directors that granted the AGAP)
- Attrition rate: 0%;



- Expected dividends: 0%;
- Volatility: 48% based on the historical volatility observed on the ERYP index;
- Repo margin: 5%
- Maturity: 3 years

The fair value of the plan was estimated at &180 thousand. This expense will be recorded gradually over the duration of the 1-year, 2-year and 3-year plan in accordance with IFRS 2 (graded vesting method). An expense of &27 thousand was recognized in the consolidated statement of income (loss) under R&D personnel expenses for &22 thousand and under G&A personnel expenses for &5 thousand, for the year ended December 31, 2017.

### Allocation of 30,000 stock options (SO2016) on October 3, 2017

The assumptions used to determine the fair value of these instruments are:

- Exercise price: €23.59
- Price of the underlying share: €24.70 (based on the quoted market price of the ordinary shares of the Company as of the date of the Board of Directors that granted the SO)
- Attrition rate: 0%;
- Expected dividends: 0%;
- Volatility: 48% based on the historical volatility observed on the ERYP index;
- Repo margin: 5%
- Maturity: 3 years

The fair value of the plan was estimated at &208 thousand. This expense will be recorded gradually over the duration of the 2-year and 3-year plan in accordance with IFRS 2 (graded vesting method). An expense of &23 thousand was recognized in the consolidated statement of income (loss) under R&D personnel expenses for &9 thousand and under G&A personnel expenses for &14 thousand, for the year ended December 31, 2017.

### Allocation of 16,650 free shares (AGA<sub>2016</sub>) on October 3, 2017

The assumptions used to determine the fair value of these instruments are:

- Price of the underlying share: €24.48 (based on the quoted market price of the ordinary shares of the Company as of the date of the Board of Directors that granted the AGA)
- Attrition rate: 0%;
- Expected dividends: 0%;
- Volatility: 48% based on the historical volatility observed on the ERYP index;
- Repo margin: 5%
- Maturity: 3 years

The fair value of the plan was estimated at  $\pounds$ 180 thousand. This expense will be recorded gradually over the duration of the 1-year, 2-year and 3-year plan in accordance with IFRS 2 (graded vesting method). An expense of  $\pounds$ 27 thousand was recognized in the consolidated statement of income (loss) under R&D personnel expenses for  $\pounds$ 22 thousand and under G&A personnel expenses for  $\pounds$ 5 thousand, for the year ended December 31, 2017.

#### Allocation of 30,000 stock options (SO<sub>2016</sub>) on October 3, 2017

The assumptions used to determine the fair value of these instruments are:

- Exercise price: €23.59
- Price of the underlying share: €23.59 (based on the quoted market price of the ordinary shares of the Company as of the date of the Board of Directors that granted the AGAP)
- Attrition rate: 0%;
- Expected dividends: 0%;
- Volatility: 48% based on the historical volatility observed on the ERYP index;
- Repo margin: 5%
- Maturity: 3 years

The fair value of the plan was estimated at &208 thousand. This expense will be recorded gradually over the duration of the 2-year and 3-year plan in accordance with IFRS 2 (graded vesting method). An expense of &23 thousand was recognized in the consolidated statement of income (loss) under R&D personnel expenses for &9 thousand and under G&A personnel expenses for &14 thousand, for the year ended December 31, 2017.

#### <u>"2017 Plan"</u>

On June 27, 2017 and on October 3, 2017, the Board of Directors used the delegation granted by the mixed general shareholders meeting of June 27, 2017, to grant a free allocation including a service condition of 83,127 free shares (hereinafter entitled AGAP<sub>2017</sub>) to ERYTECH Pharma S.A senior management and employees, 40,200 stock options (hereinafter entitled SO<sub>2017</sub>) to ERYTECH Pharma, Inc. and 55,000 share subscription warrants (hereinafter entitled BSA<sub>2017</sub>) to members of the Board of Directors.

At the end of 2017, the subscription warrants for the 2017 plan are as follows:

Types of securities	AGAP2017	SO2017	<b>BSA2017</b>
Number of shares that the company is authorized to issue		420,000	
Number of free shares / stock options / warrants granted	74,475	22,200	55,000
Date of General Meeting	27-June-17	27-June-17	27-June-17
Number of tranches	3	2	3
Vesting period	Tranche 1: 1 year	Tranche 1: 2 years	Tranche 1: 1 year
	Tranche 2: 2 years	Tranche 2: 3 years	Tranche 2: 2 years
	Tranche 3: 3 years		Tranche 3: 3 years
General conditions of exercise	NA	NA	NA
Maximum number of new shares that can be issued	74,475	22,200	55,000

### Allocation of 74,475 free shares (AGA2017) on June 27, 2017

The assumptions used to determine the fair value of these instruments are:

- Price of the underlying share: €26.47 (based on the quoted market price of the ordinary shares of the Company as of the date of the Board of Directors that granted the AGAP)
- Attrition rate: 0%;
- Expected dividends: 0%;
- Volatility: 48% based on the historical volatility observed on the ERYP index;
- Repo margin: 5%
- Maturity: 3 years
- Performance criteria: progression of the quoted market share price between the allocation date and the tranche acquisition date
  - ERYP2017: average price of the 40-quoted market share price days before the allocation date, which was €24.48
  - ERYPi: average price of the 40-quoted market share price days before the acquisition date,
  - Tri: ERYPi / (ERYP2017-1)
    - If TRi <=0 % no shares granted are acquired
    - If Tri>100% all the shares granted are acquired
    - If 0%<TRi<100% shares granted are acquired following the TRi percentage

The fair value of the plan was estimated at  $\pounds$ 1,081 thousand. This expense will be recorded gradually over the duration of the 1-year, 2-year and 3-year plan in accordance with IFRS 2 (graded vesting method). An expense of  $\pounds$ 348 thousand was recognized in the consolidated statement of income (loss) under R&D personnel expenses for  $\pounds$ 180 thousand and under G&A personnel expenses for  $\pounds$ 168 thousand, for the year ended December 31, 2017.

### Allocation of 22,200 stock options (SO<sub>2017</sub>) on June 27, 2017

The assumptions used to determine the fair value of these instruments are:

- Exercise price: €26.47
- Price of the underlying share: €26.47 (based on the quoted market price of the ordinary shares of the Company as of the date of the Board of Directors that granted the SO)

- Attrition rate: 0%;
- Expected dividends: 0%;
- Volatility: 48% based on the historical volatility observed on the ERYP index;
- Repo margin: 5%
- Maturity: 3 years

The fair value of the plan was estimated at &308 thousand. This expense will be recorded gradually over the duration of the 3-year plan in accordance with IFRS 2 (graded vesting method). An expense of &65 thousand was recognized in the consolidated statement of income (loss) under R&D personnel expenses for &50 thousand and under G&A personnel expenses for &15 thousand, for the year ended December 31, 2017.

## Allocation of 55,000 share subscription warrants (BSA2017) on June 27, 2017

The assumptions used to determine the fair value of these instruments are:

- Exercise price: €26.47
- Price of the underlying share: €26.47 (based on the quoted market price of the ordinary shares of the Company as of the date of the Board of Directors that granted the AGA)
- Attrition rate: 0%;
- Expected dividends: 0%;
- Volatility: 48% based on the historical volatility observed on the ERYP index;
- Repo margin: 5%
- Maturity: 3 years

The fair value of the plan was estimated at &394 thousand. This expense will be recorded gradually over the duration of the 2-year plan in accordance with IFRS 2 (graded vesting method). An expense of &165 thousand was recognized in the consolidated statement of income (loss) under G&A expenses for the year ended December 31, 2017.

## Breakdown of allocations plan

Plan name	Amount in P&L in euros thousands as of December 31, 2017	of which employees	of which Executive	of which Directors
Allocation of AGAP on 3 October 2016	533	250	283	
Allocation of SO on 3 October 2016	90	45	44	_
Allocation of BSA on 3 October 2016	126	_	_	126
Allocation of AGAP on 7 January 2017	92	—	92	—
Allocation of SO on 7 January 2017	46	46	—	—
Allocation of BSA on 7 January 2017	10		—	10
Total allocation October, 2016	896	341	419	135
Allocation of BSPCE on 6 May 2016	138	94	44	
Allocation of BSPCE on 22 January 2014	7	_	7	—
Allocation of BSPCE on 1 September 2015	51	—	51	—
Allocation of BSA on 23 June 2015	50	—	50	—
Total allocation 2014	245	94	152	
Allocation of AGAP on 26 June 2017	348	156	192	
Allocation of SO on 26 June 2017	65	44	21	—
Allocation of BSA on 26 June 2017	165	_	_	165
Total allocation June, 2017	578	200	213	165
Allocation of AGAP on 3 October 2017	27	27		
Allocation of SO on 3 October 2017	23	23	_	_
Total allocation October, 2017	49	49		
TOTAL IFRS 2 EXPENSES	1,769	685	784	300
	Amount in P&L in euros thousands as of December 31,	of which	of which	of which
Plan name	P&L in euros thousands as of December 31, 2016	<u>employees</u>	Executive	of which <u>Directors</u>
Allocation of AGAP on 3 October 2016	P&L in euros thousands as of December 31, <u>2016</u> 151	employees 71	<u>Executive</u> 80	
Allocation of AGAP on 3 October 2016 Allocation of SO on 3 October 2016	P&L in euros thousands as of December 31, 2016 151 22	<u>employees</u> 71 11	Executive	<u>Directors</u> — —
Allocation of AGAP on 3 October 2016 Allocation of SO on 3 October 2016 Allocation of BSA on 3 October 2016	P&L in euros thousands as of December 31, <u>2016</u> 151	employees 71	<u>Executive</u> 80	
Allocation of AGAP on 3 October 2016 Allocation of SO on 3 October 2016 Allocation of BSA on 3 October 2016 Allocation of AGAP on 7 January 2017	P&L in euros thousands as of December 31, 2016 151 22	<u>employees</u> 71 11 —	<u>Executive</u> 80 11 —	<u>Directors</u> — — 37
Allocation of AGAP on 3 October 2016 Allocation of SO on 3 October 2016 Allocation of BSA on 3 October 2016 Allocation of AGAP on 7 January 2017 Allocation of SO on 7 January 2017	P&L in euros thousands as of December 31, 2016 151 22 37 — —	<u>employees</u> 71 11 — — —	<u>Executive</u> 80	<u>Directors</u> — —
Allocation of AGAP on 3 October 2016Allocation of SO on 3 October 2016Allocation of BSA on 3 October 2016Allocation of AGAP on 7 January 2017Allocation of SO on 7 January 2017Allocation of BSA on 7 January 2017	P&L in euros thousands as of December 31, 2016 151 22 37 — — — —	<u>employees</u> 71 11 — — —	Executive 80 11 — — —	<u>Directors</u> — — 37 — —
Allocation of AGAP on 3 October 2016Allocation of SO on 3 October 2016Allocation of BSA on 3 October 2016Allocation of AGAP on 7 January 2017Allocation of SO on 7 January 2017Allocation of BSA on 7 January 2017	P&L in euros thousands as of December 31, 2016 151 22 37    210	<u>employees</u> 71 11 — — — — 82	Executive 80 11 — — — — 91	<u>Directors</u> — — 37
Allocation of AGAP on 3 October 2016Allocation of SO on 3 October 2016Allocation of BSA on 3 October 2016Allocation of AGAP on 7 January 2017Allocation of SO on 7 January 2017Allocation of BSA on 6 May 2016	P&L in euros thousands as of December 31, 2016 151 22 37 — — — — — — — — — — — — — — — — — —	<u>employees</u> 71 11 — — —	<u>Executive</u> 80 11 — — — — — — 91 159	<u>Directors</u> — — 37 — —
Allocation of AGAP on 3 October 2016Allocation of SO on 3 October 2016Allocation of BSA on 3 October 2016Allocation of AGAP on 7 January 2017Allocation of SO on 7 January 2017Allocation of BSA on 7 January 2017Allocation of BSPCE on 6 May 2016Allocation of BSPCE on 22 January 2014	P&L in euros thousands as of December 31, 2016 151 22 37 —— —— —— —— —— —— —— —— —— —— —— —— ——	<u>employees</u> 71 11 — — — — 82	<u>Executive</u> 80 11 — — — — — 91 159 21	<u>Directors</u> — — 37 — —
Allocation of AGAP on 3 October 2016Allocation of SO on 3 October 2016Allocation of BSA on 3 October 2016Allocation of AGAP on 7 January 2017Allocation of SO on 7 January 2017Allocation of BSA on 7 January 2017Allocation of BSA on 7 January 2017Total allocation 10.2016Allocation of BSPCE on 6 May 2016Allocation of BSPCE on 22 January 2014Allocation of BSPCE on 1 September 2015	P&L in euros thousands as of December 31, 2016 151 22 37 —— —— —— —— —— —— —— —— —— —— —— —— ——	<u>employees</u> 71 11 — — — — — <u>82</u> 339 — —	Executive 80 11 — — — — — — 91 159 21 261	<u>Directors</u> — — 37 — —
Allocation of AGAP on 3 October 2016Allocation of SO on 3 October 2016Allocation of BSA on 3 October 2016Allocation of AGAP on 7 January 2017Allocation of SO on 7 January 2017Allocation of BSA on 7 January 2017 <b>Total allocation 10.2016</b> Allocation of BSPCE on 6 May 2016Allocation of BSPCE on 1 September 2015Allocation of BSA on 23 June 2015	P&L in euros thousands as of December 31, 2016 22 37 —— —— —— —— —— —— —— —— —— —— —— —— ——	<u>employees</u> 71 11 — — — — — <u>82</u> 339 — — — — —	Executive 80 11 — — — — — — — — — 91 159 21 261 187	<u>Directors</u> — — 37 — —
Allocation of AGAP on 3 October 2016Allocation of SO on 3 October 2016Allocation of BSA on 3 October 2016Allocation of AGAP on 7 January 2017Allocation of SO on 7 January 2017Allocation of BSA on 7 January 2017Total allocation 10.2016Allocation of BSPCE on 6 May 2016Allocation of BSPCE on 1 September 2015Allocation of BSA on 23 June 2015Total allocation 2014	P&L in euros thousands as of December 31, 2016 151 22 37 —— —— —— —— —— —— —— —— —— —— —— —— ——	<u>employees</u> 71 11 — — — — — <u>82</u> 339 — —	Executive 80 11 — — — — — — 91 159 21 261	<u>Directors</u> — — 37 — —
Allocation of AGAP on 3 October 2016Allocation of SO on 3 October 2016Allocation of BSA on 3 October 2016Allocation of AGAP on 7 January 2017Allocation of SO on 7 January 2017Allocation of BSA on 7 January 2017Allocation of BSA on 7 January 2017Total allocation 10.2016Allocation of BSPCE on 6 May 2016Allocation of BSPCE on 1 September 2015Allocation of BSA on 23 June 2015Total allocation 2014Allocation of BSA on 26 June 2017	P&L in euros thousands as of December 31, 2016 22 37 —— —— —— —— —— —— —— —— —— —— —— —— ——	<u>employees</u> 71 11 — — — — — <u>82</u> 339 — — — — —	Executive 80 11 — — — — — — — — — 91 159 21 261 187	<u>Directors</u> — — 37 — —
Allocation of AGAP on 3 October 2016Allocation of SO on 3 October 2016Allocation of BSA on 3 October 2016Allocation of AGAP on 7 January 2017Allocation of SO on 7 January 2017Allocation of BSA on 7 January 2017 <b>Total allocation 10.2016</b> Allocation of BSPCE on 6 May 2016Allocation of BSPCE on 22 January 2014Allocation of BSPCE on 1 September 2015Allocation of BSA on 23 June 2015 <b>Total allocation 2014</b> Allocation of BSA on 26 June 2017Allocation of SO on 26 June 2017	P&L in euros thousands as of December 31, 2016 22 37 —— —— —— —— —— —— —— —— —— —— —— —— ——	<u>employees</u> 71 11 — — — — — <u>82</u> 339 — — — — —	Executive 80 11 — — — — — — — — — 91 159 21 261 187	<u>Directors</u> — — 37 — —
Allocation of AGAP on 3 October 2016Allocation of SO on 3 October 2016Allocation of BSA on 3 October 2016Allocation of AGAP on 7 January 2017Allocation of SO on 7 January 2017Allocation of BSA on 7 January 2017Allocation of BSA on 7 January 2017 <b>Total allocation 10.2016</b> Allocation of BSPCE on 6 May 2016Allocation of BSPCE on 1 September 2015Allocation of BSA on 23 June 2015 <b>Total allocation 2014</b> Allocation of BSA on 26 June 2017Allocation of SO on 26 June 2017	P&L in euros thousands as of December 31, 2016 22 37 —— —— —— —— —— —— —— —— —— —— —— —— ——	<u>employees</u> 71 11 — — — — — <u>82</u> 339 — — — — —	Executive 80 11 — — — — — — — — — 91 159 21 261 187	<u>Directors</u> — — 37 — —
Allocation of AGAP on 3 October 2016Allocation of SO on 3 October 2016Allocation of BSA on 3 October 2016Allocation of AGAP on 7 January 2017Allocation of SO on 7 January 2017Allocation of BSA on 7 January 2017Allocation of BSA on 7 January 2017 <b>Total allocation 10.2016</b> Allocation of BSPCE on 6 May 2016Allocation of BSPCE on 22 January 2014Allocation of BSPCE on 1 September 2015Allocation of BSA on 23 June 2015 <b>Total allocation 2014</b> Allocation of SO on 26 June 2017Allocation of SO on 26 June 2017Allocation of BSA on 26 June 2017Allocation of BSA on 26 June 2017Allocation of BSA on 26 June 2017	P&L in euros thousands as of December 31, 2016 22 37 —— —— —— —— —— —— —— —— —— —— —— —— ——	<u>employees</u> 71 11 — — — — — <u>82</u> 339 — — — — —	Executive 80 11 — — — — — — — — — 91 159 21 261 187	<u>Directors</u> — — 37 — —
Allocation of AGAP on 3 October 2016Allocation of SO on 3 October 2016Allocation of BSA on 3 October 2016Allocation of AGAP on 7 January 2017Allocation of SO on 7 January 2017Allocation of BSA on 7 January 2017Allocation of BSA on 7 January 2017Total allocation 10.2016Allocation of BSPCE on 6 May 2016Allocation of BSPCE on 22 January 2014Allocation of BSPCE on 1 September 2015Allocation of BSA on 23 June 2015Total allocation 2014Allocation of AGAP on 26 June 2017Allocation of BSA on 26 June 2017Allocation of BSA on 30 Ctober 2017Allocation of AGAP on 3 October 2017	P&L in euros thousands as of December 31, 2016 22 37 —— —— —— —— —— —— —— —— —— —— —— —— ——	<u>employees</u> 71 11 — — — — — <u>82</u> 339 — — — — —	Executive 80 11 — — — — — — — — — 91 159 21 261 187	<u>Directors</u> — — 37 — —
Allocation of AGAP on 3 October 2016Allocation of SO on 3 October 2016Allocation of BSA on 3 October 2016Allocation of AGAP on 7 January 2017Allocation of SO on 7 January 2017Allocation of BSA on 7 January 2017Allocation of BSA on 7 January 2017 <b>Total allocation 10.2016</b> Allocation of BSPCE on 6 May 2016Allocation of BSPCE on 22 January 2014Allocation of BSPCE on 22 January 2014Allocation of BSPCE on 1 September 2015Allocation of BSA on 23 June 2015 <b>Total allocation 2014</b> Allocation of AGAP on 26 June 2017Allocation of SO on 26 June 2017Allocation of BSA on 23 October 2017Allocation of AGAP on 3 October 2017Allocation of SO on 3 October 2017	P&L in euros thousands as of December 31, 2016 22 37 —— —— —— —— —— —— —— —— —— —— —— —— ——	<u>employees</u> 71 11 — — — — — <u>82</u> 339 — — — — —	Executive 80 11 — — — — — — — — — 91 159 21 261 187	<u>Directors</u> — — 37 — —
Allocation of AGAP on 3 October 2016Allocation of SO on 3 October 2016Allocation of BSA on 3 October 2016Allocation of AGAP on 7 January 2017Allocation of SO on 7 January 2017Allocation of BSA on 7 January 2017Allocation of BSA on 7 January 2017Total allocation 10.2016Allocation of BSPCE on 6 May 2016Allocation of BSPCE on 22 January 2014Allocation of BSPCE on 1 September 2015Allocation of BSA on 23 June 2015Total allocation 2014Allocation of AGAP on 26 June 2017Allocation of BSA on 26 June 2017Allocation of BSA on 30 Ctober 2017Allocation of AGAP on 3 October 2017	P&L in euros thousands as of December 31, 2016 22 37 —— —— —— —— —— —— —— —— —— —— —— —— ——	<u>employees</u> 71 11 — — — — — <u>82</u> 339 — — — — —	Executive 80 11 — — — — — — — — — 91 159 21 261 187	<u>Directors</u> — — 37 — —

Plan name	Amount in P&L in euros thousands as of December 31, 2015	of which employees	of which Executive	of which Directors
Allocation of BSPCE on 22 January 2014	12		12	
Allocation of BSPCE on 23 June 2015	517	517	—	_
Allocation of BSPCE on 1 September 2015	209	—	209	
Allocation of BSA on 23 June 2015	385		385	
Total plan 2014	1,124	517	607	—
Allocation of BSA on 29 April 2015	512			512
Allocation of BSA on 31 August 2015	1,081	_	_	1,081
Total plan 2012	1,593			1,593
TOTAL IFRS 2 EXPENSES	2,716	517	607	1,593

# 5.4 Depreciation and amortization expense

	For the	For the year ended December 31,		
	2015	2016	2017	
(in thousands of euros)				
Clinical studies	224	252	169	
Other research and development expenses	26	26	94	
Research and development expenses	250	277	263	
General and administrative expenses	39	148	266	
Total	288	425	530	

### 5.5 Financial income and expense

	For the year ended December 31,		
	2015	2016	2017
(in thousands of euros)			
Interest expense on finance leases	(5)	(4)	(8)
Interest expense related to borrowings	—	_	(7)
Interest expense on repayable loan	(25)	—	
Other finance expenses	(34)	(66)	(3,168)
Total finance expense	(64)	(70)	(3,183)
Income from short term deposits	523	545	405
Other finance income	108	13	134
Total finance income	631	558	539
	567	488	(2,644)

Other finance expenses are related to foreign currency exchange losses related to the bank account in U.S. dollars and purchases of services in U.S. dollars.

Finance income consists of interest accrued on short term deposits as well as foreign exchange gains related to purchases of services in U.S. dollars.

Financial expenses increased significantly by &3,113 thousand as at December 31, 2017. These financial expenses are related mainly to the conversion into euros of the USD bank account as at December 31, 2017. The impact in the financial result is the difference of the exchange rate between the date of the global offering in the United States and a listing on Nasdaq (1&=1.1630& on November 9, 2017) and the closing of the period (1&=1.1993& on December 31, 2017).

## 5.6 Deferred tax balances

## Reconciliation of effective tax rate

	1 2015	For the year ended December 31, 2016	2017
(in thousands of euros)			(
Loss before tax	(15,016)	(21,902)	(33,533)
Theoretical tax expense or income	5,170	7,541	11,545
Current year loss not capitalized	(5,001)	(8,303)	(12,071)
CICE (employment and competitiveness tax credit) not included in taxable income	18	24	34
Research tax credits	764	1,144	1,097
Tax rate differences	(7)	(51)	0
Share-based compensation expense	(935)	(398)	(592)
Permanent differences			(10)
Other differences	(6)	33	0
Effective tax (loss)/income	3	(10)	3

As of December 31, 2015, 2016 and 2017, the amount of accumulated tax loss carryforwards since inception was €59,682 thousand, €80,281 thousand and €128,802 thousand respectively with no expiration date. The tax proof has been calculated based on the French tax rate which is 34.43%.

### **6** Notes related to the consolidated statements of financial position

### 6.1 Intangible assets

	As of December 31,		31,
(in thousands of euros)	2015	2016	2017
Other intangible assets	184	209	234
Total historical cost	184	209	234
Accumulated amortization of other intangible assets	(122)	(152)	(180)
Total accumulated amortization and depreciation	(122)	(152)	(180)
Total, net	61	57	53

## 6.2 Property, plant and equipment

At December 31, 2017, property, plant and equipment are composed as follows:

(in thousands of euros)	As of January 1, 2017	Increase	Decrease	As of December 31, 2017
Laboratory equipment	974	merease	Decrease	974
Assets under construction	862	868		1,730
Plant, equipment, and tooling	850	270		1,121
General equipment, fixtures and fittings	1,466	389	—	1,855
Office equipment and computers	531	137		668
Total gross value	4,684	1,664		6,349
Accumulated depreciation of laboratory equipment	(882)	(48)		(930)
Accumulated depreciation of plant, equipment and tooling	(523)	(118)		(641)
Accumulated depreciation of general equipment, fixtures and fittings	(909)	(207)		(1,116)
Accumulated depreciation of office equipment and computers	(125)	(129)		(255)
Total accumulated depreciation	(2,439)	(503)		(2,439)
Total net value	2,245	1,161		3,407

Property, plant and equipment held under finance leases amounts to €203 thousand and €116 thousand as of December 31, 2016 and 2017, respectively.

At December 31, 2016, property, plant and equipment are composed as follows:

(in thousands of euros)	As of January 1, 2016	Increase	Decrease	As of December 31, 2016
Laboratory equipment	974			974
Assets under construction	44	862	(44)	862
Plant, equipment, and tooling	727	123		850
General equipment, fixtures and fittings	1,079	387		1,466
Office equipment and computers	134	397		531
Total gross value	2,958	1,770	(44)	4,684
Accumulated depreciation of laboratory equipment	(831)	(51)	_	(882)
Accumulated depreciation of plant, equipment and tooling	(426)	(98)		(523)
Accumulated depreciation of general equipment, fixtures and fittings	(733)	(175)		(909)
Accumulated depreciation of office equipment and computers	(51)	(74)	—	(125)
Total accumulated depreciation	(2,041)	(398)		(2,439)
Total net value	918	1,372	(44)	2,245

Property, plant and equipment held under finance leases amounts to €143 thousand and €203 thousand as of December 31, 2015 and 2016, respectively.

At December 31, 2015, property, plant and equipment are composed as follows:

(in thousands of euros)	As of January 1, 2015	Increase	Decrease	As of December 31, 2015
Laboratory equipment	974			974
Assets under construction	112	29	(98)	44
Plant, equipment, and tooling	617	110	_	727
General equipment, fixtures and fittings	959	120	_	1,079
Office equipment and computers	76	59		134
Total gross value	2,738	318	(98)	2,958
Accumulated depreciation of laboratory equipment	(753)	(78)		(831)
Accumulated depreciation of plant, equipment and tooling	(346)	(79)		(426)
Accumulated depreciation of general equipment, fixtures and fittings	(636)	(98)		(733)
Accumulated depreciation of office equipment and computers	(36)	(15)	—	(51)
Total accumulated depreciation	(1,771)	(270)		(2,041)
Total net value	967	48	(98)	918

## 6.3 Other non-current financial assets

The other non-current financial assets correspond mainly to deposits paid in relation to the rental of our premises for  $\notin$ 97 thousand,  $\notin$ 132 thousand and  $\notin$ 168 thousand as of December 31, 2015, 2016 and 2017, respectively.

### **6.4 Inventories**

	As o	As of December 31,		
	2015	2016	2017	
(in thousands of euros)				
Production inventory	79	71	104	
Laboratory inventory	87	74	72	
Total inventory	166	145	176	

### 6.5 Trade and other receivables

The receivables relate mainly to the receivables on Orphan Europe as regards the re-invoicing of the clinical studies AML 2012-10 and NOPHO, and amounted to  $\notin$ 424 thousand,  $\notin$ 218 thousand and  $\notin$ 76 thousand as of December 31, 2015, 2016 and 2017, respectively.

#### 6.6 Other current assets

	As of December 31,		
	2015	2016	2017
(in thousands of euros)			
Research Tax Credit	3,743	3,321	3,326
Tax receivables (e.g. VAT) and other receivables	1,190	863	1,114
Cash to be received from bank related to exercise of warrants	553		23
Prepayments	220	339	1,327
Total	5,705	4,524	5,791

#### Research Tax Credit

The Company benefits from the provisions in Articles 244 *quater* B and 49 *septies* F of the French Tax Code related to the Research Tax Credit. In compliance with the principles described in Note 4.16, the Research Tax Credit is recognized in the consolidated statement of income (loss) in "other income" during the year in which the eligible research expenditures are incurred.

The amount as of December 31, 2017 is mainly the CIR receivable for the 2017 period.

Prepayments as at December 31, 2017 relate to the building leases for 2018 first quarter, the D&O insurance for one-year period amounting to €373 thousand and an invoice received for a payment in advance for purchase ordered from MEDAC for an amount of €570 thousand, for which the payment in advance occurred in January 2018.

#### 6.7 Cash and cash equivalents

	As of December 31,		31,
(in thousands of euros)	2015	2016	2017
Cash and cash equivalents	45,634	37,646	185,525
Total cash and cash equivalents as reported in statement of financial position	45,634	37,646	185,525
Bank overdrafts			10
Total cash and cash equivalents as reported in statement of cash flow	45,634	37,646	185,515

At December 31, 2015, the cash position is composed of the following items: (i)  $\notin$  20.2 million in current accounts and (ii)  $\notin$  25.4 million in term deposits, with maturities of 1 month to 3 years, but readily available without penalty subject to a 32-day notice.

At December 31, 2016, the cash position is composed of the following items: (i)  $\in$  10.6 million in current accounts and (ii)  $\in$  27.0 million in term deposits, with maturities of 1 month to 3 years, but readily available without penalty subject to a 32-day notice.

At December 31, 2017, the cash position is composed of the following items: (i)  $\notin$ 174.5 million in current accounts and (ii)  $\notin$ 11.0 million in term deposits, with a maturity as of January 1, 2019, but readily available without penalty subject to a 32-day notice.

#### 6.8 Shareholders' equity

We manage our capital to ensure that the Company will be able to continue as a going concern while maximizing the return to shareholders through the optimization of the debt and equity balance. Our capital structure consists of financial liabilities as detailed in Notes 6.10 offset by cash and bank balances and equity (comprising issued capital, reserves and retained earnings). We are not subject to any externally imposed capital requirements.

As of December 31, 2016, the capital of the Parent Company consisted of 8,732,648 shares, fully paid up, with a nominal value of 0.10 euro. Following the private placement completed in April 2017 and the IPO in November 2017, as well as the exercise of subscription warrants, the capital was increased to 17,937,559 shares with a nominal value of 0.10 euro as at December 31, 2017.

Nature of transactions	Number of shares
Balance as of January 1, 2015	6,882,761
Exercise of share warrants	101,850
Private placement with institutional investors	940,000
Balance as of January 1, 2016	7,924,611
Follow-on offering	793,877
Exercise of share warrants	14,160
Balance as of January 1, 2017	8,732,648
Exercise of share warrants	17,200
Free shares / Stock options / Share warrants	7,574
Private placement with institutional investors in April	3,000,000
Initial Public Offering (including 5,389,021 ordinary shares in the form of ADSs)	6,180,137
Total as of December 31, 2017	17,937,559

The costs of issuing ordinary shares amounted to €16,722 thousand and were deducted from the share premium increase. These costs were related to bank fees, legal counsels, advisors and auditors' fees.

### Basic earnings per share and diluted earnings (loss) per share

	For the year ended December 31,		
(in thousands of euros)	2015	2016	2017
Net loss (in thousands of euros)	(15,013)	(21,913)	(33,530)
Weighted number of shares for the period	6,957,654	7,983,642	11,370,557
Basic loss per share (€/share)	(2,16)	(2.74)	(2.95)
Diluted loss per share (€/share)	(2.16)	(2.74)	(2.95)

At December 31, 2015, 2016 and 2017, the potential shares that could be issued within the context of exercising warrants issued (455,330, 626,000 and 858,186 as at December 31, 2015, 2016 and 2017, respectively) were not taken into consideration in the calculation of the diluted earnings, as their effect would be anti-dilutive.

2,500 shares are held by the Company as treasury shares (and recognized as a deduction of shareholders' equity) and will be cancelled.

#### **6.9** Provisions

The provisions can be detailed as follows:

		As of		
	D	December 31,		
(in thousands of euros)	2015	2016	2017	
Provision for retirement indemnities	<u>2015</u> 100	163	2017 214	
Provisions for disputes	81			
Total	181	163	214	

The regime for retirement indemnities applicable at the Parent Company, is defined by the collective agreement for the pharmaceutical industry in France.

The Company recognizes actuarial differences in other comprehensive income. The pension commitments are not covered by plan assets. The portion of the provision for which the maturity is less than one year is not significant.

As part of the estimate of the retirement commitments, the following assumptions were used for all categories of employees:

	2015	2016	2017
Discount rate	2.03%	1.36%	1.30%
Wage increase	2%	2%	2%
Social welfare contribution rate	Non-executive 44%	Non-executive 44%	Non-executive 44%
	Executive 54%	Executive 54%	Executive 54%
Expected staff turnover	0-10%	0-10%	0-10%
Age of retirement:	65-67 years	65-67 years	65-67 years
Mortality table	INSEE 2014	<b>INSEE 2014</b>	<b>INSEE 2014</b>

The Company has settled the dispute with BPI France related to the GR-SIL subsidy for &1 thousand as well as the residual conditional advance for &23 thousand. The reimbursement was made in January 2016 for &104 thousand.

The breakdown of provisions is as follows:

Closing
100
81
181
163
—
163
214
—
214

(1) The "Other" differences relate to actuarial gains and losses

## 6.10 Financial liabilities

## Financial liabilities by type

	As of December 31,		
(in thousands of euros)	2015	2016	2017
Financial liabilities related to finance leases	144	204	117
Bank overdrafts	—	—	11
Conditional advances	563	1,182	1,182
Bank loans		1,480	1,534
Total financial liabilities	707	2,865	2,843

## Financial liabilities by maturity

Maturity dates of financial liabilities as of December 31, 2015 are as follows:

(in thousands of euros) Financial liabilities	Less than one year	One to three years	Three to five years	More than five years	<u>Total</u>
Bank loans			—		_
Conditional advances	501			63	563
Liabilities related to leases	56	88			144
Total financial liabilities	556	88		63	707

Maturity dates of financial liabilities as of December 31, 2016 are as follows:

(in thousands of euros) Financial liabilities	Less than one year	One to three years	Three to five years	More than five years	Total
Bank loans		1,480			1,480
Conditional advances		—		1,182	1,182
Liabilities related to leases	50	154	—	—	204
Total financial liabilities	50	1,634		1,182	2,865

Maturity dates of financial liabilities as of December 31, 2017 are as follows:

(in thousands of euros)	Less than one year	One to three years	Three to five years	More than five years	Total
Financial liabilities					
Bank loans	735	799		_	1,534
Conditional advances	—	—	—	1,182	1,182
Liabilities related to leases	79	39	—	—	117
Bank overdrafts	11				11
Total financial liabilities	824	838		1,182	2,843

The company has received a bank loan amounting to €1.900 thousand with Société Générale with a 0.4% interest rate and 36 monthly repayment terms to finance its investments.

The conditional advances from public authorities relate to contracts with BPI France. The Company has three contracts related to conditional advances with BPI France. These advances are not interest-bearing and are 100% repayable (nominal value) in the event of technical and/or commercial success.

Under IFRS, the fact that a conditional advance does not require an annual interest payment is akin to obtaining a zero-interest loan, i.e., more favorable than market conditions. The difference between the amount of the advance at its historical cost and that of the advance discounted at the risk-free rate (10 year forward bonds) increased by an estimated credit spread is considered to be a grant received from the State. These grants are recognized in the consolidated statement of net income (loss) over the estimated duration of the projects financed by these advances.

The portion of the conditional advances due in more than one year is recorded under financial debts—non-current portion, while the portion due in less than one year is recorded under financial debts—current portion.

Since its creation, the Company has received 3 conditional advances from BPI France, repayable under certain conditions. The main terms of the agreements as well as the balances as of December 31, 2016 and 2017 respectively are presented below:

Conditional advances (amounts received/paid)	€ '000
Conditional advance granted by BPI France / Pancreas project	735
Conditional advance granted by BPI France / GR-SIL project	81
Conditional advance granted by BPI France / Tedac project	63
Total conditional advances granted by BPI France as of 31 December 2012 (nominal	
value)	879
Effect of the discount	(122)
Total conditional advances granted by BPI France as of 31 December 2012 (present	
value)	757
Repayment in 2013	(115)
Of which BPI France / Pancreas project	(100)

Of which GR-SIL project	(15)
Interest capitalized in 2013	52
Financial liabilities as of December 31, 2013	694
Repayment in 2014	(184)
Of which BPI France / Pancreas project	(150)
Of which GR-SIL project	(34)
Interest capitalized in 2014	39
Financial liabilities as of December 31, 2014	549
Repayment in 2015	(9)
Interest capitalized in 2015	23
Financial liabilities as of December 31, 2015	563
Repayment in 2016	(508)
Of which BPI France / Pancreas project	(485)
Of which GR-SIL project	(23)
Conditional advance granted by BPI France / Tedac project	1,118
Interest capitalized in 2016	7
Financial liabilities as of December 31, 2016	1,181
Repayment in 2017	
Interest capitalized in 2017	_
Financial liabilities as of December 31, 2017	1,181

#### • BPI FRANCE / PANCREAS

The first conditional advance, granted by BPI France for a total amount of €735,000, related to the development of a new treatment against pancreatic cancer through the administration of allogenic red blood cells incorporating L-asparaginase program.

The repayment of this conditional advance was according to a fixed payment schedule that ended on June 30, 2016 following the last payment of €260,000.

As at December 31, 2017, all the payment due had been reimbursed (see below).

## • BPI FRANCE / GR-SIL

The second conditional advance, granted by BPI France, which provided for a total amount of €135,000, concerns a program for the preclinical validation of the encapsulation of interfering RNA for therapeutic use in red blood cells, notably to limit inflammation of the cirrhotic liver and/or prevent the development of hepatocellular carcinomas.

The Company has reimbursed the entire amount of the conditional advance in January 2016 for  $\leq 23$  thousand (representing the balance) and also reimbursed the related subsidy of  $\leq 81$  thousand to settle the dispute with BPI France.

## **BPI FRANCE / TEDAC:**

The third conditional advance, granted by BPI France within the scope of the TEDAC project, is for a total amount of €4,895,052. This conditional advance is paid upon completion of the following key milestones:

- €62,607 upon signature of the agreement (paid in 2012)
- €1,118,735 upon the milestones n°4
- the remainder upon calls for funds when key milestones are reached (not yet received)
- as at December 31, 2017, the Company has reached milestone n°4; the Company has received €1,181 thousand of reimbursable advances and €1,455 thousand of cumulated subsidies.

The Company undertakes to repay BPI France initially:

- a) an amount of €5,281,000 upon achieving cumulative sales (excluding VAT) equal to or greater than €10 million, according to the following payment schedule:
  - €500,000 at the latest on June 30 of the first year in which the cumulative sales condition is achieved,
  - €750,000 at the latest on June 30 of the second year,

  - €2,531,000 at the latest on June 30 of the fourth year,
- b) and, where applicable, an annuity equal to 50% of the income generated through the sale of intellectual property rights resulting from the project, within the limit of a total repayment of €5.3 million.

In a second phase, when the cumulative sales reach  $\leq 60,000,000$ , the Company undertakes to pay BPI France 2.5% of sales generated by the products developed within the project, limited to a total amount of  $\leq 15$  million over 15 years once sales begin.

#### 6.11 Trade and other payables

	As of December 31,			
(in thousands of euros)	2015	2016	2017	
Domestic vendors	1,904	2,802	2,335	
Foreign vendors	1,371	745	2,631	
Vendors—Accruals	498	1,292	3,211	
Other	(101)	(7)	(101)	
Total trade and other payables	3,672	4,832	8,076	

Trades and other payables have increased by  $\notin$  3,244 thousand as of December 31, 2017 of which  $\notin$  1,919 thousand relate to accruals. This trade and other payables increase is related to the increase in research and development activities in 2017.

The increase between 2015 and 2016 of €1,160 thousand is due to the same reason.

#### 6.12 Other current liabilities

	j	As of December 31,	
(in thousands of euros)	2015	2016	2017
Social liabilities, taxation and social security	1,241	1,465	2017 2,706
Deferred revenue		—	
Other payables	71	—	—
Total other current liabilities	1,311	1,465	2,706

The increase in other current liabilities between 2016 and 2017 is mainly due to the increase of accruals for bonuses and social tax on bonuses. The increase is related to the increase of wages and headcounts over the two periods.

## 6.13 Related parties

Related parties include the Chief Executive Officer of the Company Gil Beyen, members of the Board of Directors (6 Board members) and members of the executive committee (5 members).

The remuneration of directors and other members of the executive committee during the year amounted to  $\pounds$ 2,402 thousand for wages and  $\pounds$ 1,120 thousand for share based-payments (see Note 5.3).

		2017			2016			2015	
			Share			Share			Share
	Salary	Retirement	based	Salary	Retirement	based	Salary	Retirement	based
In thousand of euros	/ Fees	benefits	payments	/ Fees	benefits	payments	/ Fees	benefits	payments
Executive officers / VP and Qualified person	654	19	306	498	15	226	825	6	241
Executive committee	1,519	25	478	818	10	495	279	1	554
Board of directors	229		336	184	—	37	172	—	1,593
Total	2,402	44	1,120	1,500	25	758	1,276	7	2,387

The Company has no other related parties.

# 6. 14 Financial instruments recognized in the consolidated statement of financial position and effect on net income (loss)

As of December 31, 2015 (in thousands of euros)	Carrying amount on the statement of financial position (1)	Fair value through profit and loss	Loans and receivables	Debt at amortized cost	Fair value
Non-current financial assets	97		97		97
Trade and other receivables	424	—	424	—	424
Other current assets	5,705	_	5,705	—	5,705
Cash and cash equivalents (2)	45,634	45,634			45,634
Total financial assets	51,860	45,634	6,226	_	51,860
Financial liabilities – Non-current portion (3)	151			151	151
Financial liabilities – Current portion <sup>(3)</sup>	557	_		557	557
Trade payables and related accounts	3,672			3,672	3,672
Total financial liabilities	4,380			4,380	4,380

As of December 31, 2016 (in thousands of euros)	Carrying amount on the statement of financial position (1)	Fair value through profit and loss	Loans and receivables	Debt at amortized cost	Fair value
Non-current financial assets	132		132		132
Trade and other receivables	218	—	218	—	218
Other current assets	4,524	—	4,524	—	4,524
Cash and cash equivalents <sup>(2)</sup>	37,646	37,646			37,646
Total financial assets	42,520	37,646	4,874	_	42,520
Financial liabilities – Non-current portion (3)	2,816			2,816	2,816
Financial liabilities – Current portion (3)	50	—		50	50
Trade payables and related accounts	4,832			4,832	4,832
Total financial liabilities	7,697		_	7,697	7,697

	Carrying amount on the				
	statement of	Fair value		Debt at	
A. of December 21, 2017 (in the second of summe)	financial	through profit	Loans and	amortized	Tain malus
As of December 31, 2017 (in thousands of euros)	position (1)	and loss	receivables	cost	Fair value
Non-current financial assets	234	—	234	—	234
Trade and other receivables	76	—	76	—	76
Other current assets	5,790	—	5,790	—	5,790
Cash and cash equivalents (2)	185,525	185,525			185,525
Total financial assets	191,626	185,525	6,100	_	191,626
Financial liabilities – Non-current portion	2,019			2,019	2,019
Financial liabilities – Current portion <sup>(3)</sup>	824		—	824	824
Trade payables and related accounts (3)	8,076			8,076	8,076
Total financial liabilities	10,919			10,919	10,919

(1) The carrying amount of these assets and liabilities is a reasonable approximation of their fair value.

- (2) Cash and cash equivalents are comprised of money market funds and time deposit accounts, which are measured using level 1 and level 2 measurements, respectively.
- (3) The fair value of financial liabilities is determined using level 2 measurements.

#### 7 MANAGEMENT OF FINANCIAL RISKS

The principal financial instruments held by the Company are securities that are classified as cash and cash equivalents. The purpose of holding these instruments is to finance the ongoing business activities of the Company. It is not the Company's policy to invest in financial instruments for speculative purposes. The Company does not utilize derivatives.

The principal risks to which the Company is exposed are liquidity risk, foreign currency exchange risk, interest rate risk and credit risk.

#### Liquidity risk

The Company has been structurally loss-generating since its creation. The net cash flows used by the Company's operating activities were respectively  $\leq 14.6$  million,  $\leq 17.6$  million and  $\leq 24.7$  million for the years ended December 31, 2015, 2016 and 2017, respectively.

The Company does not believe that it is exposed to short-term liquidity risk, considering the cash and cash equivalents that it had available as of December 31, 2017, amounting to  $\in$ 185.5 million which was primarily cash at hand and term deposits that are convertible into cash immediately without penalty. Management believes that the amount of cash and cash equivalents available is sufficient to fund the Company's planned operations through the next twenty-four months.

Historically, the Company has financed its growth by strengthening its shareholders' equity in the form of capital increases and the issue of convertible bonds. The Company believes that the capital increase associated with its initial public offering completed in May 2013, as well as the capital increases completed in 2014, 2015, 2016 and a private placement and an initial public offering in 2017, enable the Company to continue as a going concern for at least the twenty-four-month period starting in January 1, 2018.

The contractual cash flows of the financial liabilities as at December 31, 2015, 2016 and 2017 are as follows:

(in thousands of euros)		(	Contractual cash flows			
As of December 31, 2015 Financial liabilities	Book value	Total	Less than one year	One to five years		
Bank loans	_	—		_		
Conditional advances	563	(570)	(507)	(63)		
Liabilities related to finance leases	144	(149)	(59)	(91)		
Trade payables and related accounts	3,672	(3,672)	(3,672)			
Total financial liabilities	4,380	(4,392)	(4,238)	(153)		

(in thousands of euros)		Contractual cash flows Less than On			
As of December 31, 2016	Book value	Total	one year	five years	
Financial liabilities					
Bank loans	1,480	(1,480)		(1,480)	
Conditional advances	1,182	(1,182)		(1,182)	
Liabilities related to finance leases	204	(149)	(59)	(91)	
Trade payables and related accounts	4,832	(4,832)	(4,832)		
Total financial liabilities	7,697	(7,644)	(4,891)	(2,753)	

(in thousands of euros)		<b>Contractual cash flows</b>			
As of December 31, 2017	Book value	Total	Less than one year	One to five years	
Financial liabilities					
Bank loans	1,534	(1,534)	(735)	(799)	
Conditional advances	1,182	(1,182)		(1,182)	
Liabilities related to finance leases	117	(117)	(79)	(39)	
Bank overdrafts	11	(11)	(11)		
Trade payables and related accounts	8,076	(8,076)	(8,076)	_	
Total financial liabilities	10,919	(10,919)	(8,900)	(2,020)	

### Foreign currency exchange risk

The Company's functional currency is the Euro. However, a significant portion of about 30% of its operating expenses is denominated in U.S. dollars (agency office in Cambridge, MA, cooperation relating to the production of clinical batches with the American Red Cross, business development consultants, consultants for the development of clinical trials in the United States, and various collaborations relating to tests and clinical projects in the United States). As a result, the Company is exposed to foreign exchange risk inherent in operating expenses incurred. The Company does not currently have revenues in euros, dollars nor in any other currency. Due to the relatively low level of these expenditures, the exposure to foreign exchange risk is unlikely to have a material adverse impact on the results of operations or financial position of the Company. However, this dependency is expected to increase, as the Company expects to perform clinical trials in the United States and, in the longer term, sell on this market. The Company will opt to use exchange rate hedging techniques. Expenses in U.S. Dollars totaled \$11,620 thousand during 2017. However, the EUR/USD rate rose considerably at the period end, reaching \$1.1993 per €1.00 at December 29, 2017, the last business day of 2017. As noted in Note 4.9, the Company does not use derivative financial instruments to hedge the foreign currency exchange risk.

Change in exchange rate (decrease) from 1% would have an impact as of December 31, 2017 of €102 thousand.

Change in exchange rate (decrease) from 5% would have an impact as of December 31, 2017 of €490 thousand.

Change in exchange rate (decrease) from 10% would have an impact as of December 31, 2017 of €935 thousand.

The bank account position held in USD amounted to \$113,385 thousand.

Change in exchange rate (decrease) from 1% would have an impact as of December 31, 2017 of €936 thousand.

Change in exchange rate (decrease) from 5% would have an impact as of December 31, 2017 of €4,502 thousand.

Change in exchange rate (decrease) from 10% would have an impact as of December 31, 2017 of €8,595 thousand.

As the Company further increases its business, particularly in the United States, the Company expects to face greater exposure to exchange rate risk.

#### Interest rate risk

The Company has very low exposure to interest rate risk. Such exposure primarily involves money market funds and time deposit accounts. Changes in interest rates have a direct impact on the rate of return on these investments and the cash flows generated.

The Company's currently outstanding bank loan bears interest at a fixed rate, and therefore the company is not subject to interest rate risk with respect to this loan.

The repayment flows of the conditional advances from BPI France are not subject to interest rate risk.

#### Credit risk

The credit risk related to the Company's cash and cash equivalents is not significant in light of the quality of the co-contracting financial institutions.

#### Inflation Risk

We do not believe that inflation has had a material effect on our business, financial condition or results of operations. If our costs were to become subject to significant inflationary pressures, we may not be able to fully offset such higher costs through price increases. Our inability or failure to do so could harm our business, financial condition and results of operations.

#### **8 OFF-BALANCE SHEET COMMITMENTS**

#### **Operating leases**

The off-balance sheet commitments relating to operating leases amount to €726 thousand and essentially correspond to the lease of buildings. The maturities on these expenses are as follows:

Less than 1 year: €484 thousand Between 1 year and 5 years: €242 thousand More than 5 years: €0

#### **Collaborative arrangements**

#### Agreement with Orphan Europe

In November 2012, the Company entered into a marketing agreement with Orphan Europe, a subsidiary of Recordati Group, to market and distribute GRASPA<sup>®</sup> for the treatment of ALL and AML in 38 countries in Europe, including all of the countries in the European Union. The Company received a payment of €5 million on signing the agreement, which provides for sharing in the development costs

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for GRASPA® in AML. The Company may be entitled to receive future payments of up to  $\notin$ 37.5 million, subject to the achievement of specified clinical, regulatory and commercial milestones. Orphan Europe will invest in the development costs for GRASPA® in AML, and we will receive a payment for product delivered and royalties on the sales for a total of up to 45% of the sale price. The agreement provides that Orphan Europe may automatically terminate the agreement, recoup certain expenses, and reduce milestone payments in the event that the intellectual property the Company would license to them under the agreement is deemed to be counterfeited or invalid.

## Agreement with the Teva Group

In March 2011, the Company entered into a partnership agreement with the Teva Group (through Abic Marketing Limited), or Teva, to distribute GRASPA® in Israel. Under the terms of the agreement, Teva will submit the request for approval of GRASPA® for ALL in Israel and is responsible for the marketing and distribution of GRASPA® in Israel. Teva will pay interim payments to the Company and will share net earnings of product sales in Israel with us. Early termination of the agreement may be requested by either party in the event of a change in control in the other party.

# SIGNATURES

The registrant hereby certifies that it meets all of the requirements for filing on Form 20-F and that it has duly caused and authorized the undersigned to sign this annual report on its behalf.

# ERYTECH Pharma S.A.

/s/ Gil Beyen

By: Gil Beyen Title: Chief Executive Officer

Date: April 24, 2018

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# **ERYTECH PHARMA** Corporation with a board of directors and a capital of 1,794,003.50 Euros Head office: 60 avenue Rockefeller (69008) LYON 479 560 013 Lyon Trade and Companies Register

# BYLAWS

## Updated by the Board of Directors on March 9, 2018

True copy certified by the Chairman of the Board of Directors and Chief Executive Officer

Gil BEYEN

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#### SECTION I

### FORM - NAME - CORPORATE PURPOSE HEAD OFFICE - DURATION

#### ARTICLE 1. FORM

The Company was established in the form of a French simplified limited company, by way of a private deed in Lyon on October 26, 2004.

The company was transformed into a corporation by decision of the Extraordinary General Meeting of September 29, 2005.

It exists and is shared between the owners of shares created after this date and all future shareholders, and is governed by laws and regulations in force, as well as by the present articles of incorporation.

## ARTICLE 2. NAME

The Company's name is:

#### ERYTECH PHARMA

In all deeds and documents created by the Company and intended for third parties, its name shall be immediately preceded or followed by the words "Société Anonyme" or the abbreviation "SA" and a declaration of its capital stock, head office, and registration number in the trade and companies register.

## ARTICLE 3. CORPORATE PURPOSE

The Company has the purpose, in France and in any country, of:

- The research, manufacture, import, distribution, and marketing of experimental drugs, drugs, devices, and medical equipment;
- the provision of all advisory services associated therewith;

and generally, all financial, commercial, industrial, civil, property, or security-related transactions, such as may directly or indirectly relate to one of the purposes specified or such as may facilitate their fulfillment.

The Company may act directly or indirectly and perform all these operations in any country, on its own behalf and on behalf of third parties, either alone or with third parties in a joint venture, association, grouping, or company, through the creation of new companies, contributions, partnerships, subscription, purchase of company securities or rights, merger, alliance, joint venture companies, or the obtaining or provision, under lease or management, of any assets and rights or other items.

## ARTICLE 4. HEAD OFFICE - BRANCHES

The Company's head office is located at: 60, avenue Rockefeller (69008) LYON.

It may be transferred to any location within the same French département or to a neighboring département by way of a simple decision of the Board of Directors, subject to the ratification this decision by the next ordinary general meeting, and to any other location by virtue of a decision by an extraordinary general meeting, subject to legal provisions in force.

In the event of a transfer decided on by the Board of Directors in conformity with the law, the Board is authorized to modify the articles of incorporation accordingly.

#### ARTICLE 5. DURATION - FINANCIAL YEAR

The Company's duration is set at 99 years from the date of its registration in the Trade and Companies Register, save in the event of extension or early dissolution.

The financial year begins on January 1 and ends on December 31.

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#### SECTION II

#### **CAPITAL - SHARES**

#### ARTICLE 6. ESTABLISHMENT OF THE CAPITAL

All the original shares constituting the initial capital represent cash contributions and have been fully paid up, as showing on the certificate issued by the Banque Populaire Loire et Lyonnais – Agence Lyon Monplaisir, custodian of the funds.

The total amount paid by the shareholders, i.e., thirty-nine thousand, two hundred and sixteen (39,216) Euros, has been deposited into an account in the Company's name at this bank.

In accordance with a resolution by the Combined General Meeting of December 31, 2004, the capital stock was increased to 41,770 Euros through the creation and issue of 2,554 new shares paid up in cash, for a nominal amount of 1 Euro each, fully paid up upon subscription.

In accordance with a resolution by the Extraordinary General Meeting of September 29, 2005, the capital stock was increased to 51,020 Euros through the creation and issue (i) of 6,266 new shares pursuant to share subscription warrants with a nominal value of 1 Euro each, which was fully paid up upon subscription, and (ii) 2,984 new shares paid up in cash, for a nominal value of 1 Euro each, fully paid up upon subscription.

In accordance with an Executive Board decision of October 3, 2006, the Company's capital stock was increased by 13,127 Euros through the issue of 13,127 class "P" shares with a nominal value of 1 Euro, fully paid up upon subscription.

In accordance with an Executive Board decision of December 21, 2006, the Company's capital stock was increased by 17,353 Euros through the issue of 17,353 class "O" shares with a nominal value of 1 Euro, fully paid up upon subscription.

In accordance with a resolution by the Combined General Meeting of December 22, 2006, the Company's capital stock was increased by 54,333 Euros, through the issue of 54,333 class "A" shares with a nominal value of 1 Euro, fully paid up upon subscription.

In accordance with an Executive Board decision of January 23, 2008, the Company's capital stock was increased by an amount of 54,333 Euros, through the creation of 54,333 new class A shares with a nominal value of 1 Euro, fully paid up upon subscription.

In accordance with an Executive Board decision of January 15, 2009, the Company's capital stock was increased by an amount of 54,333 Euros, through the creation of 54,333 new class A shares with a nominal value of 1 Euro, fully paid up upon subscription.

In accordance with an Executive Board decision of July 16, 2010, the Company's capital stock was increased by an amount of 63,283 Euros, through the creation of 63,283 new class A shares with a nominal value of 1 Euro, fully paid up upon subscription.

In accordance with an Executive Board decision of July 29, 2010, the Company's capital stock was increased by an amount of 7,573 Euros, through the creation of 7,573 new class A shares with a nominal value of 1 Euro, fully paid up upon subscription.

In accordance with a resolution by the Combined General Meeting of April 2, 2013, all the share classes were canceled and the existing preferential shares were all converted into common shares. As such, the Company's shares are all common shares.

In this same meeting, the nominal value of the Company's shares was divided by 10.

In accordance with Executive Board decisions of April 30, 2013 recognizing the listing of the Company's shares on the market NYSE Euronext Paris, the convertible bonds issued by the Company were converted into new shares. The Company's capital stock was increased by an amount of 86,206.80 Euros, from 315,355 Euros to 401,561.80 Euros through the issue of 862,068 shares with a nominal value of 0.10 Euro.

In accordance with resolutions of the Combined General Meeting of April 2, 2013 granting delegations of power to the Executive Board, and in accordance with Executive Board decisions of April 4, 2013, April 12, 2013, and April 30, 2013 making use of these delegations, the capital stock was increased by an amount of 152,433.40 Euros, from 401,561.80 Euros to 553,995.20 Euros, through the issue of 1,524,334 shares with a nominal value of 0.10 Euro.

In accordance with resolutions of the Combined General Meeting of May 21, 2012 granting delegations of power to the Executive Board/Board of Directors, and in accordance with Board of Directors' decisions of July 18, 2013 making use of these delegations, the capital stock was increased by an amount of 816 Euros, from 553,995.20 Euros to 554,811.20 Euros, through the issue of 8,160 shares with a nominal value of 0.10 Euro.

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In accordance with resolutions of the Combined General Meeting of May 21, 2012 granting delegations of power to the Executive Board/Board of Directors, and in accordance with Board of Directors' decisions of December 3, 2013 making use of these delegations, the capital stock was increased by an amount of 1,084 Euros, from 554,811.20 Euros to 555,895.20 Euros, through the issue of 10,840 shares with a nominal value of 0.10 Euro.

In accordance with resolutions of the Combined General Meeting of May 21, 2012 granting delegations of power to the Executive Board/Board of Directors, and in accordance with Board of Directors' decisions of May 5, 2014 making use of these delegations, the capital stock was increased by an amount of 762 Euros, from 555,895.20 Euros to 556,657.20 Euros, through the issue of 7,620 shares with a nominal value of 0.10 Euro.

In accordance with resolutions of the Extraordinary General Meeting of May 21, 2012 and the Combined General Meeting of June 17, 2014 granting delegations of power to the Executive Board/Board of Directors, and in accordance with the Board of Directors' decisions of December 4, 2014 making use of these delegations, the capital stock was increased by an amount of 131,618.90 Euros, from 556,657.20 Euros to 688,276.10 Euros, through the issue of 1,316,189 shares with a nominal value of 0.10 Euro.

In accordance with resolutions of the Extraordinary General Meeting of May 21, 2012 granting delegations of power to the Executive Board/Board of Directors, and in accordance with the Board of Directors' decisions of June 23<sup>rd</sup>, 2015 making use of these delegations, the capital stock was increased by an amount of 653.00 Euros, from 688,276.10 Euros to 688,929.10 Euros, through the issue of 6,530 shares with a nominal value of 0.10 Euro.

In accordance with resolutions of the Combined General Meeting of May 21, 2012 and the Extraordinary General Meeting of April 2<sup>nd</sup>, 2013 granting delegations of power to the Executive Board/Board of Directors, and in accordance with the Board of Directors' decisions of December 2<sup>nd</sup>, 2015 making use of these delegations, the capital stock was increased by an amount of 1,375 Euros, from 688,929,10 Euros to 690,304.10 Euros, through the issue of 13,750 shares with a nominal value of 0.10 Euro.

In accordance with resolutions of the Combined General Meeting of May 21, 2012 and the Extraordinary General Meeting of April 2nd, 2013 granting delegations of power to the Executive Board/Board of Directors, and in accordance with the Board of Directors' decisions of December 2nd, 2015 making use of these delegations, the capital stock was increased by an amount of 649 Euros, from 690,304.10 Euros to 690,953.10 Euros, through the issue of 6,490 shares with a nominal value of 0.10 Euro.

In accordance with resolutions of the Combined General Meeting of June 23, 2015 granting delegations of power to the Board of Directors and in accordance with the Board of Directors' decisions of December 2<sup>nd</sup>, 2015 and with the Chief Executive Officer's decisions of December 3<sup>rd</sup>, 2015 making use of these delegations, the capital stock was increased by an amount of 94,000 Euros, from 690,953.10 Euros to 784,953.10 Euros, through the issue of 940,000 shares with a nominal value of 0.10 Euro.

In accordance with resolutions of the Combined General Meeting of May 21, 2012 granting delegations of power to the Executive Board/Board of Directors and in accordance with the Board of Directors' decisions of January 10, 2016 making use of these delegations, the capital stock was increased by an amount of 7,508 Euros, from 784,953.10 Euros to 792,461.10 Euros, through the issue of 75,080 shares with a nominal value of 0.10 Euro.

In accordance with resolutions of the Combined General Meeting of May 21, 2012 and the General Meeting of April 2<sup>nd</sup>, 2013 granting delegations of power to the Executive Board/Board of Directors and in accordance with the Board of Directors' decisions of December 6, 2016 making use of these delegations, the capital stock was increased by an amount of 1,416 Euros, from 792,461.10 Euros to 793,877.10 Euros, through the issue of 14,160 shares with a nominal value of 0.10 Euro.

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In accordance with resolutions of the Combined General Meeting of June 24, 2016 granting delegations of power to the Executive Board/Board of Directors and in accordance with the Board of Directors' decisions of January 8, 2017 making use of these delegations, the capital stock was increased by an amount of 79,387.70 Euros, from 793,877.10 Euros to 873,264.80 Euros, through the issue of 793,877 shares with a nominal value of 0.10 Euro.

In accordance with resolutions of the Combined General Meeting of May 21, 2012 and the General Meeting of April 2nd, 2013 granting delegations of power to the Executive Board/Board of Directors and in accordance with the Board of Directors' decisions of April 12, 2017 making use of these delegations, the capital stock was increased by an amount of 800 Euros, from 873,264.80 Euros to 874,064.80 Euros, through the issue of 8,000 shares with a nominal value of 0.10 Euro.

In accordance with resolutions of the Combined General Meeting of June 24, 2016 granting delegations of power to the Executive Board/Board of Directors and in accordance with the Chief Executive Officer's decision of April 19, 2017 making use of these delegations, the capital stock was increased by an amount of 300,000 Euros, from 874,064.80 Euros to 1,174,064.80 Euros, through the issue of 3,000,000 shares with a nominal value of 0.10 Euro.

In accordance with resolutions of the Extraordinary General Meeting of April 2, 2013 granting delegations of power to the Executive Board/Board of Directors, and in accordance with the decision of the Board of Directors of November 6, 2017 making use of these delegations, the capital stock was increased by an amount of 500 Euros, from 1,174,064.80 Euros to 1,174,564.80 Euros through the issue of 5,000 shares with a nominal value of 0.10 Euro.

In accordance with the resolutions of the Combined General Meeting of April 2, 2013 and June 24, 2016 granting delegations of authority to the Board of Directors, and pursuant to the decision of the Board of Directors on November 6, 2017 making use of these delegations, the capital stock was increased by an amount of 877.4 Euros from 1,174,564.80 Euros to 1,175,442.20 Euros, through the issue of 8,774 shares with a nominal value of 0.10 Euros.

In accordance with resolutions of the Combined General Meeting of June 27, 2017 granting delegations of power to the Board of Directors and in accordance with the Chief Executive Officer's decision of November 14, 2017 making use of these delegations, the capital stock was increased by an amount of 537,403.30 Euros, from 1,175,442.20 Euros to 1,712,845,50 Euros, through the issue of 5,374,033 shares with a nominal value of 0.10 Euro.

In accordance with resolutions of the Combined General Meeting of June 27, 2017 granting delegations of power to the Board of Directors and in accordance with the Board of Directors' decision of November 27, 2017 making use of these delegations, the capital stock was increased by an amount of 80,610.40 Euros, from 1,712,845,50 Euros to 1,793,455,90 Euros, through the issue of 806,104 shares with a nominal value of 0.10 Euro.

In accordance with resolutions of the Extraordinary General Meeting of April 2, 2013 granting delegations of power to the Executive Board/Board of Directors, and in accordance with the decision of the Board of Directors of January 7, 2018 making use of these delegations the capital stock was increased by an amount of 300 Euros, from 1,793,455.90 Euros to 1,793,755.90 Euros, through the issue of 3,000 shares with a nominal value of 0.10 Euro.

In accordance with resolutions of the Extraordinary General Meeting of June 24, 2016 granting delegations of power to the Executive Board/Board of Directors and in accordance with the decision of the Board of Directors of March 9, 2018 making use of these delegations the capital stock was increased by an amount of 247,60 Euros, from 1,793,755.90 Euros to 1,794,003.50 Euros, through the issue of 2,476 shares with a nominal value of 0.10 Euro.

# ARTICLE 7. CAPITAL STOCK

The capital stock is set at an amount of one million, seven hundred and ninety-four thousand, three Euros and fifty Euro cents (€1,794,003.50).

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It is divided into seventeen million, nine hundred and forty thousand, and thirty-five (17,940,035) shares with a nominal value of ten Eurocents (0.10) each, all in the same category and fully paid up.

# ARTICLE 8. IDENTIFICATION OF SHAREHOLDERS

The Company remains informed on the composition of its shareholding structure in accordance with the conditions established by law. To this end, it may make use of established legal provisions on the identification of bearers of securities such as grant an immediate or future voting right in general shareholders' meetings.

## ARTICLE 9. CROSSING OF THRESHOLDS

All shareholders who come to hold or cease to hold, directly or indirectly, alone or jointly with another person, a number of shares or similar securities representing a portion of the capital or voting rights established by law must inform the Company of this, in accordance with the conditions established by the law and regulations.

Shareholders who have not respected these provisions shall be deprived of the voting rights attached to the shares exceeding the portion that should have been declared. The loss of voting rights shall apply to all shareholders' meetings held up to the expiry of a two-year period following the date on which the declaration was normalized.

# ARTICLE 10. INCREASES IN SHARE CAPITAL

The share capital shall be increased by any means and according to any methods established by law.

An extraordinary general meeting, acting on a report by the Board of Directors, is the sole entity with competency to decide on a capital increase. It may delegate such competency or powers to the Board of Directors.

The shareholders have, proportionately to the amount of their shares, a preferential right to the subscription of shares issued by way of a cash contribution to perform a capital increase, a right that they may waive individually. An extraordinary general meeting may decide to withdraw this preferential subscription right under legally established conditions.

The right to the assignment of new shares to shareholders, following an incorporation of reserves, income, or issue premiums into the capital, belongs to the bare owner, without prejudice to the rights of the usufructuary.

## ARTICLE 11. PAYMENT OF SHARES

All the original shares constituting the initial capital and representing cash contributions must be paid up in the amount of at least half their nominal value at the time of their subscription.

Shares subscribed during a cash-based capital increase must be paid up in the amount of at least one quarter of their nominal value at the time of their subscription and, where applicable, the entirety of the issue premium.

Payment of the remainder must take place on one or more occasions on the decision of the Board of Directors within a period of five years, i.e., this period starting on the day of registration in the Trade and Companies Register or, for a capital increase, on the day on which the capital increase became final.

Calls for funds shall be brought to the knowledge of subscribers by registered letter with confirmation of receipt sent at least fifteen days prior to the date established for each payment. Payments shall be made either at the head office or at any other location indicated to this end.

Any delays in the payment of sums owing on the share amount not paid up shall result, duly and without the need to proceed with any formalities whatsoever, in the payment of interest at the legal rate, starting on the due date, without prejudice to any personal action that the Company may exercise against the defaulting shareholder and the enforcement measures established by law.

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## ARTICLE 12. REDUCTION - AMORTIZATION OF THE SHARE CAPITAL

A reduction of the capital may be authorized or decided on in an extraordinary general meeting, which may delegate to the Board of Directors all powers to perform such reduction. In no case shall this harm the equal treatment of the shareholders.

A reduction in share capital for an amount below the legal minimum can only be decided pursuant to the suspensive condition of a capital increase intended to return the share capital to an amount at least equal to this minimum amount, except where the Company is transformed into another form of company.

In the event of non-compliance with these provisions, any interested parties may seek dissolution of the Company through the courts.

Nevertheless, the court cannot order its dissolution where, on the date on which it rules based on grounds, the situation has been normalized.

The capital may be liquidated in conformity with legal provisions. Liquidation of the capital may be decided in an extraordinary general meeting and must be performed using sums distributable in accordance with Article L. 232-11 of the Code of Commerce, by way of an equal reimbursement on each share of the same class. It shall not result in a reduction of the capital. Shares fully or partially liquidated shall lose the right to reimbursement at their nominal value, up to the amount of this liquidation. They shall retain all their other rights.

# ARTICLE 13. SHARE TYPES

The shares are nominal, up to their full payment. When they are fully paid up, they may be nominal or bearer, as decided by the shareholders.

They shall give rise to the registration of an account opened pursuant to the conditions and methods established under current legal and regulatory provisions, by the issuing company or by a financial broker mentioned on paragraphs 2° to 7° of Article L.542-1 of the *Code Monétaire et Financier*.

## ARTICLE 14. INDIVISIBILITY OF THE SHARES – BARE OWNERSHIP – USUFRUCT

Shares are indivisible in the eyes of the company. Indivisible co-owners of shares shall be represented in general meetings by one of the co-owners or by a joint representative of their choice. In default of an agreement between them on the choice of a representative, this representative shall be designated by order of the president of the commercial court, ruling in an interim order on the application of the co-owner first making such request.

The voting right attached to a share belongs to the usufructuary for ordinary general meetings and to the bare owner for extraordinary general meetings. However, the shareholders may agree amongst themselves on any other distribution for the exercise of a voting right in general meetings. In this case, they must bring their agreement to the knowledge of the Company by registered letter sent to the head office, the Company being required to respect this agreement for any general meetings held after the expiry of a one-month period following mailing of the registered letter, the postmark being considered proof of the mailing date.

The shareholder's right to obtain the communication of company documents or to consult these documents may likewise be exercised by each co-owner of an undivided share, by the usufructuary, and the bare owner of shares.

# ARTICLE 15. ASSIGNMENT AND TRANSFER OF SHARES

Shares can be freely traded, without prejudice to legal and regulatory provisions.

The ownership of shares issued in registered form shall result from their registration in the name of the owners on the registers held to this end. Shares that are designated as registered shares may only be traded on the market where they have first been placed in a management account with an authorized broker.

Shares that are not registered as necessarily being nominal may only be traded on the market where they are converted to bearer shares.

Ownership of bearer shares shall result from their registration in a bearer account with an authorized financial broker.

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The assignment of nominal or bearer shares shall take place, with regard to third parties and the company, by an account-to-account transfer into the accounts of the issuing company or those of the authorized financial broker.

The transfer of shares, free or charge or following a death, shall likewise take place by an account-to-account transfer upon the provision of evidence supporting the change in legal conditions.

# ARTICLE 16. RIGHTS AND OBLIGATIONS ATTACHED TO THE SHARES

Each share gives right to the profits, the company assets in a share proportional to the proportion of capital that it represents.

Except where the law or the articles of incorporation stipulate otherwise, each share confers on its owner a vote in the shareholders' General Meetings.

All shareholders shall have the right to be informed of the Company's performance and to obtain the communication of certain company documents at the times and in accordance with the conditions established by the law and regulations.

Shareholders shall only sustain losses up to the amount of their contributions.

The possession of a share requires due adherence to the decisions of general meetings and the present articles of incorporation. Assignment shall include all dividends matured and not paid or maturing in future, as well as any share in the reserve funds, save where provisions to the contrary are disclosed to the Company.

Whenever it is necessary to hold a certain number of shares to exercise a right, in the event of an exchange, regrouping, or assignment of title, or at the time of a capital increase or reduction, a merger, or any other operation, the shareholders holding a number of shares less than that required can only exercise these rights on the condition that they personally arrange to obtain the number of shares required.

## SECTION III ADMINISTRATION AND CONTROL OF THE COMPANY

## ARTICLE 17. BOARD OF DIRECTORS

## I. Appointment/removal of directors

The Company is governed by a Board of Directors composed of at least three members and at most eighteen members, without prejudice to the derogation established by law in the event of merger.

The Board of Directors is composed by seeking a balanced representation of women and men.

During the life of the Company, directors shall be appointed, renewed, or removed in ordinary general meetings. They may always be re-elected.

The duration of a director position is three (3) years; this position ends at the end of the Ordinary General Meeting called to rule on the annual financial statements for the year just ended and held during the year in which their term of office expires.

A person cannot be appointed as director where, having surpassed seventy-five years of age, this person's appointment has the effect of bringing the number of Board members having surpassed this age to more than one-third of the number of directors. Where this limit has been exceeded, the oldest director shall be deemed as having duly resigned.

Directors can be shareholders or non-shareholders of the Company.

A Company employee cannot be appointed director where his/her employment contract corresponds to an effective job. The number of directors tied to the Company by way of an employment contract cannot exceed one third of the directors in office.

## II. Directors as legal persons

Directors may be natural persons or legal persons. In the latter case, upon its appointment, the legal person is required to designate a permanent representative, who is subject to the same conditions and obligations and who incurs the same civil and criminal liability as if this person was a director in his/her own name, without prejudice to the joint and several liability of the legal person that he/she represents. The permanent representative of a director as a legal entity is subject to the age conditions pertaining to directors as natural persons.

The term of office of the permanent representative designated by the legal person appointed as director is given to him/her for the duration of the latter's term of office.

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Where the legal person revokes the term of office of its permanent representative, the legal person is required to provide the Company, without delay and by registered letter, this revocation as well as the identify of its new permanent representative. The same is applicable in the event of the death or resignation of the permanent representative.

Designation of the permanent representative and discontinuation of his/her term of office are subject to the same publication formalities applicable as if he/she had been a director in his/her own name.

## III. Vacancy, death, resignation

In the event of a vacancy, due to death or resignation, of one or more director positions, the Board of Directors may, between two general meetings, proceed with temporary appointments.

Where the number of directors has become lower than the legal minimum, the remaining directors shall immediately call an Ordinary General Meeting with a view to supplementing the Board's numbers.

Temporary appointments made by the Board are subject to ratification at the next ordinary general meeting. In default of such ratification, the resolutions made and acts performed by the Board prior to this meeting shall no longer be considered valid.

In the event of absence of a director at more than four consecutive Board of Directors' meetings, this director shall be considered as having duly resigned.

## ARTICLE 18. ORGANIZATION OF THE BOARD

The Board of Directors shall elect a chairman from among its members, the chairman being a natural person, on penalty of invalidity of this appointment. It shall determine the chairman's remuneration.

Any person older than seventy-five years of age may not be appointed chairman. Where the chairman in office comes to surpass this age, he/she shall be deemed as having duly resigned.

The chairman is appointed for a duration that cannot exceed that of his/her director mandate. He/she may be re-elected. The Board of Directors may remove the chairman at any time.

The Board may likewise appoint a Vice President from among its members who are natural persons, and he/she shall preside over Board meetings in the Chairman's absence.

The Board may designate, within a maximum limit of two, one or more observers who are natural persons, directors or otherwise, and who are 65 years of age at most at the day of their appointment.

These observers are appointed for a duration of two years.

These observer positions shall be fulfilled free of charge. The observers shall be summoned to all meetings of the Board of Directors, and shall take part in deliberations for consultation purposes only. In its relations with the Board of Directors, the observers shall perform a general mission of consultation and supervision.

## ARTICLE 19. BOARD DELIBERATIONS

The Board of Directors shall meet as often as the Company's interests so require, upon summons by its chairman or the managing director. Where the Board has not met for more than two months, at least one third of the directors may request that the chairman, who is bound by this request, call a Board of Directors' meeting on a specific agenda.

Summonses shall be given by any means, including verbally.

Meetings shall take place either at the headquarters or at any other location indicated in the summons.

The Board may only validly deliberate where half of its directors are present.

Decisions shall be made by the majority of members present or represented.

In the event of a tie, the meeting Chairman's vote shall carry the decision.

Pursuant to the provisions of internal rules established by the Board of Directors, for calculation of the quorum and the majority, the directors participating in a Board meeting by videoconference or other means of telecommunications allowing for identification of the participants and guaranteeing their effective participation shall be deemed present, in compliance with current regulations.

This provision is not applicable for decisions on the annual financial statements, the consolidated financial statements, and preparation of the annual report and the group's annual report.

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## ARTICLE 20. POWERS OF THE BOARD OF DIRECTORS

The Board of Directors determines the orientations of the Company's activities and oversees their implementation. Without prejudice to the powers expressly assigned by law to the shareholders and within the limit of the corporate purpose, the Board of Directors is responsible for all matters relating to the successful operation of the Company and governs matters concerning the Company, through its resolutions.

In relations with third parties, the Company is committed by the actions of the Board of Directors including where not pertaining to the corporate object, except where it can prove that the third party knew that such action fell outside this purpose or that it could not be ignorant of such fact, given the circumstances, mere publication of the articles of incorporation not being sufficient to constitute such proof.

The Board of Directors shall perform the controls and verifications that it deems appropriate. Each director may arrange for the communication to him/her of all documents and information necessary to the fulfillment of his/her mission.

The Board of Directors may decide on the creation of a study committee responsible for studying matters that the Board of Directors or its Chairman submits to it.

## ARTICLE 21. SENIOR MANAGEMENT

#### 1 - Operating methods

General management is provided under its responsibility, by a natural person appointed by the Board of Directors and holding the title of managing director. This natural person may be the chairman of the Board of Directors.

The Board of Directors chooses between two operating methods for the Senior Management.

The Board resolution relative to the choice of operating method for the executive division shall be carried by the majority of directors present or represented. Shareholders and third parties shall be informed of this choice in accordance with the conditions established under current regulations.

#### 2 - Senior Management

The Chief Executive Officer shall be a natural person selected from among the directors or elsewhere.

The duration of the managing director's term of office is determined by the Board at the time of his/her appointment. However, where the managing director is a director, the duration of his/her term of office cannot exceed that of the director mandate.

Any person older than seventy years of age cannot be appointed as managing director. Where the managing director reaches this age limit, he/she shall be deemed as having duly resigned.

The managing director may be removed by the Board of Directors at any time. Where the removal is decided without just cause, it may result in the payment of damages, save where the managing director holds the position of chairman of the Board of Directors.

The managing director is vested with the broadest of powers to act in all circumstances in the name of the Company. He shall exercise his powers within the limits of the corporate object and without prejudice to the powers that the law expressly assigns to the shareholders and to the Board of Directors.

He represents the Company in its relations with third parties. The Company is committed by the actions of the managing director including where not pertaining to the corporate object, save where it can prove that the third party knew that such action fell outside this object or that it could not be ignorant of such fact, given the circumstances, mere publication of the articles of incorporation not being sufficient to constitute such proof.

The Board of Directors may limit the powers of the Chief Executive Officer, but these limitations are not binding against third parties.

## 3 - Deputy Managing Director

Upon the proposal of the Chief Executive Officer that this position be assumed by the Chairman of the Board of Directors or by another person, the Board of Directors may appoint one or more natural persons assigned to assist the Chief Executive Officer, with the title of Deputy Managing Director.

The Board of Directors may choose the Deputy Managing Directors from among the directors or elsewhere, and cannot appoint more than five (5) persons.

The age limit is set at seventy (70) years of age. Where a deputy managing director reaches this age limit, he/she shall be deemed as having duly resigned.

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The deputy managing directors may be removed at any time by the Board of Directors, upon such proposal by the managing director. Where such removal is decided on without just cause, it may result in the payment of damages.

Where the Chief Executive Officer ceases or is unable to perform his/her duties, the Deputy Managing Directors shall retain, except where decided otherwise by the Board, their duties and powers until the appointment of a new Chief Executive Officer.

In accordance with the managing director, the Board of Directors shall determine the extent and duration of powers granted to the deputy managing directors. The deputy managing directors shall have, in relation to third parties, the same powers as the managing director.

#### ARTICLE 22. REMUNERATION OF DIRECTORS

1 - A general meeting may allocate to the directors, in remuneration for their activity and in the form of attendance fees, a fixed annual sum, the amount of which shall be reported under operating expenses and shall be maintained until a decision is made to the contrary. Its distribution among the directors shall be determined by the Board of Directors.

2 - The Board of Directors shall determine the remuneration for the chairman of the Board of Directors, the managing director, and the deputy managing directors. This remuneration may be fixed and/or proportional.

# ARTICLE 23. PLURALITY OF TERMS OF OFFICE

The limitation on the plurality of terms of office as director and Chief Executive Officer applies in accordance with the conditions and subject to the derogations established by law.

## ARTICLE 24. REGULATED AGREEMENTS

**24.1** All regulated agreements taking place, directly or through a third party, between the Company and one of its directors, its managing director, one of its deputy managing directors, one of its shareholders holding a portion of the voting rights greater than 10% or, where relating to a shareholder company, the company controlling it as defined under Article L. 233-3 of the Code of Commerce, must be submitted for the prior authorization of the Board of Directors.

The same is likewise applicable for agreements in which one of the persons outlined in the previous paragraph has an indirect interest, and for agreements taking place between the Company and another company, where the managing director, one of the deputy managing directors, or one of the Company's directors is the owner, shareholder with unlimited liability, manager, director, member of the supervisory board, or generally any director of this company.

The prior authorization of the Board of Directors shall be supported by reasons justifying the Company's interests in stipulating the agreement, and shall notably specify the financial conditions associated with this agreement.

Agreements stipulated and authorized during previous financial years, the fulfillment of which was continued into the last financial year, shall be examined each year by the Board of Directors and disclosed to the external auditors as established under the law.

The provisions of the preceding paragraphs shall not be applicable either to agreements relating to day-to-day operations stipulated under normal conditions or to agreements stipulated between two companies where one of these companies directly or indirectly holds the entirety of the other's capital, where applicable after deducting the minimum number of shares required to satisfy the requirements of Article 1832 of the Civil Code and Articles L. 225-1 and L. 226-1 of the Code of Commerce.

**24.2** The report outlined under Article L. 225-102 of the Code of Commerce mentions, save where these are agreements relating to day-to-day operations stipulated under normal conditions, agreements reached directly or through a third party and between, on one part and as applicable, the managing director, one of the deputy managing directors, one of the directors, or one of the shareholders holding a portion of voting rights greater than 10% of the Company's capital and, on the other part, another company in which the Company directly or indirectly holds more than half the capital."

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## ARTICLE 25. STATUTORY AUDITORS

One or more statutory auditors shall be appointed and shall perform their audit assignment in conformity with the law.

Their permanent assignment, to the exclusion of any involvement in the Company's management, is to review the Company's books and financial figures and to verify the accuracy and fairness of the corporate financial statements.

One or more deputy auditors shall be appointed, who shall be called upon to replace any statutory auditors in the event of an impediment, rejection, resignation, or death.

#### SECTION IV

#### SHAREHOLDERS' MEETINGS

#### ARTICLE 26. NATURE OF THE MEETINGS

Shareholder decisions shall be made in General Meetings.

Ordinary General Meetings are those that are called to make all decisions that do not modify the articles of incorporation.

Extraordinary General Meetings are those called to decide on or authorize direct or indirect modifications to the articles of incorporation.

The resolutions of General Meetings create an obligation on all shareholders, including those who are absent, dissenting, or incompetent.

## ARTICLE 27. SUMMONSES AND MEETINGS OF THE GENERAL SHAREHOLDERS

All shareholders have the right to participate in General Meetings or to arrange for their representation in accordance with the conditions established by law.

General Meetings are called either by the Board of Directors or by the statutory auditors, or by a representative designated by the President of the Commercial Court in an interim ruling on the application of one or more shareholders constituting at least one tenth of the capital or, in an emergency, on the application of the participative Management Committee.

Where the Company's shares are admitted for trading on a regulated market or where all its shares are not nominal, it is required, at least thirty-five (35) days prior to any meeting, to publish in the French Bulletin des Annonces Légales Obligatoires (BALO) a meeting notice containing the information outlined in current regulations.

The summons to a General Meeting is made by a notice in a newspaper authorized to publish legal notices in the French département where the headquarters is located, and a notice, furthermore, in the Bulletin des Annonces Légales et Obligatoires (BALO).

Nevertheless, the notices outlined in the previous paragraph may be replaced by a summons made, at the Company's expense, by simple or registered letter sent to each shareholder. This summons may likewise be sent by a means of electronic telecommunications implemented in accordance with regulatory conditions.

Meetings shall take place at the headquarters or at any other location indicated in the notice of summons.

General Meetings shall be composed of all the shareholders, whatever the number of shares they hold.

Participation in the General Meetings, in any form whatsoever, is subject to the registration or recording of shares in accordance with the conditions and timelines established under current regulations.

A shareholder may arrange for his/her representation at general meetings by any natural or legal person of his/her choice, in conformity with legal provisions. Shareholders who are legal persons shall participate in meetings through their legal representatives or through any representative designated to this end.

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Shareholders may likewise vote remotely in accordance with the methods established by the law and regulations, sending their remote voting form either in paper format or, on the decision of the Board of Directors, by a means of telecommunications.

The Board of Directors has the right to decide, at the time a meeting is called, whether the shareholders may participate and vote in any meetings by video conference or any other means of telecommunications or electronic transmission (including via the internet), in accordance with the conditions established by the law and regulations applicable at the time of its utilization. This decision shall be communicated in the meeting notice and the notice of summons published in the Bulletin des annonces légales obligatoires (BALO).

Shareholders who use, to this end and within the required time lines, the electronic voting form offered on the web site arranged by the coordinator of the shareholders' meeting shall be considered equivalent to the shareholders present or represented. The submission and signature of the electronic form may be directly performed on this site through any process approved by the Board of Directors and meeting the conditions defined under the paragraph two, sentence one, Article 1316-4 of the French Civil Code, i.e., the usage of a reliable identification process guaranteeing a link with the form, notably such as consists of an identifier and a password.

The proxy or vote, thus expressed prior to the shareholders' meeting by any means of telecommunications or electronic transmission, and the confirmation of receipt given therefor, shall be considered a submission irrevocable and binding on all parties, it being specified that, in the event of an assignment of shares taking place prior to the second (2nd) business day preceding the shareholders' meeting, local Paris time, the Company shall consequently invalidate or modify, as applicable, the proxy or vote expressed prior to the meeting by any means of telecommunications.

## ARTICLE 28. AGENDA

The agenda for Meetings is provided by the person issuing the summons.

One or more shareholders, representing at least the portion of share capital required and acting in accordance with the conditions and timeframes established by law, have the right to request, by registered letter with acknowledgment of receipt or by electronic telecommunications, the inclusion of points or draft resolutions on a Meeting agenda.

The participative management committee may likewise request that draft resolutions be included on a Meeting agenda.

Shareholders' meetings cannot deliberate on a matter that is not included on the agenda, which cannot be modified in the event of a second summons. Such meetings may nevertheless, in all circumstances, remove one or more members of the Board of Directors and proceed with their replacement.

## ARTICLE 29. HOLDING OF MEETINGS - CHAIR COMMITTEE - MINUTES

Meetings shall be presided over by the chairman of the Board of Directors or, in his absence, by a deputy chairman or by a director specially deputy to this end by the Board. Failing this, the shareholders' meeting shall itself designate a meeting chairman.

In the event of a summons by a statutory auditor or by an agent appointed by the court, the Meeting shall be presided over by the person issuing the summons.

The two shareholders, present and accepting such duties, representing, both for themselves and as representatives, the largest number of votes shall act as scrutineers and vote counters.

The committee thus established shall designate a secretary, who may be taken from outside the members of the Meeting.

An attendance sheet shall be kept, in accordance with the conditions established by law.

Deliberations and resolutions of the General Meetings are recorded in minutes signed by the committee members and kept in a special register, in accordance with the law. Copies and extracts of these minutes shall be validly certified in accordance with the conditions established by law.

# ARTICLE 30. QUORUM - VOTE

General Meetings, whether they are ordinary, extraordinary, or mixed, shall deliberate in accordance with the conditions for a quorum and majority as established in the provisions governing them, and shall exercise the powers assigned to them by the law.

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The voting right attached to capital or dividend shares is proportional to the portion of capital that they represent. Each share gives the right to one vote.

A double voting right is nevertheless assigned, in accordance with legal conditions, to all shares fully paid up for which evidence is provided of nominal registration for at least two years in the name of the same shareholder, or in the name of a person holding such rights following a succession, a sharing of the community of property between spouses, or an inter vivos gift granted by a shareholder to his/her spouse or to a relative in the direct line of succession, or following a transfer resulting from a merger or a division of a shareholder company.

In the event of a capital increase through the incorporation of reserves, income, or issue premiums, the double voting right is granted, upon their issue, to nominal shares assigned free of charge to replace the previous shares already receiving such benefit.

The double voting right shall be duly withdrawn from any share having been converted to a bearer share or been subject to a transfer of ownership, except where this transfer results from a succession, a sharing of the community of property between spouses, or an inter vivos gift granted by a shareholder to his/her spouse or to a relative in the direct line of succession, or following a transfer resulting from a merger or a division of a shareholder company.

## SECTION V

## CORPORATE FINANCIAL YEAR - CORPORATE FINANCIAL STATEMENTS -ALLOCATION AND DISTRIBUTION OF PROFITS

# ARTICLE 31. CORPORATE FINANCIAL YEAR

The corporate financial year is defined under Article 5.

# ARTICLE 32. INVENTORY - ANNUAL FINANCIAL STATEMENTS - STATEMENT OF FINANCIAL POSITION

Regular accounts of Company operations shall be kept, in conformity with the law and commercial practices.

At the end of each financial year, the Board of Directors shall conduct an inventory of all the assets and liabilities. It shall also prepare the annual financial statements in conformity with the provisions of Part II, Book 1 of the Commercial Code.

It shall attach to the statement of financial position a statement of sureties, endorsements, and guarantees given by the Company and a statement of collateral pledged by it.

It shall prepare an annual report containing the information required by law.

The annual report shall include, where applicable, the Group's annual report where the Company must prepare and publish consolidated financial statements as required law.

Where applicable, the Board of Directors shall prepare accounting estimates as required by the law and regulations.

All these documents shall be provided to the auditor in accordance with legal and regulatory conditions.

## ARTICLE 33. ALLOCATION AND DISTRIBUTION OF PROFITS

Amounts required by law for allocation to reserves shall be firstly withdrawn on the profits of each financial year, where applicable, decreased by prior losses.

As such, 5% of profits shall be allocated to establish the legal reserve; this allocation is no longer obligatory when this fund reaches ten percent of the capital stock; it shall resume its obligatory status where, for any reason, the legal reserve falls below this proportion.

The distributable profits are composed of the annual profits, less any prior losses and amounts allocated to reserves in application of the law or articles of incorporation, and increased by any profits carried forward.

From these profits, general meetings shall determine the portion assignable to shareholders in the form of a dividend, and may allocate any amounts such as it sees fit, to any funds whether optional, ordinary, or extraordinary, or to be carried forward.

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However, in the event of a reduction in the capital, no distribution may be made to shareholders where the shareholders' equity is or becomes, following such capital reduction, lower than the amount of the capital, increased by any reserves for which the law and the articles of incorporation prohibit distribution.

General meetings may decide on the distribution of amounts withdrawn from optional reserves, either to provide or to supplement a dividend, or by way of an exceptional distribution; in this case, the meeting's decision shall expressly indicate the reserve items from which such withdrawal shall be made. However, dividends shall be given priority distribution over any distributable profits from the financial year.

Where existing and upon approval of the financial statements by the general meeting, losses shall be recorded in a special account to be offset by any profits in future financial years, until such losses have been completely discharged.

## ARTICLE 34. PAYMENT OF DIVIDENDS

For all or part of a regularly distributed dividend or interim dividends, general meetings may grant shareholders an option between payment in cash or in shares, in accordance with legal conditions.

The methods for payment of dividends in cash shall be set by the general meeting or, failing this, by the Board of Directors.

## ARTICLE 35. SHAREHOLDERS' EQUITY AT LESS THAN HALF THE CAPITAL STOCK

Where, due to losses identified in the accounting documents, the shareholders' equity in the Company falls below half the capital stock, the Board of Directors is required, within four months following approval of the financial statements showing these losses, to call an extraordinary general meeting for the purpose of deciding whether early dissolution of the Company should take place.

Where dissolution is not decided on, the Company is required, at the latest by the end of the second financial year following that in which identification of the losses took place and subject to the provisions of Article L. 224-2 of the Commercial Code, to reduce its capital by an amount at least equal to that of the losses that could not be allocated to the reserves where, within this period, the shareholders' equity has not been reestablished up to a value at least equal to half of the capital stock. In the event of non-fulfillment of these requirements, any interested party may seek dissolution of the Company through legal measures. However, the courts may not hand down a dissolution decision where, at the date on which the courts rule on the basis of substance, the situation has been regularized.

#### SECTION VI

## **DISSOLUTION - DISPUTES**

#### ARTICLE 36. DISSOLUTION

Upon expiry of the Company's established duration or in the event of early dissolution, a general meeting shall decide on the liquidation methods and appoint one or more liquidators, whose powers it shall determine, and who shall perform their duties in compliance with the law.

#### ARTICLE 37. DISPUTES

All disputes such as may arise within the duration of the Company or after its dissolution during liquidation operations, either between the shareholders and the Company's management and control bodies, or between the shareholders themselves, relative to business affairs or to the fulfillment of provisions of the articles of incorporation shall be decided on in conformity with the law and submitted to the jurisdiction of the competent courts.

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# ERYTECH PHARMA S.A.

AND

# THE BANK OF NEW YORK MELLON

As Depositary

AND

# OWNERS AND HOLDERS OF AMERICAN DEPOSITARY SHARES

Amended and Restated Deposit Agreement

Dated as of November 9, 2017

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#### AMENDED AND RESTATED DEPOSIT AGREEMENT

AMENDED AND RESTATED DEPOSIT AGREEMENT dated as of November 9, 2017 among ERYTECH PHARMA S.A., a company incorporated under the laws of France (herein called the Company), THE BANK OF NEW YORK MELLON, a New York banking corporation (herein called the Depositary), and all Owners and Holders (each as hereinafter defined) from time to time of American Depositary Shares issued hereunder.

#### WITNESSETH:

WHEREAS, the Company and the Depositary entered into a deposit agreement dated as of January 9, 2015 (the "Prior Deposit Agreement") for the purposes stated in that agreement;

WHEREAS, the Company and the Depositary now wish to amend the Prior Deposit Agreement and the form of Receipt to reflect that the American Depositary Shares are listed on the Nasdaq Global Market and the Company has become a reporting company under the Securities Exchange Act of 1934 and to provide additional disclosure language regarding the conversion of foreign currency;

WHEREAS, the Company desires to provide, as set forth in this Amended and Restated Deposit Agreement (herein called this Deposit Agreement), for the deposit of Shares (as hereinafter defined) of the Company from time to time with the Depositary or with the Custodian (as hereinafter defined) under this Deposit Agreement, for the creation of American Depositary Shares representing the Shares so deposited and for the execution and delivery of American Depositary Receipts evidencing the American Depositary Shares; and

WHEREAS, the American Depositary Receipts are to be substantially in the form of Exhibit A annexed to this Deposit Agreement, with appropriate insertions, modifications and omissions, as set forth in this Deposit Agreement;

NOW, THEREFORE, in consideration of the premises, it is agreed by and between the parties hereto that the Prior Deposit Agreement is hereby amended and restated as follows:

## ARTICLE 1. DEFINITIONS

The following definitions shall for all purposes, unless otherwise clearly indicated, apply to the respective terms used in this Deposit

Agreement:

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## SECTION 1.1. American Depositary Shares.

The term "<u>American Depositary Shares</u>" shall mean the securities created under this Deposit Agreement representing rights with respect to the Deposited Securities. American Depositary Shares may be certificated securities evidenced by Receipts or uncertificated securities. The form of Receipt annexed as Exhibit A to this Deposit Agreement shall be the prospectus required under the Securities Act of 1933 for sales of both certificated and uncertificated American Depositary Shares. Except for those provisions of this Deposit Agreement that refer specifically to Receipts, all the provisions of this Deposit Agreement shall apply to both certificated and uncertificated American Depositary Shares.

Each American Depositary Share shall represent the number of Shares specified in Exhibit A to this Deposit Agreement, <u>except that</u>, if there is a distribution upon Deposited Securities covered by Section 4.3, a change in Deposited Securities covered by Section 4.8 with respect to which additional American Depositary Shares are not delivered or a sale of Deposited Securities under Section 3.2 or 4.8, each American Depositary Share shall thereafter represent the amount of Shares or other Deposited Securities that are then on deposit per American Depositary Share after giving effect to that distribution, change or sale.

#### SECTION 1.2. Commission.

The term "<u>Commission</u>" shall mean the Securities and Exchange Commission of the United States or any successor governmental agency in the United States.

#### SECTION 1.3. Company.

The term "Company" shall mean ERYTECH Pharma S.A., a company incorporated under the laws of France, and its successors.

## SECTION 1.4. Custodian.

The term "<u>Custodian</u>" shall mean Société Générale, as custodian for the Depositary in Paris for the purposes of this Deposit Agreement, and any other firm or corporation the Depositary appoints under Section 5.5 as a substitute or additional custodian under this Deposit Agreement, and shall also mean all of them collectively.

## SECTION 1.5. Delisting Event.

A "<u>Delisting Event</u>" occurs if the American Depositary Shares are delisted from a securities exchange on which the American Depositary Shares were listed and the Company has not listed or applied to list the American Depositary Shares on any other securities exchange.

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## SECTION 1.6. Deliver; Surrender.

(a) The term "<u>deliver</u>", or its noun form, when used with respect to Shares or other Deposited Securities, shall mean (i) book-entry transfer of those Shares or other Deposited Securities to an account maintained by an institution authorized under applicable law to effect transfers of such securities designated by the person entitled to that delivery or (ii) physical transfer of certificates evidencing those Shares or other Deposited Securities registered in the name of, or duly endorsed or accompanied by proper instruments of transfer to, the person entitled to that delivery.

(b) The term "<u>deliver</u>", or its noun form, when used with respect to American Depositary Shares, shall mean (i) registration of those American Depositary Shares in the name of DTC or its nominee and book-entry transfer of those American Depositary Shares to an account at DTC designated by the person entitled to that delivery, (ii) registration of those American Depositary Shares not evidenced by a Receipt on the books of the Depositary in the name requested by the person entitled to that delivery and mailing to that person of a statement confirming that registration or (iii) if requested by the person entitled to that delivery, execution and delivery at the Depositary's Office to the person entitled to that delivery of one or more Receipts evidencing those American Depositary Shares registered in the name requested by that person.

(c) The term "<u>surrender</u>", when used with respect to American Depositary Shares, shall mean (i) one or more book-entry transfers of American Depositary Shares to the DTC account of the Depositary, (ii) delivery to the Depositary at its Office of an instruction to surrender American Depositary Shares not evidenced by a Receipt or (iii) surrender to the Depositary at its Office of one or more Receipts evidencing American Depositary Shares.

## SECTION 1.7. Deposit Agreement.

The term "<u>Deposit Agreement</u>" shall mean this Amended and Restated Deposit Agreement, as it may be amended from time to time in accordance with the provisions hereof.

#### SECTION 1.8. Depositary; Depositary's Office.

The term "<u>Depositary</u>" shall mean The Bank of New York Mellon, a New York banking corporation, and any successor as depositary under this Deposit Agreement. The term "<u>Office</u>", when used with respect to the Depositary, shall mean the office at which its depositary receipts business is administered, which, at the date of this Deposit Agreement, is located at 101 Barclay Street, New York, New York 10286.

## SECTION 1.9. Deposited Securities.

The term "<u>Deposited Securities</u>" as of any time shall mean Shares at such time deposited or deemed to be deposited under this Deposit Agreement, including without limitation, Shares that have not been successfully delivered upon surrender of American Depositary Shares, and any and all other securities, property and cash received by the Depositary or the Custodian in respect of Deposited Securities and at that time held under this Deposit Agreement.

## SECTION 1.10. Disseminate.

The term "<u>Disseminate</u>," when referring to a notice or other information to be sent by the Depositary to Owners, shall mean (i) sending that information to Owners in paper form by mail or another means or (ii) with the consent of Owners, another procedure that has the effect of making the information available to Owners, which may include (A) sending the information by electronic mail or electronic messaging or (B) sending in paper form or by electronic mail or messaging a statement that the information is available and may be accessed by the Owner on an Internet website and that it will be sent in paper form upon request by the Owner, when that information is so available and is sent in paper form as promptly as practicable upon request.

## SECTION 1.11. Dollars.

The term "Dollars" shall mean United States dollars.

#### SECTION 1.12. DTC.

The term "DTC" shall mean The Depository Trust Company or its successor.

## SECTION 1.13. Foreign Registrar.

The term "<u>Foreign Registrar</u>" shall mean the entity that carries out the duties of registrar for the Shares and any other agent of the Company for the transfer and registration of Shares, including, without limitation, any securities depository for the Shares.

## SECTION 1.14. Holder.

The term "<u>Holder</u>" shall mean any person holding a Receipt or a security entitlement or other interest in American Depositary Shares, whether for its own account or for the account of another person, but that is not the Owner of that Receipt or those American Depositary Shares.

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## SECTION 1.15. Insolvency Event.

An "<u>Insolvency Event</u>" occurs if the Company institutes proceedings to be adjudicated as bankrupt or insolvent, consents to the institution of bankruptcy or insolvency proceedings against it, files a petition or answer or consent seeking reorganization or relief under any applicable law in respect of bankruptcy or insolvency, consents to the filing of any petition of that kind or to the appointment of a receiver, liquidator, assignee, trustee, custodian or sequestrator (or other similar official) of it or any substantial part of its property or makes an assignment for the benefit of creditors, or if information becomes publicly available indicating that unsecured claims against the Company are not expected to be paid.

## SECTION 1.16. Owner.

The term "<u>Owner</u>" shall mean the person in whose name American Depositary Shares are registered on the books of the Depositary maintained for that purpose.

## SECTION 1.17. Receipts.

The term "<u>Receipts</u>" shall mean the American Depositary Receipts issued under this Deposit Agreement evidencing certificated American Depositary Shares, as the same may be amended from time to time in accordance with the provisions of this Deposit Agreement.

## SECTION 1.18. Registrar.

The term "<u>Registrar</u>" shall mean any corporation or other entity that is appointed by the Depositary to register American Depositary Shares and transfers of American Depositary Shares as provided in this Deposit Agreement.

## SECTION 1.19. Replacement.

The term "Replacement" shall have the meaning assigned to it in Section 4.8.

#### SECTION 1.20. Restricted Securities.

The term "<u>Restricted Securities</u>" shall mean Shares that (i) are "restricted securities," as defined in Rule 144 under the Securities Act of 1933, except for Shares that could be resold in reliance on Rule 144 without any conditions, (ii) are beneficially owned by an officer, director (or person performing similar functions) or other affiliate of the Company, (iii) otherwise would require registration under the Securities Act of 1933 in connection with the public offer and sale thereof in the United States or (iv) are subject

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to other restrictions on sale or deposit under the laws of France, a shareholder agreement or the articles of association or similar document of the Company.

#### SECTION 1.21. Securities Act of 1933.

The term "Securities Act of 1933," shall mean the United States Securities Act of 1933, as from time to time amended.

#### SECTION 1.22. Shares.

The term "<u>Shares</u>" shall mean ordinary shares of the Company that are validly issued and outstanding, fully paid and nonassessable and that were not issued in violation of any pre-emptive or similar rights of the holders of outstanding securities of the Company; <u>provided</u>, <u>however</u>, that, if there shall occur any change in nominal or par value, a split-up or consolidation or any other reclassification or, upon the occurrence of an event described in Section 4.8, an exchange or conversion in respect of the Shares of the Company, the term "Shares" shall thereafter also mean the successor securities resulting from such change in nominal value, split-up or consolidation or such other reclassification or such exchange or conversion.

#### SECTION 1.23. SWIFT.

The term "<u>SWIFT</u>" shall mean the financial messaging network operated by the Society for Worldwide Interbank Financial Telecommunication, or its successor.

#### SECTION 1.24. Termination Option Event.

The term "Termination Option Event" shall mean an event of a kind defined as such in Section 4.1, 4.2 or 4.8.

# ARTICLE 2. FORM OF RECEIPTS, DEPOSIT OF SHARES, DELIVERY, TRANSFER AND SURRENDER OF AMERICAN DEPOSITARY SHARES

#### SECTION 2.1. Form of Receipts; Registration and Transferability of American Depositary Shares.

Definitive Receipts shall be substantially in the form set forth in Exhibit A to this Deposit Agreement, with appropriate insertions, modifications and omissions, as permitted under this Deposit Agreement. No Receipt shall be entitled to any benefits under this Deposit Agreement or be valid or obligatory for any purpose, unless that Receipt has been (i) executed by the Depositary by the manual signature of a duly authorized officer of the Depositary or (ii) executed by the facsimile signature of a duly authorized officer of the Depositary of the Depositary or the Registrar or a co-registrar. The Depositary

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shall maintain books on which (x) each Receipt so executed and delivered as provided in this Deposit Agreement and each transfer of that Receipt and (y) all American Depositary Shares delivered as provided in this Deposit Agreement and all registrations of transfer of American Depositary Shares, shall be registered. A Receipt bearing the facsimile signature of a person that was at any time a proper officer of the Depositary shall, subject to the other provisions of this paragraph, bind the Depositary, even if that person was not a proper officer of the Depositary on the date of issuance of that Receipt.

The Receipts and statements confirming registration of American Depositary Shares may have incorporated in or attached to them such legends or recitals or modifications not inconsistent with the provisions of this Deposit Agreement as may be required by the Depositary or required to comply with any applicable law or regulations thereunder or with the rules and regulations of any securities exchange upon which American Depositary Shares may be listed or to conform with any usage with respect thereto, or to indicate any special limitations or restrictions to which any particular Receipts and American Depositary Shares are subject by reason of the date of issuance of the underlying Deposited Securities or otherwise.

American Depositary Shares evidenced by a Receipt, when the Receipt is properly endorsed or accompanied by proper instruments of transfer, shall be transferable as certificated registered securities under the laws of the State of New York. American Depositary Shares not evidenced by Receipts shall be transferable as uncertificated registered securities under the laws of the State of New York. The Depositary, notwithstanding any notice to the contrary, may treat the Owner of American Depositary Shares as the absolute owner thereof for the purpose of determining the person entitled to distribution of dividends or other distributions or to any notice provided for in this Deposit Agreement and for all other purposes, and neither the Depositary nor the Company shall have any obligation or be subject to any liability under this Deposit Agreement to any Holder of American Depositary Shares (but only to the Owner of those American Depositary Shares).

#### SECTION 2.2. Deposit of Shares.

Subject to the terms and conditions of this Deposit Agreement, Shares or evidence of rights to receive Shares may be deposited under this Deposit Agreement by delivery thereof to any Custodian, accompanied by any appropriate instruments or instructions for transfer, or endorsement, in form satisfactory to the Custodian.

As conditions of accepting Shares for deposit, the Depositary may require (i) any certification required by the Depositary or the Custodian in accordance with the provisions of this Deposit Agreement, (ii) a written order directing the Depositary to deliver to, or upon the written order of, the person or persons stated in that order American Depositary Shares representing those deposited Shares, (iii) evidence satisfactory to the Depositary that those Shares have been re-registered in the books of the Company or the Foreign Registrar in the name of the Depositary, a Custodian or a

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nominee of the Depositary or a Custodian, (iv) evidence satisfactory to the Depositary that any necessary approval has been granted by any governmental body in each applicable jurisdiction and (v) an agreement or assignment, or other instrument satisfactory to the Depositary, that provides for the prompt transfer to the Custodian of any dividend, or right to subscribe for additional Shares or to receive other property, that any person in whose name those Shares are or have been recorded may thereafter receive upon or in respect of those Shares, or, in lieu thereof, such agreement of indemnity or other agreement as shall be satisfactory to the Depositary.

At the request and risk and expense of a person proposing to deposit Shares, and for the account of that person, the Depositary may receive certificates for Shares to be deposited, together with the other instruments specified in this Section, for the purpose of forwarding those Share certificates to the Custodian for deposit under this Deposit Agreement.

The Depositary shall instruct each Custodian that, upon each delivery to a Custodian of a certificate or certificates for Shares to be deposited under this Deposit Agreement, together with the other documents specified in this Section, that Custodian shall, as soon as transfer and recordation can be accomplished, present that certificate or those certificates to the Company or the Foreign Registrar, if applicable, for transfer and recordation of the Shares being deposited in the name of the Depositary or its nominee or that Custodian or its nominee.

Deposited Securities shall be held by the Depositary or by a Custodian for the account and to the order of the Depositary or at such other place or places as the Depositary shall determine.

# SECTION 2.3. Delivery of American Depositary Shares.

The Depositary shall instruct each Custodian that, upon receipt by that Custodian of any deposit pursuant to Section 2.2, together with the other documents or evidence required under that Section, that Custodian shall notify the Depositary of that deposit and the person or persons to whom or upon whose written order American Depositary Shares are deliverable in respect thereof. Upon receiving a notice of a deposit from a Custodian, or upon the receipt of Shares or evidence of the right to receive Shares by the Depositary, the Depositary, subject to the terms and conditions of this Deposit Agreement, shall deliver, to or upon the order of the person or persons entitled thereto, the number of American Depositary Shares issuable in respect of that deposit, but only upon payment to the Depositary of the fees and expenses of the Depositary for the delivery of those American Depositary Shares as provided in Section 5.9, and of all taxes and governmental charges and fees payable in connection with that deposit and the transfer of the deposited Shares. However, the Depositary shall deliver only whole numbers of American Depositary Shares.

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#### SECTION 2.4. <u>Registration of Transfer of American Depositary Shares; Combination and Split-up of Receipts; Interchange of Certificated and</u> Uncertificated American Depositary Shares.

The Depositary, subject to the terms and conditions of this Deposit Agreement, shall register a transfer of American Depositary Shares on its transfer books upon (i) in the case of certificated American Depositary Shares, surrender of the Receipt evidencing those American Depositary Shares, by the Owner or by a duly authorized attorney, properly endorsed or accompanied by proper instruments of transfer or (ii) in the case of uncertificated American Depositary Shares, receipt from the Owner of a proper instruction (including, for the avoidance of doubt, instructions through DRS and Profile as provided in Section 2.10), and, in either case, duly stamped as may be required by the laws of the State of New York and of the United States of America. Upon registration of a transfer, the Depositary shall deliver the transferred American Depositary Shares to or upon the order of the person entitled thereto.

The Depositary, subject to the terms and conditions of this Deposit Agreement, shall upon surrender of a Receipt or Receipts for the purpose of effecting a split-up or combination of such Receipt or Receipts, execute and deliver a new Receipt or Receipts for any authorized number of American Depositary Shares requested, evidencing the same aggregate number of American Depositary Shares as the Receipt or Receipts surrendered.

The Depositary, upon surrender of certificated American Depositary Shares for the purpose of exchanging for uncertificated American Depositary Shares, shall cancel the Receipt evidencing those certificated American Depositary Shares and send the Owner a statement confirming that the Owner is the owner of the same number of uncertificated American Depositary Shares. The Depositary, upon receipt of a proper instruction (including, for the avoidance of doubt, instructions through DRS and Profile as provided in Section 2.10) from the Owner of uncertificated American Depositary Shares for the purpose of exchanging for certificated American Depositary Shares, shall cancel those uncertificated American Depositary Shares and register and deliver to the Owner a Receipt evidencing the same number of certificated American Depositary Shares.

The Depositary may appoint one or more co-transfer agents for the purpose of effecting registration of transfers of American Depositary Shares and combinations and split-ups of Receipts at designated transfer offices on behalf of the Depositary, and the Depositary shall notify the Company of any such appointment. In carrying out its functions, a co-transfer agent may require evidence of authority and compliance with applicable laws and other requirements by Owners or persons entitled to American Depositary Shares and will be entitled to protection and indemnity to the same extent as the Depositary.

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#### SECTION 2.5. Surrender of American Depositary Shares and Withdrawal of Deposited Securities.

Upon surrender at the Depositary's Office of American Depositary Shares for the purpose of withdrawal of the Deposited Securities represented thereby and payment of the fee of the Depositary for the surrender of American Depositary Shares as provided in Section 5.9 and payment of all taxes and governmental charges payable in connection with that surrender and withdrawal of the Deposited Securities, and subject to the terms and conditions of this Deposit Agreement, the Owner of those American Depositary Shares shall be entitled to delivery (to the extent delivery can then be lawfully and practicably made), to or as instructed by that Owner, of the amount of Deposited Securities at the time represented by those American Depositary Shares, but not any money or other property as to which a record date for distribution to Owners has passed. That delivery shall be made, as provided in this Section, without unreasonable delay.

As a condition of accepting a surrender of American Depositary Shares for the purpose of withdrawal of Deposited Securities, the Depositary may require (i) that each surrendered Receipt be properly endorsed in blank or accompanied by proper instruments of transfer in blank and (ii) that the surrendering Owner execute and deliver to the Depositary a written order directing the Depositary to cause the Deposited Securities being withdrawn to be delivered to or upon the written order of a person or persons designated in that order.

Thereupon, the Depositary shall direct the Custodian to deliver, subject to Sections 2.6, 3.1 and 3.2, the other terms and conditions of this Deposit Agreement and local market rules and practices, to the surrendering Owner or to or upon the written order of the person or persons designated in the order delivered to the Depositary as above provided, the amount of Deposited Securities represented by the surrendered American Depositary Shares.

At the request, risk and expense of an Owner surrendering American Depositary Shares for withdrawal of Deposited Securities, and for the account of that Owner, the Depositary shall direct the Custodian to forward any cash or other property comprising, and forward a certificate or certificates, if applicable, and other proper documents of title, if any, for, the Deposited Securities represented by the surrendered American Depositary Shares to the Depositary for delivery at the Depositary's Office or to another address specified in the order received from the surrendering Owner.

The Depositary shall direct the Custodian to make delivery of Deposited Securities and may charge the surrendering Owner a fee and the Depositary's expenses for doing so.

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#### SECTION 2.6. Limitations on Delivery, Transfer and Surrender of American Depositary Shares.

As a condition precedent to the delivery, registration of transfer or surrender of any American Depositary Shares or split-up or combination of any Receipt or withdrawal of any Deposited Securities, the Depositary, Custodian or Registrar may require payment from the depositor of Shares or the presenter of the Receipt or instruction for registration of transfer or surrender of American Depositary Shares not evidenced by a Receipt of a sum sufficient to reimburse it for any tax or other governmental charge and any stock transfer or registration fee with respect thereto (including any such tax or charge and fee with respect to Shares being deposited or withdrawn) and payment of any applicable fees as provided in this Deposit Agreement, may require the production of proof satisfactory to it as to the identity and genuineness of any signature and may also require compliance with any regulations the Depositary may establish consistent with the provisions of this Deposit Agreement, including, without limitation, this Section 2.6.

The delivery of American Depositary Shares against deposit of Shares generally or against deposit of particular Shares may be suspended, or the registration of transfer of American Depositary Shares in particular instances may be refused, or the registration of transfer of outstanding American Depositary Shares generally may be suspended, during any period when the transfer books of the Depositary are closed, or if any such action is deemed necessary or advisable by the Depositary or the Company at any time or from time to time because of any requirement of law or of any government or governmental body or commission, or under any provision of this Deposit Agreement, or for any other reason. Notwithstanding anything to the contrary in this Deposit Agreement, the surrender of outstanding American Depositary or the Company or the Company or the Foreign Registrar, if applicable, or the deposit of Shares in connection with voting at a shareholders' meeting, or the payment of dividends, (ii) the payment of fees, taxes and similar charges, and (iii) compliance with any U.S. or foreign laws or governmental regulations relating to the American Depositary Shares or to the withdrawal of the Deposited Securities; in each case, the Depositary shall notify the Company as promptly as practicable of any such suspension or delay that is outside the ordinary course of business.

The Depositary shall not knowingly accept for deposit under this Deposit Agreement any Shares that, at the time of deposit, are Restricted Securities.

## SECTION 2.7. Lost Receipts, etc.

If a Receipt is mutilated, destroyed, lost or stolen, the Depositary shall deliver to the Owner the American Depositary Shares evidenced by that Receipt in uncertificated form or, if requested by the Owner, execute and deliver a new Receipt of like tenor in exchange and substitution for such mutilated Receipt, upon surrender and

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cancellation of that mutilated Receipt, or in lieu of and in substitution for that destroyed, lost or stolen Receipt. <u>However</u>, before the Depositary will deliver American Depositary Shares in uncertificated form or execute and deliver a new Receipt, in substitution for a destroyed, lost or stolen Receipt, the Owner must (a) file with the Depositary (i) a request for that replacement before the Depositary has notice that the Receipt has been acquired by a bona fide purchaser and (ii) a sufficient indemnity bond and (b) satisfy any other reasonable requirements imposed by the Depositary.

#### SECTION 2.8. Cancellation and Destruction of Surrendered Receipts.

The Depositary shall cancel all Receipts surrendered to it and is authorized to destroy Receipts so cancelled.

#### SECTION 2.9. Pre-Release of American Depositary Shares.

Notwithstanding Section 2.3, and unless otherwise instructed in writing by the Company, the Depositary may deliver American Depositary Shares prior to the receipt of Shares pursuant to Section 2.2 (a "<u>Pre-Release</u>"). The Depositary may, pursuant to Section 2.5, deliver Shares upon the surrender of American Depositary Shares that have been Pre-Released, whether or not that surrender is prior to the termination of that Pre-Release or the Depositary knows that those American Depositary Shares have been Pre-Released. The Depositary may receive American Depositary Shares in lieu of Shares in satisfaction of a Pre-Release. Each Pre-Release must be (a) preceded or accompanied by a written representation from the person to whom American Depositary Shares or Shares are to be delivered, that such person, or its customer, owns the Shares or American Depositary Shares to be remitted, as the case may be, (b) at all times fully collateralized with cash or such other collateral as the Depositary deems appropriate, (c) terminable by the Depositary on not more than five (5) business days' notice, and (d) subject to all indemnities and credit regulations that the Depositary deems appropriate. The number of American Depositary Shares outstanding at any time as a result of Pre-Release will not normally exceed thirty percent (30%) of all American Depositary Shares outstanding; provided, however, that the Depositary reserves the right to change or disregard that limit from time to time as it deems appropriate.

The Depositary may retain for its own account any compensation received by it in connection with Pre-Release.

#### SECTION 2.10. DTC Direct Registration System and Profile Modification System.

(a) Notwithstanding the provisions of Section 2.4, the parties acknowledge that DTC's Direct Registration System ("<u>DRS</u>") and Profile Modification System ("<u>Profile</u>") apply to the American Depositary Shares upon acceptance thereof to DRS by DTC. DRS is the system administered by DTC that facilitates interchange between registered holding of uncertificated securities and holding of security

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entitlements in those securities through DTC and a DTC participant. Profile is a required feature of DRS that allows a DTC participant, claiming to act on behalf of an Owner of American Depositary Shares, to direct the Depositary to register a transfer of those American Depositary Shares to DTC or its nominee and to deliver those American Depositary Shares to the DTC account of that DTC participant without receipt by the Depositary of prior authorization from the Owner to register that transfer.

(b) In connection with DRS/Profile, the parties acknowledge that the Depositary will not determine whether the DTC participant that is claiming to be acting on behalf of an Owner in requesting a registration of transfer and delivery as described in paragraph (a) above has the actual authority to act on behalf of that Owner (notwithstanding any requirements under the Uniform Commercial Code). For the avoidance of doubt, the provisions of Sections 5.3 and 5.8 apply to the matters arising from the use of the DRS/Profile. The parties agree that the Depositary's reliance on and compliance with instructions received by the Depositary through the DRS/Profile system and otherwise in accordance with this Deposit Agreement shall not constitute negligence or bad faith on the part of the Depositary.

#### ARTICLE 3. CERTAIN OBLIGATIONS OF OWNERS AND HOLDERS OF AMERICAN DEPOSITARY SHARES

## SECTION 3.1. Filing Proofs, Certificates and Other Information.

Any person presenting Shares for deposit or any Owner or Holder may be required from time to time to file with the Depositary or the Custodian such proof of citizenship or residence, exchange control approval, or such information relating to the registration on the books of the Company or the Foreign Registrar, if applicable, to execute such certificates and to make such representations and warranties, as the Depositary may deem necessary or proper. The Depositary may withhold the delivery or registration of transfer of American Depositary Shares, the distribution of any dividend or other distribution or of the proceeds thereof or the delivery of any Deposited Securities until that proof or other information is filed or those certificates are executed or those representations and warranties are made.

Each Holder and Owner agrees to comply with requests from the Company pursuant to applicable law and regulations, the rules and requirements of the Euronext Paris stock exchange, the Nasdaq Global Market and of any other stock exchange on which the Shares or American Depositary Shares are, or may be, registered, traded or listed and any book-entry settlement system or the articles of association or similar document of the Company, which are made to provide information, inter alia, as to the capacity in which such Holder or Owner owns American Depositary Shares (and Shares, as the case may be) and regarding the identity of any other person(s) interested in such American Depositary Shares and the nature of such interest and various other matters, whether or not they are Holders or Owners at the time of such request. The Depositary agrees to use its reasonable efforts to forward, upon the request of the

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Company and at the Company's expense (unless otherwise agreed between the Company and the Depositary), any such request from the Company to the Owners and to forward to the Company any such responses to such requests received by the Depositary, to the extent that disclosure is permitted under applicable law.

Holders and Owners of American Depositary Shares may be required from time to time, and in a timely manner, to file such proof of taxpayer status, residence and beneficial ownership (as applicable), to execute such certificates and to make such representations and warranties, or to provide any other information or documents, as the Company, the Depositary or the Custodian may deem necessary or proper to fulfill the Company's, the Depositary's or the Custodian's obligations under applicable law.

## SECTION 3.2. Liability of Owner for Taxes.

If any tax or other governmental charge shall become payable by the Company, the Custodian or the Depositary with respect to or in connection with any American Depositary Shares or any Deposited Securities represented by any American Depositary Shares or in connection with a transaction to which Section 4.8 applies, that tax or other governmental charge shall be payable by the Owner of those American Depositary Shares to the Company or the Depositary (for further payment to the Custodian if applicable). The Depositary may refuse to register any transfer of those American Depositary Shares or any withdrawal of Deposited Securities represented by those American Depositary Shares until that payment is made, and may withhold any dividends or other distributions or the proceeds thereof, or may sell for the account of the Owner any part or all of the Deposited Securities represented by those American Depositary Shares and apply those dividends or other distributions or the net proceeds of any sale of that kind in payment of that tax or other governmental charge <u>but</u>, even after a sale of that kind, the Owner of those American Depositary Shares shall remain liable for any deficiency. The Depositary shall distribute any net proceeds of a sale made under this Section that are not used to pay taxes or governmental charges to the Owners entitled to them in accordance with Section 4.1. If the number of Shares represented by each American Depositary Share decreases as a result of a sale of Deposited Securities under this Section, the Depositary may call for surrender of the American Depositary Shares to be exchanged on a mandatory basis for a lesser number of American Depositary Shares and may sell American Depositary Shares to the extent necessary to avoid distributing fractions of American Depositary Shares in that exchange and distribute the net proceeds of that sale to the Owners entitled to them.

Every Holder and Owner agrees to indemnify the Depositary, the Company, the Custodian, and any of their respective agents, directors, officers, employees and affiliates (as such term is defined in Regulation C under the Securities Act of 1933) for, and to hold each of them harmless from, any claims by any governmental authority or any other entity or person with respect to taxes, additions to tax, penalties or interest arising out of any refund of taxes, reduced rate of withholding at source or other

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tax benefit obtained. The obligations of Holders and Owners of American Depositary Shares under this Section 3.2 of the Deposit Agreement shall survive any transfer of American Depositary Shares, any surrender of American Depositary Shares and withdrawal of Deposited Securities, as well as the termination of the Deposit Agreement.

#### SECTION 3.3. Warranties on Deposit of Shares.

Every person depositing Shares under this Deposit Agreement shall be deemed thereby to represent and warrant that those Shares and each certificate therefor, if applicable, are validly issued, fully paid and nonassessable and were not issued in violation of any preemptive or similar rights of the holders of outstanding securities of the Company and that the person making that deposit is duly authorized so to do. Every depositing person shall also be deemed to represent that the Shares, at the time of deposit, are not Restricted Securities. All representations and warranties deemed made under this Section shall survive the deposit of Shares and delivery of American Depositary Shares.

#### SECTION 3.4. Disclosure of Interests.

In order to comply with applicable laws and regulations or the articles of association or similar document of the Company, the Company may from time to time request each Owner and Holder to provide to the Depositary information relating to: (a) the capacity in which it holds American Depositary Shares, (b) the identity of any Holders or other persons or entities then or previously interested in those American Depositary Shares and the nature of those interests and (c) any other matter where disclosure of such matter is required for that compliance. Each Owner and Holder agrees to provide all information known to it in response to a request made pursuant to this Section. Each Holder consents to the disclosure by the Owner or any other Holder through which it holds American Depositary Shares, directly or indirectly, of all information responsive to a request made pursuant to this Section relating to that Holder that is known to that Owner or other Holder. The Depositary agrees to use reasonable efforts, at the Company's expense (unless otherwise agreed between the Company and the Depositary), to comply with written instructions requesting that the Depositary forward any request authorized under this Section to the Owners and to forward to the Company any responses it receives in response to that request.

Each Owner and Holder of American Depositary Shares further agrees to comply with the laws and regulations of the United States and the Republic of France (if and to the extent applicable) with respect to the disclosure requirements regarding beneficial ownership of Shares, all as if the American Depositary Shares were the Shares represented thereby, which is deemed to include, inter alia, requirements to make notifications and filings within the required timeframes to the Company, to the Commission, to the French Autorité des Marchés Financiers and any other authorities in the United States or in the Republic of France. The Company reserves the right to instruct Holders to deliver their American Depositary Shares for cancellation and withdrawal of the Deposited Securities so as to permit the Company to deal directly with the Holder

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thereof as a holder of Shares and Holders agree to comply with such instructions. The Depositary agrees to cooperate with the Company in its efforts to inform Holders of the Company's exercise of its rights under this paragraph and agrees to consult with, and provide reasonable assistance without risk, liability or expense on the part of the Depositary, to the Company on the manner or manners in which it may enforce such rights with respect to any Holder.

# ARTICLE 4. THE DEPOSITED SECURITIES

#### SECTION 4.1. Cash Distributions.

Whenever the Depositary receives any cash dividend or other cash distribution on Deposited Securities, the Depositary shall, subject to the provisions of Section 4.5, convert that dividend or other distribution into Dollars and distribute the amount thus received (net of the fees and expenses of the Depositary as provided in Section 5.9) to the Owners entitled thereto, in proportion to the number of American Depositary Shares representing those Deposited Securities held by them respectively; <u>provided</u>, <u>however</u>, that if the Custodian or the Depositary shall be required to withhold and does withhold from that cash dividend or other cash distribution an amount on account of taxes or other governmental charges, the amount distributed to the Owners of the American Depositary Shares representing those Deposited Securities shall be reduced accordingly. <u>However</u>, the depositary will not pay any Owner a fraction of one cent, but will round each Owner's entitlement to the nearest whole cent.

The Company or its agent will remit to the appropriate governmental agency in each applicable jurisdiction all amounts withheld and owing to such agency. The Depositary will forward to the Company or its agent such information from its records as the Company may reasonably request to enable the Company or its agent to file necessary reports with governmental agencies.

If a cash distribution would represent a return of all or substantially all the value of the Deposited Securities underlying American Depositary Shares, the Depositary may require surrender of those American Depositary Shares and may require payment of or deduct the fee for surrender of American Depositary Shares (whether or not it is also requiring surrender of American Depositary Shares) as a condition of making that cash distribution. A distribution of that kind shall be a <u>Termination Option Event</u>.

#### SECTION 4.2. Distributions Other Than Cash, Shares or Rights.

Subject to the provisions of Sections 4.11 and 5.9, whenever the Depositary receives any distribution other than a distribution described in Section 4.1, 4.3 or 4.4 on Deposited Securities (but not in exchange for or in conversion or in lieu of Deposited Securities), the Depositary shall cause the securities or property received by it

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to be distributed to the Owners entitled thereto, after deduction or upon payment of any fees and expenses of the Depositary and any taxes or other governmental charges, in proportion to the number of American Depositary Shares representing such Deposited Securities held by them respectively, in any manner that the Depositary deems equitable and practicable for accomplishing that distribution (which may be a distribution of depositary shares representing the securities received); <u>provided</u>, <u>however</u>, that if in the opinion of the Depositary such distribution cannot be made proportionately among the Owners entitled thereto, or if for any other reason (including, but not limited to, any requirement that the Company or the Depositary withhold an amount on account of taxes or other governmental charges or that securities received must be registered under the Securities Act of 1933 in order to be distributed to Owners or Holders) the Depositary, after consultation with the Company to the extent practicable, deems such distribution, including, but not limited to, the public or private sale of the securities or property thus received, or any part thereof, and distribution of the net proceeds of any such sale (net of the fees and expenses of the Depositary as provided in Section 5.9) to the Owners entitled thereto, all in the manner and subject to the conditions set forth in Section 4.1. The Depositary may withhold any distribution of securities Act of 1933. The Depositary may sell, by public or private sale, an amount of securities or other property it would otherwise distribute under this Section 4.2 that is sufficient to pay its fees and expenses in respect of that distribution.

If a distribution under this Section 4.2 would represent a return of all or substantially all the value of the Deposited Securities underlying American Depositary Shares, the Depositary may require surrender of those American Depositary Shares and may require payment of or deduct the fee for surrender of American Depositary Shares (whether or not it is also requiring surrender of American Depositary Shares) as a condition of making that distribution. A distribution of that kind shall be a <u>Termination Option Event</u>.

## SECTION 4.3. Distributions in Shares.

Whenever the Depositary receives any distribution on Deposited Securities consisting of a dividend in, or free distribution of, Shares, the Depositary may deliver to the Owners entitled thereto, in proportion to the number of American Depositary Shares representing those Deposited Securities held by them respectively, an aggregate number of American Depositary Shares representing the amount of Shares received as that dividend or free distribution, subject to the terms and conditions of the Deposit Agreement with respect to the deposit of Shares and issuance of American Depositary Shares, including withholding of any tax or governmental charge as provided in Section 4.11 and payment of the fees and expenses of the Depositary as provided in

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Section 5.9 (and the Depositary may sell, by public or private sale, an amount of the Shares received (or American Depositary Shares representing those Shares) sufficient to pay its fees and expenses in respect of that distribution). In lieu of delivering fractional American Depositary Shares, the Depositary may sell the amount of Shares represented by the aggregate of those fractions (or American Depositary Shares representing those Shares) and distribute the net proceeds, all in the manner and subject to the conditions described in Section 4.1. If and to the extent that additional American Depositary Shares are not so delivered and Shares or American Depositary Shares are not so sold, each American Depositary Share shall thenceforth also represent the additional Shares distributed on the Deposited Securities represented thereby.

If the Company declares a distribution in which holders of Deposited Securities have a right to elect whether to receive cash, Shares or other securities or a combination of those things, or a right to elect to have a distribution sold on their behalf, the Depositary may, after consultation with the Company, make that right of election available for exercise by Owners in any manner the Depositary considers to be lawful and practical. As a condition of making a distribution election right available to Owners, the Depositary may require satisfactory assurances from the Company that doing so does not require registration of any securities under the Securities Act of 1933.

# SECTION 4.4. Rights.

(a) If rights are granted to the Depositary in respect of deposited Shares to purchase additional Shares or other securities, the Company and the Depositary shall endeavor to consult as to the actions, if any, the Depositary should take in connection with that grant of rights. The Depositary may, to the extent deemed by it to be lawful and practical (i) if requested in writing by the Company, grant to all or certain Owners rights to instruct the Depositary to purchase the securities to which the rights relate and deliver those securities or American Depositary Shares representing those securities to Owners, (ii) if requested in writing by the Company, or (iii) sell the rights to the extent practicable and distribute the net proceeds of that sale to Owners entitled to those proceeds. To the extent rights are not exercised, delivered or disposed of under (i), (ii) or (iii) above, the Depositary shall permit the rights to lapse unexercised.

(b) If the Depositary will act under (a)(i) above, the Company and the Depositary will enter into a separate agreement setting forth the conditions and procedures applicable to the particular offering. Upon instruction from an applicable Owner in the form the Depositary specified and upon payment by that Owner to the Depositary of an amount equal to the purchase price of the securities to be received upon the exercise of the rights, the Depositary shall, on behalf of that Owner, exercise the rights and purchase the securities. The purchased securities shall be delivered to, or as instructed by, the Depositary shall (i) deposit the purchased Shares under this Deposit Agreement and deliver American Depositary Shares representing

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those Shares to that Owner or (ii) deliver or cause the purchased Shares or other securities to be delivered to or to the order of that Owner. The Depositary will not act under (a)(i) above unless the offer and sale of the securities to which the rights relate are registered under the Securities Act of 1933 or the Depositary has received an opinion of United States counsel that is satisfactory to it to the effect that those securities may be sold and delivered to the applicable Owners without registration under the Securities Act of 1933.

(c) If the Depositary will act under (a)(ii) above, the Company and the Depositary will enter into a separate agreement setting forth the conditions and procedures applicable to the particular offering. Upon (i) the request of an applicable Owner to deliver the rights allocable to the American Depositary Shares of that Owner to an account specified by that Owner to which the rights can be delivered and (ii) receipt of such documents as the Company and the Depositary agreed to require to comply with applicable law, the Depositary will deliver those rights as requested by that Owner.

(d) If the Depositary will act under (a)(iii) above, the Depositary will use reasonable efforts to sell the rights in proportion to the number of American Depositary Shares held by the applicable Owners and pay the net proceeds to the Owners otherwise entitled to the rights that were sold, upon an averaged or other practical basis without regard to any distinctions among such Owners because of exchange restrictions or the date of delivery of any American Depositary Shares or otherwise.

(e) Payment or deduction of the fees of the Depositary as provided in Section 5.9 and payment or deduction of the expenses of the Depositary and any applicable taxes or other governmental charges shall be conditions of any delivery of securities or payment of cash proceeds under this Section 4.4.

(f) The Depositary shall not be responsible for any failure to determine that it may be lawful or feasible to make rights available to or exercise rights on behalf of Owners in general or any Owner in particular, or to sell rights.

# SECTION 4.5. Conversion of Foreign Currency.

Whenever the Depositary or the Custodian receives foreign currency, by way of dividends or other distributions or the net proceeds from the sale of securities, property or rights, and if at the time of the receipt thereof the foreign currency so received can in the judgment of the Depositary be converted on a reasonable basis into Dollars and the resulting Dollars transferred to the United States, the Depositary shall convert or cause to be converted by sale or in any other manner that it may determine that foreign currency into Dollars, and those Dollars shall be distributed to the Owners entitled thereto. A cash distribution may be made upon an averaged or other practicable basis without regard to any distinctions among Owners based on exchange restrictions, the date of delivery of any American Depositary Shares or otherwise and shall be net of

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any expenses of conversion into Dollars incurred by the Depositary as provided in Section 5.9.

If a conversion of foreign currency or the repatriation or distribution of Dollars can be effected only with the approval or license of any government or agency thereof, the Depositary may, but will not be required to, file an application for that approval or license.

If the Depositary, after consultation with the Company to the extent practicable, determines that in its judgment any foreign currency received by the Depositary or the Custodian is not convertible on a reasonable basis into Dollars transferable to the United States, or if any approval or license of any government or agency thereof that is required for such conversion is not filed or sought by the Depositary, or if any required approval or license is not obtained within a reasonable period as determined by the Depositary, the Depositary may distribute the foreign currency received by the Depositary to, or in its discretion may hold such foreign currency uninvested and without liability for interest thereon for the respective accounts of, the Owners entitled to receive the same.

If any conversion of foreign currency, in whole or in part, cannot be effected for distribution to some of the Owners entitled thereto, the Depositary may in its discretion make that conversion and distribution in Dollars to the extent practicable and permissible to the Owners entitled thereto and may distribute the balance of the foreign currency received by the Depositary to, or hold that balance uninvested and without liability for interest thereon for the account of, the Owners entitled thereto.

The Depositary may convert currency itself or through any of its affiliates and, in those cases, acts as principal for its own account and not as agent, advisor, broker or fiduciary on behalf of any other person and earns revenue, including, without limitation, transaction spreads, that it will retain for its own account. The revenue is based on, among other things, the difference between the exchange rate assigned to the currency conversion made under this Deposit Agreement and the rate that the Depositary or its affiliate receives when buying or selling foreign currency for its own account. The Depositary makes no representation that the exchange rate used or obtained in any currency conversion under this Deposit Agreement will be the most favorable rate that could be obtained at the time or that the method by which that rate will be determined will be the most favorable to Owners, subject to the Depositary's obligations under Section 5.3. The methodology used to determine exchange rates used in currency conversions is available upon request.

## SECTION 4.6. Fixing of Record Date.

Whenever a cash dividend, cash distribution or any other distribution is made on Deposited Securities or rights to purchase Shares or other securities are issued with respect to Deposited Securities (which rights will be delivered to or exercised or



sold on behalf of Owners in accordance with Section 4.4) or the Depositary receives notice that a distribution or issuance of that kind will be made, or whenever the Depositary receives notice that a meeting of holders of Shares will be held in respect of which the Company has requested the Depositary to send a notice under Section 4.7, or whenever the Depositary will assess a fee or charge against the Owners, or whenever the Depositary causes a change in the number of Shares that are represented by each American Depositary Share, or whenever the Depositary otherwise finds it necessary or convenient, the Depositary shall fix a record date, which shall be the same as, or as near as practicable to, any corresponding record date set by the Company with respect to Shares, (a) for the determination of the Owners (i) who shall be entitled to receive the benefit of that dividend or other distribution or those rights, (ii) who shall be entitled to give instructions for the exercise of voting rights at that meeting or (iii) who shall be responsible for that fee or charge or (iv) for any other purpose for which the record date was set, or (b) on or after which each American Depositary Share will represent the changed number of Shares. Subject to the provisions of Sections 4.1 through 4.5 and to the other terms and conditions of this Deposit Agreement, the Owners on a record date fixed by the Depositary shall be entitled to receive the amount distributable by the Depositary with respect to such dividend or other distribution or such rights or the net proceeds of sale thereof in proportion to the number of American Depositary Shares held by them respectively, to give voting instructions or to act in respect of the other matter for which that record date was fixed, or be responsible for that fee or charge, as the case may be.

## SECTION 4.7. Voting of Deposited Shares.

(a) Upon receipt of notice of any meeting of holders of Shares at which holders of Shares will be entitled to vote, if requested in writing by the Company, the Depositary shall, as soon as practicable thereafter, Disseminate to the Owners a notice, the form of which shall be in the sole discretion of the Depositary, that shall contain (a) the information contained in the notice of meeting received by the Depositary from the Company, (b) a statement that the Owners as of the close of business on a specified record date will be entitled, subject to any applicable provision of French law and of the articles of association or similar documents of the Company, to instruct the Depositary as to the exercise of the voting rights pertaining to the number of Shares represented by their respective American Depositary Shares (c) a statement as to the manner in which those instructions may be given and (d) the last date on which the Depositary will accept instructions (the "Instruction Cutoff Date").

(b) Upon the written request of an Owner of American Depositary Shares, as of the date of the request or, if a record date was specified by the Depositary, as of that record date, received on or before any Instruction Cutoff Date established by the Depositary, the Depositary may, and if the Depositary sent a notice under the preceding paragraph shall, endeavor, in so far as practicable, to vote or cause to be voted the amount of deposited Shares represented by those American Depositary Shares in

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accordance with the instructions set forth in that request. The Depositary shall not vote or attempt to exercise the right to vote that attaches to the deposited Shares other than in accordance with instructions given by Owners and received by the Depositary.

(c) There can be no assurance that Owners generally or any Owner in particular will receive the notice described in paragraph (a) above in time to enable Owners to give instructions to the Depositary prior to the Instruction Cutoff Date.

(d) In order to give Owners a reasonable opportunity to instruct the Depositary as to the exercise of voting rights relating to Shares, if the Company will request the Depositary to Disseminate a notice under paragraph (a) above, the Company shall give the Depositary notice of the meeting, details concerning the matters to be voted upon and copies of materials to be made available to holders of Shares in connection with the meeting not less than 30 days prior to the meeting date, except where under French law the notice period for such meeting is less than 30 days, in which case the Depositary shall upon receipt of the request use its commercially reasonable efforts to distribute to Owners the material described in the first paragraph of this Section 4.7 and carry out the further actions set forth in this Section 4.7.

Notwithstanding anything in this Section 4.7 to the contrary, the Depositary and the Company may modify, amend or adopt additional procedures from time to time as they determine may be necessary or appropriate.

Without prejudice to the Depositary's rights under Section 2.9, the Depositary will take no action to impair the ability of the Custodian to vote the number of Shares (including the Shares held by the Depositary in registered form) necessary to carry out the instructions of all Owners under this Section 4.7.

## SECTION 4.8. Tender and Exchange Offers; Redemption, Replacement or Cancellation of Deposited Securities.

(a) The Depositary shall not tender any Deposited Securities in response to any voluntary cash tender offer, exchange offer or similar offer made to holders of Deposited Securities (a "<u>Voluntary Offer</u>") except when instructed in writing to do so by an Owner surrendering American Depositary Shares and subject to any conditions or procedures the Depositary may require.

(b) If the Depositary receives a written notice that Deposited Securities have been redeemed for cash or otherwise purchased for cash in a transaction that is mandatory and binding on the Depositary as a holder of those Deposited Securities (a "<u>Redemption</u>"), the Depositary, at the expense of the Company (unless otherwise agreed between the Company and the Depositary), shall (i) if required, surrender Deposited Securities that have been redeemed to the issuer of those securities or its agent on the redemption date, (ii) Disseminate a notice to Owners (A) notifying them of that Redemption, (B) calling for surrender of a corresponding number of American

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Depositary Shares and (C) notifying them that the called American Depositary Shares have been converted into a right only to receive the money received by the Depositary upon that Redemption and those net proceeds shall be the Deposited Securities to which Owners of those converted American Depositary Shares shall be entitled upon surrenders of those American Depositary Shares in accordance with Section 2.5 or 6.2 and (iii) distribute the money received upon that Redemption to the Owners entitled to it upon surrender by them of called American Depositary Shares in accordance with Section 2.5 (and, for the avoidance of doubt, Owners shall not be entitled to receive that money under Section 4.1 or 4.2). If the Redemption affects less than all the Deposited Securities, the Depositary shall call for surrender a corresponding portion of the outstanding American Depositary Shares and only those American Depositary Shares will automatically be converted into a right to receive the net proceeds of the Redemption. The Depositary shall allocate the American Depositary Shares converted under the preceding sentence among the Owners pro-rata to their respective holdings of American Depositary Shares immediately prior to the Redemption, <u>except that</u> the allocations may be adjusted so that no fraction of a converted American Depositary Share is allocated to any Owner. A Redemption of all or substantially all of the Deposited Securities shall be a <u>Termination Option Event</u>.

(c) If the Depositary is notified of or there occurs any change in nominal value or any subdivision, combination or any other reclassification of the Deposited Securities or any recapitalization, reorganization, sale of assets substantially as an entirety, merger or consolidation affecting the issuer of the Deposited Securities or to which it is a party that is mandatory and binding on the Depositary as a holder of Deposited Securities and as a result securities or other property have been or will be delivered in exchange, conversion, replacement or in lieu of, Deposited Securities (a "<u>Replacement</u>"), then (i) the Depositary shall, if required surrender the old Deposited Securities affected by that Replacement of Shares and hold, as new Deposited Securities under this Deposited Securities if in the opinion of the Depositary, after consultation with the Company or its successor entity to the extent practicable, it is not lawful or not practical for it to hold those new Deposited Securities under this Deposit Agreement because those new Deposited Securities may not be distributed to Owners without registration under the Securities Act of 1933 or for any other reason, at public or private sale, at such places and on such terms as it deems proper and proceed as if those new Deposited Securities had been Redeemed under paragraph (b) above. A Replacement shall be a <u>Termination Option Event</u>.

(d) In the case of a Replacement where the new Deposited Securities will continue to be held under this Deposit Agreement, the Depositary may call for the surrender of outstanding Receipts to be exchanged for new Receipts specifically describing the new Deposited Securities and the number of those new Deposited Securities represented by each American Depositary Share. If the number of Shares represented by each American Depositary Share decreases as a result of a Replacement,

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the Depositary may, after consultation with the Company to the extent practicable, call for surrender of the American Depositary Shares to be exchanged on a mandatory basis for a lesser number of American Depositary Shares and may sell American Depositary Shares to the extent necessary to avoid distributing fractions of American Depositary Shares in that exchange and distribute the net proceeds of that sale to the Owners entitled to them.

(e) If there are no Deposited Securities with respect to American Depositary Shares, including if the Deposited Securities are cancelled, or the Deposited Securities with respect to American Depositary Shares have become apparently worthless, the Depositary may call for surrender of those American Depositary Shares or may cancel those American Depositary Shares, upon notice to Owners, and a <u>Termination Option Event</u> occurs.

## SECTION 4.9. Reports.

The Depositary shall make available for inspection by Owners at its Office any reports and communications, including any proxy solicitation material, received from the Company which are both (a) received by the Depositary as the holder of the Deposited Securities and (b) made generally available to the holders of those Deposited Securities by the Company. The Company shall furnish reports and communications, including any proxy soliciting material to which this Section applies, to the Depositary in English, to the extent those materials are required to be translated into English pursuant to any regulations of the Commission.

## SECTION 4.10. Lists of Owners.

Upon written request by the Company, the Depositary shall, at the expense of the Company (unless otherwise agreed between the Company and the Depositary), furnish to it a list, as of a recent date, of the names, addresses and American Depositary Share holdings of all Owners.

## SECTION 4.11. Withholding.

In the event that the Depositary determines that any distribution received or to be made by the Depositary (including Shares and rights to subscribe therefor) is subject to any tax or other governmental charge that the Depositary is obligated to withhold, the Depositary may sell, by public or private sale, all or a portion of the distributed property (including Shares and rights to subscribe therefor) in the amounts and manner the Depositary deems necessary and practicable to pay those taxes or charges, and the Depositary shall distribute the net proceeds of that sale, after deduction of those taxes or charges, to the Owners entitled thereto in proportion to the number of American Depositary Shares held by them respectively.

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None of the Company, the Depositary or the Custodian shall be liable for the failure by any Holder or Owner to obtain the benefits of credits on the basis of any tax withheld or paid against such Holder's or Owner's tax liability.

# ARTICLE 5. THE DEPOSITARY, THE CUSTODIANS AND THE COMPANY

# SECTION 5.1. Maintenance of Office and Transfer Books by the Depositary.

Until termination of this Deposit Agreement in accordance with its terms, the Depositary shall maintain facilities for the execution and delivery, registration, registration of transfers and surrender of American Depositary Shares in accordance with the provisions of this Deposit Agreement.

The Depositary shall keep books for the registration of American Depositary Shares, which shall be open for inspection by the Owners at the Depositary's Office during regular business hours, <u>provided</u> that such inspection is not for the purpose of communicating with Owners in the interest of a business or object other than the business of the Company or a matter related to this Deposit Agreement or the American Depositary Shares.

The Depositary may close the transfer books, at any time or from time to time, when deemed expedient by it in connection with the performance of its duties under this Deposit Agreement (whereupon it shall notify the Company as promptly as practicable of any closure that is outside the ordinary course of business).

Subject to the provisions of Section 5.4, if the Company lists any American Depositary Shares on one or more stock exchanges in the United States, the Depositary shall act as Registrar or appoint a Registrar or one or more co-registrars for registry of those American Depositary Shares in accordance with any requirements of that exchange or those exchanges. The Depositary shall notify the Company of any such appointment.

# SECTION 5.2. Prevention or Delay in Performance by the Depositary or the Company.

Neither the Depositary nor the Company nor any of their respective directors, employees, agents or affiliates shall incur any liability to any Owner or Holder (i) if by reason of any provision of any present or future law or regulation of the United States or any other country, or of any governmental or regulatory authority or stock exchange, or by reason of any provision, present or future, of the articles of association or similar document of the Company, or by reason of any provision of any securities issued or distributed by the Company, or any offering or distribution thereof, or by reason of any act of God or war or terrorism or other circumstances beyond its control, the Depositary or the Company is prevented from, forbidden to or delayed in, or could be subject to any

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civil or criminal penalty on account of doing or performing and therefore does not do or perform, any act or thing that, by the terms of this Deposit Agreement or the Deposited Securities, it is provided shall be done or performed, (ii) by reason of any exercise of, or failure to exercise, any discretion provided for in this Deposit Agreement (including any determination by the Depositary to take, or not take, any action that this Deposit Agreement provides the Deposited Securities but is not, under the terms of this Deposit Agreement, made available to Owners or Holders, or (iv) for any special, consequential, indirect or punitive damages for any breach of the terms of this Deposit Agreement. Where, by the terms of a distribution to which Section 4.1, 4.2 or 4.3 applies, or an offering to which Section 4.4 applies, or for any other reason, that distribution or offering may not be made available to Owners, and the Depositary may not dispose of that distribution or offering on behalf of Owners and make the net proceeds available to Owners, then the Depositary shall not make that distribution or offering available to Owners, and shall allow any rights, if applicable, to lapse.

## SECTION 5.3. Obligations of the Depositary and the Company.

The Company assumes no obligation nor shall it be subject to any liability under this Deposit Agreement to any Owner or Holder or any other persons (other than the Depositary), except that the Company agrees to perform its obligations specifically set forth in this Deposit Agreement without negligence or bad faith.

The Depositary assumes no obligation nor shall it be subject to any liability under this Deposit Agreement to any Owner or Holder (including, without limitation, liability with respect to the validity or worth of the Deposited Securities), except that the Depositary agrees to perform its obligations specifically set forth in this Deposit Agreement without negligence or bad faith.

Neither the Depositary nor the Company shall be under any obligation to appear in, prosecute or defend any action, suit or other proceeding in respect of any Deposited Securities or in respect of the American Depositary Shares on behalf of any Owner or Holder or any other person.

Each of the Depositary and the Company may rely, and shall be protected in relying upon, any written notice, request, direction or other document believed by it to be genuine and to have been signed or presented by the proper party or parties.

Neither the Depositary nor the Company, nor any of their respective affiliates (as such term is defined in Regulation C under the Securities Act of 1933) or agents, shall be liable for any action or non-action by it in reliance upon the advice of or information from legal counsel, accountants, any person presenting Shares for deposit, any Owner or any other person believed by it in good faith to be competent to give such advice or information.

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The Depositary shall not be liable for any acts or omissions made by a successor depositary whether in connection with a previous act or omission of the Depositary or in connection with any matter arising wholly after the removal or resignation of the Depositary, provided that in connection with the issue out of which such potential liability arises the Depositary performed its obligations without negligence or bad faith while it acted as Depositary.

The Depositary shall not be liable for the acts or omissions of any securities depository, clearing agency or settlement system in connection with or arising out of book-entry settlement of American Depositary Shares or Deposited Securities or otherwise.

In the absence of bad faith on its part, the Depositary shall not be responsible for any failure to carry out any instructions to vote any of the Deposited Securities, or for the manner in which any such vote is cast or the effect of any such vote.

Neither the Company nor the Depositary shall have any duty to make any determination or provide any information as to the tax status of the Company or any liability for any tax consequences that may be incurred by Owners or Holders as a result of owning or holding American Depositary Shares, including without limitation, tax consequences resulting from the Company (or any of its subsidiaries) being treated as a "Passive Foreign Investment Company" ("<u>PFIC</u>") (in each case as defined in the U.S. Internal Revenue Code and the regulations issued thereunder) or otherwise. The Company may have been in the past and may be in the future a PFIC for U.S. Federal income tax purposes. Owners must consult their own tax advisers as to the potential application of the PFIC rules.

No disclaimer of liability under the Securities Act of 1933 is intended by any provision of this Deposit Agreement.

# SECTION 5.4. Resignation and Removal of the Depositary.

The Depositary may at any time resign as Depositary hereunder by written notice of its election so to do delivered to the Company, to become effective upon the appointment of a successor depositary and its acceptance of that appointment as provided in this Section. The effect of resignation if a successor depositary is not appointed is provided for in Section 6.2.

The Depositary may at any time be removed by the Company by 120 days' prior written notice of that removal, to become effective upon the later of (i) the 120th day after delivery of the notice to the Depositary and (ii) the appointment of a successor depositary and its acceptance of its appointment as provided in this Section.

In case at any time the Depositary acting hereunder shall resign or be removed, the Company shall use its best efforts to appoint a successor depositary, which

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shall be a bank or trust company having an office in the Borough of Manhattan, The City of New York. Every successor depositary shall execute and deliver to its predecessor and to the Company an instrument in writing accepting its appointment hereunder, and thereupon such successor depositary, without any further act or deed, shall become fully vested with all the rights, powers, duties and obligations of its predecessor; but such predecessor, nevertheless, upon payment of all sums due it and on the written request of the Company shall execute and deliver an instrument transferring to such successor all rights and powers of such predecessor hereunder, shall duly assign, transfer and deliver all right, title and interest in the Deposited Securities to such successor and shall deliver to such successor a list of the Owners of all outstanding American Depositary Shares. Any such successor depositary shall promptly mail notice of its appointment to the Owners.

Any corporation or other entity into or with which the Depositary may be merged or consolidated shall be the successor of the Depositary without the execution or filing of any document or any further act.

## SECTION 5.5. The Custodians.

The Custodian shall be subject at all times and in all respects to the directions of the Depositary and shall be responsible solely to it. The Depositary in its discretion may at any time appoint a substitute or additional custodian or custodians, each of which shall thereafter be one of the Custodians under this Deposit Agreement. If the Depositary receives notice that a Custodian is resigning and, upon the effectiveness of that resignation there would be no Custodian acting under this Deposit Agreement, the Depositary shall, as promptly as practicable after receiving that notice, appoint a substitute custodian or custodians, each of which shall thereafter be a Custodian under this Deposit Agreement. The Depositary shall require any Custodian that resigns or is removed to deliver all Deposited Securities held by it to another Custodian.

## SECTION 5.6. Notices and Reports.

On or before the first date on which the Company gives notice, by publication or otherwise, of any meeting of holders of Shares or other Deposited Securities, or of any adjourned meeting of those holders, or of the taking of any action in respect of any cash or other distributions or the granting of any rights, the Company agrees to transmit to the Depositary and the Custodian a copy of the notice thereof in English but otherwise in the form given or to be given to holders of Shares or other Deposited Securities.

The Company will arrange for the translation into English, if not already in English, to the extent required pursuant to any regulations of the Commission, and the prompt transmittal by the Company to the Depositary and the Custodian of all notices and any other reports and communications which are made generally available by the Company to holders of its Shares. If requested in writing by the Company, the

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Depositary will Disseminate, at the Company's expense unless otherwise agreed between the Company and the Depositary, those notices, reports and communications to all Owners or otherwise make them available to Owners in a manner that the Company specifies as substantially equivalent to the manner in which those communications are made available to holders of Shares and compliant with the requirements of any securities exchange on which the American Depositary Shares are listed. The Company will timely provide the Depositary with the quantity of such notices, reports, and communications, as requested by the Depositary from time to time, in order for the Depositary to effect that Dissemination.

The Company represents that as of the date of this Deposit Agreement, the statements in Article 11 of the Receipt with respect to the Company's obligation to file periodic reports under the United States Securities Exchange Act of 1934, as amended, are true and correct. The Company agrees to promptly notify the Depositary upon becoming aware of any change in the truth of any of those statements.

# SECTION 5.7. Distribution of Additional Shares, Rights, etc.

If the Company or any affiliate of the Company determines to make any issuance or distribution of (1) additional Shares, (2) rights to subscribe for Shares, (3) securities convertible into Shares, or (4) rights to subscribe for such securities (each a "<u>Distribution</u>"), the Company shall notify the Depositary in writing in English as promptly as practicable and in any event before the Distribution starts and, if requested in writing by the Depositary, the Company shall promptly furnish to the Depositary either (i) evidence satisfactory to the Depositary that the Distribution is registered under the Securities Act of 1933 or (ii) a written opinion from U.S. counsel for the Company that is reasonably satisfactory to the Depositary, stating that the Distribution does not require, or, if made in the United States, would not require, registration under the Securities Act of 1933.

The Company agrees with the Depositary that neither the Company nor any company controlled by, controlling or under common control with the Company will at any time deposit any Shares that, at the time of deposit, are Restricted Securities.

# SECTION 5.8. Indemnification.

The Company agrees to indemnify the Depositary, its directors, employees, agents and affiliates and each Custodian against, and hold each of them harmless from, any liability or expense (including, but not limited to any reasonable fees and expenses incurred in seeking, enforcing or collecting such indemnity and the fees and expenses of counsel) which may arise out of or in connection with (a) any registration with the Commission of American Depositary Shares or Deposited Securities or the offer or sale thereof in the United States or (b) acts performed or omitted, pursuant to the provisions of or in connection with this Deposit Agreement and the American Depositary Shares, as the same may be amended, modified or supplemented from time to time, (i) by

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either the Depositary or a Custodian or their respective directors, employees, agents and affiliates, except for any liability or expense arising out of the negligence or bad faith of either of them, or (ii) by the Company or any of its directors, employees, agents and affiliates.

The Depositary agrees to indemnify the Company, its directors, officers, employees, agents and affiliates and hold them harmless from any liability or expense (including, but not limited to, the reasonable fees and expenses of counsel) which may arise out of acts performed or omitted by the Depositary or any Custodian or their respective directors, employees, agents and affiliates due to their negligence or bad faith.

The obligations set forth in this Section 5.8 shall survive the termination of this Deposit Agreement and the succession or substitution of any party hereto.

Any person seeking indemnification hereunder (an "<u>indemnified person</u>") shall notify the person from whom it is seeking indemnification (the "<u>indemnifying person</u>") of the commencement of any indemnifiable action or claim promptly after such indemnified person becomes aware of such commencement (provided that the failure to make such notification shall not affect such indemnified person's rights to seek indemnification except to the extent the indemnifying person is materially prejudiced by such failure) and shall consult in good faith with the indemnifying person as to the conduct of the defense of such action or claim that may give rise to an indemnity hereunder, which defense shall be reasonable in the circumstances. No indemnified person shall compromise or settle any action or claim that may give rise to an indemnity hereunder without the consent of the indemnifying person, which consent shall not be unreasonably withheld.

# SECTION 5.9. Charges of Depositary.

The Company agrees to pay the fees and out-of-pocket expenses of the Depositary and those of any Registrar only in accordance with agreements in writing entered into between the Depositary and the Company from time to time or to the extent that the Company is a depositor of Shares or an Owner.

The following charges shall be incurred by any party depositing or withdrawing Shares or by any party surrendering American Depositary Shares or to whom American Depositary Shares are issued (including, without limitation, issuance pursuant to a stock dividend or stock split declared by the Company or an exchange of stock regarding the American Depositary Shares or Deposited Securities or a delivery of American Depositary Shares pursuant to Section 4.3), or by Owners, as applicable: (1) taxes and other governmental charges, (2) such registration fees as may from time to time be in effect for the registration of transfers of Shares generally on the Share register of the Company or Foreign Registrar and applicable to transfers of Shares to or from the name of the Depositary or its nominee or the Custodian or its nominee on the making of deposits or withdrawals hereunder, (3) such cable (including SWIFT) and facsimile

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transmission fees and expenses as are expressly provided in this Deposit Agreement, (4) such expenses as are incurred by the Depositary in the conversion of foreign currency pursuant to Section 4.5, (5) a fee of \$5.00 or less per 100 American Depositary Shares (or portion thereof) for the delivery of American Depositary Shares pursuant to Section 2.3, 4.3 or 4.4 and the surrender of American Depositary Shares pursuant to Section 2.5 or 6.2, (6) a fee of \$.05 or less per American Depositary Share (or portion thereof) for any cash distribution made pursuant to this Deposit Agreement, including, but not limited to Sections 4.1 through 4.4 and Section 4.8, (7) a fee for the distribution of securities pursuant to Section 4.2 or of rights pursuant to Section 4.4 (where the Depositary Shares referred to above which would have been charged as a result of the deposit of such securities under this Deposit Agreement (for purposes of this item 7 treating all such securities as if they were Shares) but which securities are instead distributed by the Depositary services, which will be payable as provided in item 9 below, and (9) any other charges payable by the Depositary or the Custodian, any of the Depositary's or Custodian's agents, in connection with the servicing of Shares or other Deposited Securities (which charges shall be assessed against Owners as of the date or dates set by the Depositary in accordance with Section 4.6 and shall be payable at the sole discretion of the Depositary by billing those Owners for those charges or by deducting those charges from one or more cash dividends or other cash distributions).

The Depositary may collect any of its fees by deduction from any cash distribution payable, or by selling a portion of any securities to be distributed, to Owners that are obligated to pay those fees.

In performing its duties under this Deposit Agreement, the Depositary may use brokers, dealers, foreign currency dealers or other service providers that are owned by or affiliated with the Depositary and that may earn or share fees, spreads or commissions.

The Depositary, subject to Section 2.9, may own and deal in any class of securities of the Company and its affiliates and in American Depositary Shares.

# SECTION 5.10. Retention of Depositary Documents.

The Depositary is authorized to destroy those documents, records, bills and other data compiled during the term of this Deposit Agreement at the times permitted by the laws or regulations governing the Depositary.

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# SECTION 5.11. Exclusivity.

Without prejudice to the Company's rights under Section 5.4, the Company agrees not to appoint any other depositary for issuance of depositary shares, depositary receipts or any similar securities or instruments (for the avoidance of doubt, other than instruments or securities issued directly by the Company) in the United States so long as The Bank of New York Mellon is acting as Depositary under this Deposit Agreement.

# ARTICLE 6. AMENDMENT AND TERMINATION

# SECTION 6.1. Amendment.

The form of the Receipts and any provisions of this Deposit Agreement may at any time and from time to time be amended by agreement between the Company and the Depositary without the consent of Owners or Holders in any respect that they may deem necessary or desirable. Any amendment that would impose or increase any fees or charges (other than taxes and other governmental charges, registration fees, cable, telex or facsimile transmission costs, delivery costs or other such expenses), or that would otherwise prejudice any substantial existing right of Owners, shall, however, not become effective as to outstanding American Depositary Shares until the expiration of 30 days after notice of that amendment has been Disseminated to the Owners of outstanding American Depositary Shares. Every Owner and Holder, at the time any amendment so becomes effective, shall be deemed, by continuing to hold American Depositary Shares or any interest therein, to consent and agree to that amendment and to be bound by the Deposit Agreement as amended thereby. Upon the effectiveness of an amendment to the form of Receipt, including a change in the number of Shares represented by each American Depositary Share, the Depositary may call for surrender of Receipts to be replaced with new Receipts in the amended form or call for surrender of American Depositary Shares to effect that change of ratio. In no event shall any amendment impair the right of the Owner to surrender American Depositary Shares and receive delivery of the Deposited Securities represented thereby, except in order to comply with mandatory provisions of applicable law.

## SECTION 6.2. Termination.

(a) The Company may terminate this Deposit Agreement by notice to the Depositary. The Depositary may terminate this Deposit Agreement if (i) at any time 60 days shall have expired after the Depositary delivered to the Company a written resignation notice and a successor depositary has not been appointed and accepted its appointment as provided in Section 5.4, (ii) an Insolvency Event or Delisting Event occurs with respect to the Company or (iii) a Termination Option Event has occurred or will occur. If a termination of the Depositary Shares then outstanding setting a date for termination (the

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"Termination Date"), which shall be at least 90 days after the date of that notice, and this Deposit Agreement shall terminate on that Termination Date.

(b) After the Termination Date, the Company shall be discharged from all obligations under this Deposit Agreement except for its obligations to the Depositary under Sections 5.8 and 5.9.

(c) At any time after the Termination Date, the Depositary may sell the Deposited Securities then held under this Deposit Agreement and may thereafter hold uninvested the net proceeds of any such sale, together with any other cash then held by it hereunder, unsegregated and without liability for interest, for the pro rata benefit of the Owners of American Depositary Shares that remain outstanding, and those Owners will become general creditors of the Depositary with respect to those net proceeds. After making that sale, the Depositary shall be discharged from all obligations under this Deposit Agreement, <u>except</u> (i) to account for the net proceeds and other cash (after deducting, in each case, the fee of the Depositary for the surrender of American Depositary Shares, any expenses for the account of the Owner of such American Depositary Shares in accordance with the terms and conditions of this Deposit Agreement and any applicable taxes or governmental charges) and (ii) for its obligations under Section 5.8 and (iii) to act as provided in the paragraph (d) below.

(d) After the Termination Date, the Depositary shall continue to receive dividends and other distributions pertaining to Deposited Securities (that have not been sold), may sell rights and other property as provided in this Deposit Agreement and shall deliver Deposited Securities (or sale proceeds) upon surrender of American Depositary Shares (after payment or upon deduction, in each case, of the fee of the Depositary for the surrender of American Depositary Shares, any expenses for the account of the Owner of those American Depositary Shares in accordance with the terms and conditions of this Deposit Agreement and any applicable taxes or governmental charges). <u>However</u>, after the Termination Date, (i) the Depositary may refuse to accept surrenders of American Depositary Shares for the purpose of withdrawal of Deposited Securities (that have not been sold) if in its judgment the requested withdrawal would interfere with its efforts to sell the Deposited Securities, (ii) the Depositary may discontinue the registration of transfers of American Depositary Shares and suspend the distribution of dividends and other distributions on Deposited Securities to the Owners and need not give any further notices or perform any further acts under this Deposit Agreement except as provided in this Section.

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# ARTICLE 7. MISCELLANEOUS

# SECTION 7.1. Counterparts; Signatures.

This Deposit Agreement may be executed in any number of counterparts, each of which shall be deemed an original and all of those counterparts shall constitute one and the same instrument. Copies of this Deposit Agreement shall be filed with the Depositary and the Custodians and shall be open to inspection by any Owner or Holder during regular business hours.

Any manual signature on this Deposit Agreement that is faxed, scanned or photocopied, and any electronic signature valid under the Electronic Signatures in Global and National Commerce Act, 15 U.S.C. § 7001, *et. seq.*, shall for all purposes have the same validity, legal effect and admissibility in evidence as an original manual signature, and the parties hereby waive any objection to the contrary.

# SECTION 7.2. No Third Party Beneficiaries.

This Deposit Agreement is for the exclusive benefit of the parties and shall not be deemed to give any legal or equitable right, remedy or claim whatsoever to any other person.

# SECTION 7.3. Severability.

In case any one or more of the provisions contained in this Deposit Agreement or in a Receipt should be or become invalid, illegal or unenforceable in any respect, the validity, legality and enforceability of the remaining provisions contained in this Deposit Agreement or that Receipt shall in no way be affected, prejudiced or disturbed thereby.

# SECTION 7.4. Owners and Holders as Parties; Binding Effect.

The Owners and Holders from time to time shall be parties to this Deposit Agreement and shall be bound by all of the terms and conditions of this Deposit Agreement and of the Receipts by acceptance of American Depositary Shares or any interest therein.

## SECTION 7.5. Notices.

Any and all notices to be given to the Company shall be in writing and shall be deemed to have been duly given if personally delivered or sent by domestic first class or international air mail or air courier or sent by facsimile transmission or email attaching a pdf or similar bit-mapped image of a signed writing, <u>provided</u> that receipt of the facsimile transmission or email has been confirmed by the recipient, addressed to ERYTECH Pharma S.A., 60 avenue Rockefeller, Bâtiment Adénine, 4ème étage, 69008

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Lyon, France, Attention: Gil Beyen, or any other place to which the Company may have transferred its principal office with notice to the Depositary.

Any and all notices to be given to the Depositary shall be in writing and shall be deemed to have been duly given if in English and personally delivered or sent by first class domestic or international air mail or air courier or sent by facsimile transmission or email attaching a pdf or similar bit-mapped image of a signed writing, addressed to The Bank of New York Mellon, 101 Barclay Street, New York, New York 10286, Attention: Depositary Receipt Administration, or any other place to which the Depositary may have transferred its Office with notice to the Company.

Delivery of a notice to the Company or Depositary by mail or air courier shall be deemed effected when deposited, postage prepaid, in a post-office letter box or received by an air courier service. Delivery of a notice to the Company or Depositary sent by facsimile transmission or email shall be deemed effected when the recipient acknowledges receipt of that notice.

A notice to be given to an Owner shall be deemed to have been duly given when Disseminated to that Owner. Dissemination in paper form will be effective when personally delivered or sent by first class domestic or international air mail or air courier, addressed to that Owner at the address of that Owner as it appears on the transfer books for American Depositary Shares of the Depositary, or, if that Owner has filed with the Depositary a written request that notices intended for that Owner be mailed to some other address, at the address designated in that request. Dissemination in electronic form will be effective when sent in the manner consented to by the Owner to the electronic address most recently provided by the Owner for that purpose.

## SECTION 7.6. Appointment of Agent for Service of Process; Submission to Jurisdiction; Jury Trial Waiver.

The Company hereby (i) designates and appoints the person named in Exhibit A to this Deposit Agreement, located in the United States, as the Company's U.S. registered agent upon which process may be served in any suit or proceeding arising out of or relating to the Shares or Deposited Securities, the American Depositary Shares, the Receipts or this Deposit Agreement (a "Proceeding"), (ii) consents and submits to the jurisdiction of any state or federal court in the State of New York in which any Proceeding may be instituted and (iii) agrees that service of process upon said U.S. registered agent shall be deemed in every respect effective service of process upon the Company in any Proceeding. The Company agrees to deliver to the Depositary, upon the execution and delivery of this Deposit Agreement, a written acceptance by the above-named agent of its appointment as process agent. The Company further agrees to take any and all action, including the filing of any and all such documents and instruments, as may be necessary to continue that designation and appointment in full force and effect, or to appoint and maintain the appointment of another process agent located in the United States as required above, and to deliver to the Depositary a written acceptance by that

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agent of that appointment, for so long as any American Depositary Shares or Receipts remain outstanding or this Deposit Agreement remains in force. In the event the Company fails to maintain the designation and appointment of a process agent in the United States in full force and effect, the Company hereby waives personal service of process upon it and consents that a service of process in connection with a Proceeding may be made by certified or registered mail, return receipt requested, directed to the Company at its address last specified for notices under this Deposit Agreement, and service so made shall be deemed completed five (5) days after the same shall have been so mailed.

EACH PARTY TO THIS DEPOSIT AGREEMENT (INCLUDING, FOR AVOIDANCE OF DOUBT, EACH OWNER AND HOLDER) HEREBY IRREVOCABLY WAIVES, TO THE FULLEST EXTENT PERMITTED BY APPLICABLE LAW, ANY RIGHT IT MAY HAVE TO A TRIAL BY JURY IN ANY SUIT, ACTION OR PROCEEDING AGAINST THE COMPANY AND/OR THE DEPOSITARY DIRECTLY OR INDIRECTLY ARISING OUT OF OR RELATING TO THE SHARES OR OTHER DEPOSITED SECURITIES, THE AMERICAN DEPOSITARY SHARES OR THE RECEIPTS, THIS DEPOSIT AGREEMENT OR ANY TRANSACTION CONTEMPLATED HEREIN OR THEREIN, OR THE BREACH HEREOF OR THEREOF, INCLUDING, WITHOUT LIMITATION, ANY QUESTION REGARDING EXISTENCE, VALIDITY OR TERMINATION (WHETHER BASED ON CONTRACT, TORT OR ANY OTHER THEORY).

# SECTION 7.7. Waiver of Immunities.

To the extent that the Company or any of its properties, assets or revenues may have or may hereafter become entitled to, or have attributed to it, any right of immunity, on the grounds of sovereignty or otherwise, from any legal action, suit or proceeding, from the giving of any relief in any respect thereof, from setoff or counterclaim, from the jurisdiction of any court, from service of process, from attachment upon or prior to judgment, from attachment in aid of execution or judgment, or from execution of judgment, or other legal process or proceeding for the giving of any relief or for the enforcement of any judgment, in any jurisdiction in which proceedings may at any time be commenced, with respect to its obligations, liabilities or any other matter under or arising out of or in connection with the Shares or Deposited Securities, the American Depositary Shares, the Receipts or this Deposit Agreement, the Company, to the fullest extent permitted by law, hereby irrevocably and unconditionally waives, and agrees not to plead or claim, any immunity of that kind and consents to relief and enforcement as provided above.

## SECTION 7.8. Governing Law.

This Deposit Agreement and the Receipts shall be interpreted in accordance with and all rights hereunder and thereunder and provisions hereof and thereof shall be governed by the laws of the State of New York.

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IN WITNESS WHEREOF, ERYTECH PHARMA S.A. and THE BANK OF NEW YORK MELLON have duly executed this Deposit Agreement as of the day and year first set forth above and all Owners and Holders shall become parties hereto upon acceptance by them of American Depositary Shares or any interest therein.

# ERYTECH PHARMA S.A.

# By: /s/ Gil Beyen

Name: Gil Beyen Title: Chief Executive Officer

THE BANK OF NEW YORK MELLON, as Depositary

By: /s/ Robert W. Goad

Name: Robert W. Goad Title: Managing Director

#### EXHIBIT A

AMERICAN DEPOSITARY SHARES (Each American Depositary Share represents one deposited Share)

# THE BANK OF NEW YORK MELLON AMERICAN DEPOSITARY RECEIPT FOR ORDINARY SHARES OF ERYTECH PHARMA S.A. (INCORPORATED UNDER THE LAWS OF FRANCE)

The Bank of New York Mellon, as depositary (hereinafter called the "Depositary"), hereby certifies that or registered assigns IS THE OWNER OF

# AMERICAN DEPOSITARY SHARES

representing deposited ordinary shares (herein called "Shares") of ERYTECH Pharma S.A., incorporated under the laws of France (herein called the "<u>Company</u>"). At the date hereof, each American Depositary Share represents one Share deposited or subject to deposit under the Deposit Agreement (as such term is hereinafter defined) with a custodian for the Depositary (herein called the "<u>Custodian</u>") that, as of the date of the Deposit Agreement, was Société Générale located in Paris. The Depositary's Office is located at a different address than its principal executive office. Its Office is located at 101 Barclay Street, New York, N.Y. 10286, and its principal executive office is located at One Wall Street, New York, N.Y. 10286.

THE DEPOSITARY'S OFFICE ADDRESS IS 101 BARCLAY STREET, NEW YORK, N.Y. 10286

# 1. THE DEPOSIT AGREEMENT.

This American Depositary Receipt is one of an issue (herein called "<u>Receipts</u>"), all issued and to be issued upon the terms and conditions set forth in the Amended and Restated Deposit Agreement dated as of November 9, 2017 (herein called the "<u>Deposit Agreement</u>") among the Company, the Depositary, and all Owners and Holders from time to time of American Depositary Shares issued thereunder, each of whom by accepting American Depositary Shares agrees to become a party thereto and become bound by all the terms and conditions thereof. The Deposit Agreement sets forth the rights of Owners and Holders and the rights and duties of the Depositary in respect of the Shares deposited thereunder and any and all other securities, property and cash from time to time received in respect of those Shares and held thereunder (those Shares, securities, property, and cash are herein called "<u>Deposited Securities</u>"). Copies of the Deposit Agreement are on file at the Depositary's Office in New York City and at the office of the Custodian.

The statements made on the face and reverse of this Receipt are summaries of certain provisions of the Deposit Agreement and are qualified by and subject to the detailed provisions of the Deposit Agreement, to which reference is hereby made. Capitalized terms defined in the Deposit Agreement and not defined herein shall have the meanings set forth in the Deposit Agreement.

# 2. SURRENDER OF RECEIPTS AND WITHDRAWAL OF SHARES.

Upon surrender at the Depositary's Office of American Depositary Shares for the purpose of withdrawal of the Deposited Securities represented thereby and payment of the fee of the Depositary for the surrender of American Depositary Shares as provided in Section 5.9 of the Deposit Agreement and payment of all taxes and governmental charges payable in connection with that surrender and withdrawal of the Deposited Securities, and subject to the terms and conditions of this Deposit Agreement, the Owner of those American Depositary Shares shall be entitled to delivery (to the extent delivery can then be lawfully and practicably made), to or as instructed by that Owner, of the amount of Deposited Securities at the time represented by those American Depositary Shares. That delivery will be made, at the office of the Custodian, <u>except that</u>, at the request, risk and expense of the surrendering Owner, and for the account of that Owner, the Depositary shall direct the Custodian to forward any cash or other property comprising, and forward a certificate or certificates, if applicable, and other proper documents of title, if any, for, the Deposited Securities represented by the surrendering Owner. The Depositary shall direct the Custodian with respect to delivery of Deposited Securities and may charge the surrendering Owner a fee and its expenses for doing so.

# 3. REGISTRATION OF TRANSFER OF AMERICAN DEPOSITARY SHARES; COMBINATION AND SPLIT-UP OF RECEIPTS; INTERCHANGE OF CERTIFICATED AND UNCERTIFICATED AMERICAN DEPOSITARY SHARES.

The Depositary, subject to the terms and conditions of the Deposit Agreement, shall register a transfer of American Depositary Shares on its transfer books upon (i) in the case of certificated American Depositary Shares, surrender of the Receipt evidencing those American Depositary Shares, by the Owner or by a duly authorized attorney, properly endorsed or accompanied by proper instruments of transfer or (ii) in the case of uncertificated American Depositary Shares, receipt from the Owner of a proper instruction (including, for the avoidance of doubt, instructions through DRS and Profile as provided in Section 2.10 of that Agreement), and, in either case, duly stamped as may be required by the laws of the State of New York and of the United States of America. Upon registration of a transfer, the Depositary shall deliver the transferred American Depositary Shares to or upon the order of the person entitled thereto.

The Depositary, subject to the terms and conditions of the Deposit Agreement, shall upon surrender of a Receipt or Receipts for the purpose of effecting a split-up or combination of such Receipt or Receipts, execute and deliver a new Receipt or Receipts for any authorized number of American Depositary Shares requested, evidencing the same aggregate number of American Depositary Shares as the Receipt or Receipts surrendered.

The Depositary, upon surrender of certificated American Depositary Shares for the purpose of exchanging for uncertificated American Depositary Shares, shall cancel the Receipt evidencing those certificated American Depositary Shares and send the Owner a statement confirming that the Owner is the owner of the same number of uncertificated American Depositary Shares. The Depositary, upon receipt of a proper instruction (including, for the avoidance of doubt, instructions through DRS and Profile as provided in Section 2.10 of the Deposit Agreement) from the Owner of uncertificated American Depositary Shares for the purpose of exchanging for certificated American Depositary Shares, shall cancel those uncertificated American Depositary Shares and register and deliver to the Owner a Receipt evidencing the same number of certificated American Depositary Shares.

As a condition precedent to the delivery, registration of transfer, or surrender of any American Depositary Shares or split-up or combination of any Receipt or withdrawal of any Deposited Securities, the Depositary, the Custodian, or Registrar may require payment from the depositor of the Shares or the presenter of the Receipt or instruction for registration of transfer or surrender of American Depositary Shares not evidenced by a Receipt of a sum sufficient to reimburse it for any tax or other governmental charge and any stock transfer or registration fee with respect thereto (including any such tax or charge and fee with respect to Shares being deposited or withdrawn) and payment of any

applicable fees as provided in the Deposit Agreement, may require the production of proof satisfactory to it as to the identity and genuineness of any signature and may also require compliance with any regulations the Depositary may establish consistent with the provisions of the Deposit Agreement.

The delivery of American Depositary Shares against deposit of Shares generally or against deposit of particular Shares may be suspended, or the registration of transfer of American Depositary Shares in particular instances may be refused, or the registration of transfer of outstanding American Depositary Shares generally may be suspended, during any period when the transfer books of the Depositary are closed, or if any such action is deemed necessary or advisable by the Depositary or the Company at any time or from time to time because of any requirement of law or of any government or governmental body or commission, or under any provision of the Depositary Shares and withdrawal of Deposited Securities may not be suspended subject only to (i) temporary delays caused by closing the transfer books of the Depositary or the Company or the deposit of Shares in connection with voting at a shareholders' meeting, or the payment of dividends, (ii) the payment of fees, taxes and similar charges, and (iii) compliance with any U.S. or foreign laws or governmental regulations relating to the American Depositary Shares or to the withdrawal of the Deposited Securities; in each case, the Depositary shall notify the Company as promptly as practicable of any such suspension or delay that is outside the ordinary course of business.

The Depositary shall not knowingly accept for deposit under the Deposit Agreement any Shares that, at the time of deposit, are Restricted Securities.

#### 4. LIABILITY OF OWNER FOR TAXES.

If any tax or other governmental charge shall become payable with respect to or in connection with any American Depositary Shares or any Deposited Securities represented by any American Depositary Shares or in connection with a transaction to which Section 4.8 of the Deposit Agreement applies, that tax or other governmental charge shall be payable by the Owner to the Company or the Depositary (for further payment to the Custodian if applicable). The Depositary may refuse to register any transfer of those American Depositary Shares or any withdrawal of Deposited Securities represented by those American Depositary Shares until that payment is made, and may withhold any dividends or other distributions or the proceeds thereof, or may sell for the account of the Owner any part or all of the Deposited Securities represented by those American Depositary Shares, and may apply those dividends or other distributions or the net proceeds of any sale of that kind in payment of that tax or other governmental charge but, even after a sale of that kind, the Owner shall remain liable for any deficiency. The Depositary shall distribute any net proceeds of a sale made under Section 3.2 of the Deposit Agreement that are not used to pay taxes or governmental charges to the Owners

entitled to them in accordance with Section 4.1 of the Deposit Agreement. If the number of Shares represented by each American Depositary Share decreases as a result of a sale of Deposited Securities under Section 3.2 of the Deposit Agreement, the Depositary may call for surrender of the American Depositary Shares to be exchanged on a mandatory basis for a lesser number of American Depositary Shares and may sell American Depositary Shares to the extent necessary to avoid distributing fractions of American Depositary Shares in that exchange and distribute the net proceeds of that sale to the Owners entitled to them.

Every Holder and Owner agrees to indemnify the Depositary, the Company, the Custodian, and any of their respective agents, directors, officers, employees and affiliates (as such term is defined in Regulation C under the Securities Act of 1933) for, and to hold each of them harmless from, any claims by any governmental authority or any other entity or person with respect to taxes, additions to tax, penalties or interest arising out of any refund of taxes, reduced rate of withholding at source or other tax benefit obtained. The obligations of Holders and Owners of American Depositary Shares under Section 3.2 of the Deposit Agreement shall survive any transfer of American Depositary Shares, any surrender of American Depositary Shares and withdrawal of Deposited Securities, as well as the termination of the Deposit Agreement

## 5. WARRANTIES ON DEPOSIT OF SHARES.

Every person depositing Shares under the Deposit Agreement shall be deemed thereby to represent and warrant, that those Shares and each certificate therefor, if applicable, are validly issued, fully paid and nonassessable and were not issued in violation of any preemptive or similar rights of the holders of outstanding securities of the Company and that the person making that deposit is duly authorized so to do. Every depositing person shall also be deemed to represent that the Shares, at the time of deposit, are not Restricted Securities. All representations and warranties deemed made under Section 3.3 of the Deposit Agreement shall survive the deposit of Shares and delivery of American Depositary Shares.

## 6. FILING PROOFS, CERTIFICATES, AND OTHER INFORMATION.

Any person presenting Shares for deposit or any Owner or Holder may be required from time to time to file with the Depositary or the Custodian such proof of citizenship or residence, exchange control approval, or such information relating to the registration on the books of the Company or the Foreign Registrar, if applicable, to execute such certificates and to make such representations and warranties, as the Depositary may deem necessary or proper. The Depositary may withhold the delivery or registration of transfer of any American Depositary Shares, the distribution of any dividend or other distribution or of the proceeds thereof or the delivery of any Deposited Securities until that proof or other information is filed or those certificates are executed or those representations and warranties are made. Each Holder and Owner agrees to comply with requests from the Company pursuant to applicable law and regulations, the rules and

requirements of the Euronext Paris stock exchange, the Nasdaq Global Market and of any other stock exchange on which the Shares or American Depositary Shares are, or may be, registered, traded or listed and any book-entry settlement system or the articles of association or similar document of the Company, which are made to provide information, inter alia, as to the capacity in which such Holder or Owner owns American Depositary Shares (and Shares, as the case may be) and regarding the identity of any other person(s) interested in such American Depositary Shares and the nature of such interest and various other matters, whether or not they are Holders or Owners at the time of such request. The Depositary agrees to use its reasonable efforts to forward, upon the request of the Company and at the Company's expense (unless otherwise agreed between the Company and the Depositary), any such request from the Company to the Owners and to forward to the Company any such responses to such requests received by the Depositary, to the extent that disclosure is permitted under applicable law.

Holders and Owners of American Depositary Shares may be required from time to time, and in a timely manner, to file such proof of taxpayer status, residence and beneficial ownership (as applicable), to execute such certificates and to make such representations and warranties, or to provide any other information or documents, as the Company, the Depositary or the Custodian may deem necessary or proper to fulfill the Company's, the Depositary's or the Custodian's obligations under applicable law.

As conditions of accepting Shares for deposit, the Depositary may require (i) any certification required by the Depositary or the Custodian in accordance with the provisions of the Deposit Agreement, (ii) a written order directing the Depositary to deliver to, or upon the written order of, the person or persons stated in that order, the number of American Depositary Shares representing those Deposited Shares (iii) evidence satisfactory to the Depositary that those Shares have been re-registered in the books of the Company or the Foreign Registrar in the name of the Depositary, a Custodian or a nominee of the Depositary or a Custodian, (iv) evidence satisfactory to the Depositary that any necessary approval has been granted by any governmental body in each applicable jurisdiction and (v) an agreement or assignment, or other instrument satisfactory to the Depositary, that provides for the prompt transfer to the Custodian of any dividend, or right to subscribe for additional Shares or to receive other property, that any person in whose name those Shares are or have been recorded may thereafter receive upon or in respect of those Shares, or, in lieu thereof, such agreement of indemnity or other agreement as shall be satisfactory to the Depositary.

## 7. CHARGES OF DEPOSITARY.

The following charges shall be incurred by any party depositing or withdrawing Shares or by any party surrendering American Depositary Shares or to whom American Depositary Shares are issued (including, without limitation, issuance pursuant to a stock dividend or stock split declared by the Company or an exchange of stock regarding the American Depositary Shares or Deposited Securities or a delivery of American

Depositary Shares pursuant to Section 4.3 of the Deposit Agreement), or by Owners, as applicable: (1) taxes and other governmental charges, (2) such registration fees as may from time to time be in effect for the registration of transfers of Shares generally on the Share register of the Company or Foreign Registrar and applicable to transfers of Shares to or from the name of the Depositary or its nominee or the Custodian or its nominee on the making of deposits or withdrawals hereunder, (3) such cable (including SWIFT) and facsimile transmission fees and expenses as are expressly provided in the Deposit Agreement, (4) such expenses as are incurred by the Depositary in the conversion of foreign currency pursuant to Section 4.5 of the Deposit Agreement, (5) a fee of \$5.00 or less per 100 American Depositary Shares (or portion thereof) for the delivery of American Depositary Shares pursuant to Section 2.3, 4.3 or 4.4 of the Deposit Agreement and the surrender of American Depositary Shares pursuant to Section 2.5 or 6.2 of the Deposit Agreement, (6) a fee of \$.05 or less per American Depositary Share (or portion thereof) for any cash distribution made pursuant to the Deposit Agreement, including, but not limited to Sections 4.1 through 4.4 and 4.8 of the Deposit Agreement, (7) a fee for the distribution of securities pursuant to Section 4.2 of the Deposit Agreement or of rights pursuant to Section 4.4 of that Agreement (where the Depositary will not exercise or sell those rights on behalf of Owners), such fee being in an amount equal to the fee for the execution and delivery of American Depositary Shares referred to above which would have been charged as a result of the deposit of such securities under the Deposit Agreement (for purposes of this item 7 treating all such securities as if they were Shares) but which securities are instead distributed by the Depositary to Owners, (8) in addition to any fee charged under item 6, a fee of \$.05 or less per American Depositary Share (or portion thereof) per annum for depositary services, which will be payable as provided in item 9 below, and (9) any other charges payable by the Depositary or the Custodian, any of the Depositary's or Custodian's agents or the agents of the Depositary's or Custodian's agents, in connection with the servicing of Shares or other Deposited Securities (which charges shall be assessed against Owners as of the date or dates set by the Depositary in accordance with Section 4.6 of the Deposit Agreement and shall be payable at the sole discretion of the Depositary by billing those Owners for those charges or by deducting those charges from one or more cash dividends or other cash distributions).

The Depositary may collect any of its fees by deduction from any cash distribution payable, or by selling a portion of any securities to be distributed, to Owners that are obligated to pay those fees.

In performing its duties under this Deposit Agreement, the Depositary may use brokers, dealers, foreign currency dealers or other service providers that are owned by or affiliated with the Depositary and that may earn or share fees, spreads or commissions.

The Depositary, subject to Article 8 hereof, may own and deal in any class of securities of the Company and its affiliates and in American Depositary Shares.

From time to time, the Depositary may make payments to the Company to reimburse the Company for costs and expenses generally arising out of establishment and maintenance of the American Depositary Shares program, waive fees and expenses for services provided by the Depositary or share revenue from the fees collected from Owners or Holders. In performing its duties under the Deposit Agreement, the Depositary may use brokers, dealers or other service providers that are affiliates of the Depositary and that may earn or share fees and commissions.

#### 8. PRE-RELEASE OF RECEIPTS.

Notwithstanding Section 2.3 of the Deposit Agreement, and unless otherwise instructed in writing by the Company, the Depositary may deliver American Depositary Shares prior to the receipt of Shares pursuant to Section 2.2 of the Deposit Agreement (a "<u>Pre-Release</u>"). The Depositary may, pursuant to Section 2.5 of the Deposit Agreement, deliver Shares upon the surrender of American Depositary Shares that have been Pre-Released, whether or not that surrender is prior to the termination of that Pre-Release or the Depositary knows that those American Depositary Shares have been Pre-Released. The Depositary may receive American Depositary Shares in lieu of Shares in satisfaction of a Pre-Release. Each Pre-Release must be (a) preceded or accompanied by a written representation from the person to whom American Depositary Shares or Shares are to be delivered, that such person, or its customer, owns the Shares or American Depositary Shares to be remitted, as the case may be, (b) at all times fully collateralized with cash or such other collateral as the Depositary deems appropriate, (c) terminable by the Depositary on not more than five (5) business days' notice, and (d) subject to all indemnities and credit regulations that the Depositary deems appropriate. The number of American Depositary Shares outstanding at any time as a result of Pre-Release will not normally exceed thirty percent (30%) of all American Depositary Shares outstanding; <u>provided</u>, <u>however</u>, that the Depositary reserves the right to change or disregard that limit from time to time as it deems appropriate.

The Depositary may retain for its own account any compensation received by it in connection with Pre-Release.

## 9. TITLE TO AMERICAN DEPOSITARY SHARES.

It is a condition of the American Depositary Shares, and every successive Owner and Holder of American Depositary Shares, by accepting or holding the same consents and agrees that American Depositary Shares evidenced by a Receipt, when the Receipt is properly endorsed or accompanied by proper instruments of transfer, shall be transferable as certificated registered securities under the laws of the State of New York, and that American Depositary Shares not evidenced by Receipts shall be transferable as uncertificated registered securities under the laws of the State of New York. The Depositary, notwithstanding any notice to the contrary, may treat the Owner of American Depositary Shares as the absolute owner thereof for the purpose of determining the person entitled to distribution of dividends or other distributions or to any notice provided

for in the Deposit Agreement and for all other purposes, and neither the Depositary nor the Company shall have any obligation or be subject to any liability under the Deposit Agreement to any Holder of American Depositary Shares, but only to the Owner.

# 10. VALIDITY OF RECEIPT.

This Receipt shall not be entitled to any benefits under the Deposit Agreement or be valid or obligatory for any purpose, unless this Receipt shall have been (i) executed by the Depositary by the manual signature of a duly authorized officer of the Depositary or (ii) executed by the facsimile signature of a duly authorized officer of the Depositary and countersigned by the manual signature of a duly authorized signatory of the Depositary or the Registrar or a co-registrar.

#### 11. REPORTS; INSPECTION OF TRANSFER BOOKS.

The Company is subject to the periodic reporting requirements of the Securities Exchange Act of 1934 and, accordingly, files certain reports with the Securities and Exchange Commission. Those reports will be available for inspection and copying through the Commission's EDGAR system or at public reference facilities maintained by the Commission in Washington, D.C.

The Depositary will make available for inspection by Owners at its Office any reports, notices and other communications, including any proxy soliciting material, received from the Company which are both (a) received by the Depositary as the holder of the Deposited Securities and (b) made generally available to the holders of those Deposited Securities by the Company. The Company shall furnish reports and communications, including any proxy soliciting material to which Section 4.9 of the Deposit Agreement applies, to the Depositary in English, to the extent such materials are required to be translated into English pursuant to any regulations of the Commission.

The Depositary will keep books for the registration of American Depositary Shares and transfers of American Depositary Shares, which shall be open for inspection by the Owners at the Depositary's Office during regular business hours, <u>provided</u> that such inspection shall not be for the purpose of communicating with Owners in the interest of a business or object other than the business of the Company or a matter related to the Deposit Agreement or the American Depositary Shares.

# 12. DIVIDENDS AND DISTRIBUTIONS.

Whenever the Depositary receives any cash dividend or other cash distribution on Deposited Securities, the Depositary will, if at the time of receipt thereof any amounts received in a foreign currency can in the judgment of the Depositary be converted on a reasonable basis into Dollars transferable to the United States, and subject to the Deposit Agreement, convert that dividend or other cash distribution into Dollars and distribute the amount thus received (net of the fees and expenses of the Depositary as

provided in Article 7 hereof and Section 5.9 of the Deposit Agreement) to the Owners entitled thereto; <u>provided</u>, <u>however</u>, that if the Custodian or the Depositary is required to withhold and does withhold from that cash dividend or other cash distribution an amount on account of taxes or other governmental charges, the amount distributed to the Owners of the American Depositary Shares representing those Deposited Securities shall be reduced accordingly. If a cash distribution would represent a return of all or substantially all the value of the Deposited Securities underlying American Depositary Shares, the Depositary may require surrender of those American Depositary Shares and may require payment of or deduct the fee for surrender of American Depositary Shares (whether or not it is also requiring surrender of American Depositary Shares) as a condition of making that cash distribution. A distribution of that kind shall be a <u>Termination Option Event</u>.

Subject to the provisions of Section 4.11 and 5.9 of the Deposit Agreement, whenever the Depositary receives any distribution other than a distribution described in Section 4.1, 4.3 or 4.4 of the Deposit Agreement on Deposited Securities (but not in exchange for or in conversion or in lieu of Deposited Securities), the Depositary will cause the securities or property received by it to be distributed to the Owners entitled thereto, after deduction or upon payment of any fees and expenses of the Depositary and any taxes or other governmental charges, in any manner that the Depositary deems equitable and practicable for accomplishing that distribution (which may be a distribution of depositary shares representing the securities received); provided, however, that if in the opinion of the Depositary such distribution cannot be made proportionately among the Owners of Receipts entitled thereto, or if for any other reason the Depositary, after consultation with the Company to the extent practicable, deems such distribution not to be lawful and feasible, the Depositary may adopt such other method as it may deem equitable and practicable for the purpose of effecting such distribution, including, but not limited to, the public or private sale of the securities or property thus received, or any part thereof, and distribution of the net proceeds of any such sale (net of the fees and expenses of the Depositary as provided in Article 7 hereof and Section 5.9 of the Deposit Agreement) to the Owners entitled thereto all in the manner and subject to the conditions set forth in Section 4.1 of the Deposit Agreement. The Depositary may withhold any distribution of securities under Section 4.2 of the Deposit Agreement if it has not received satisfactory assurances from the Company that the distribution does not require registration under the Securities Act of 1933. The Depositary may sell, by public or private sale, an amount of securities or other property it would otherwise distribute under this Article that is sufficient to pay its fees and expenses in respect of that distribution. If a distribution under Section 4.2 of the Deposit Agreement would represent a return of all of substantially all the value of the Deposited Securities underlying American Depositary Shares, the Depositary may require surrender of those American Depositary Shares and may require payment of or deduct the fee for surrender of American Depositary Shares (whether or not it is also requiring surrender of American Depositary Shares) as a condition of making that distribution. A distribution of that kind shall be a Termination Option Event.

Whenever the Depositary receives any distribution consisting of a dividend in, or free distribution of, Shares, the Depositary may deliver to the Owners entitled thereto, an aggregate number of American Depositary Shares representing the amount of Shares received as that dividend or free distribution, subject to the terms and conditions of the Deposit Agreement with respect to the deposit of Shares and after deduction or upon issuance of American Depositary Shares, including the withholding of any tax or other governmental charge as provided in Section 4.11 of the Deposit Agreement and the payment of the fees and expenses of the Depositary as provided in Article 7 hereof and Section 5.9 of the Deposit Agreement (and the Depositary may sell, by public or private sale, an amount of Shares received (or American Depositary Shares representing those Shares) sufficient to pay its fees and expenses in respect of that distribution). In lieu of delivering fractional American Depositary Shares, the Depositary may sell the amount of Shares represented by the aggregate of those fractions (or American Depositary Shares representing those Shares) and distribute the net proceeds, all in the manner and subject to the conditions described in Section 4.10 fthe Deposit Agreement. If and to the extent that additional American Depositary Shares are not so delivered and Shares or American Depositary Shares shall thenceforth also represent the additional Shares distributed on the Deposited Securities represented thereby.

If the Company declares a distribution in which holders of Deposited Securities have a right to elect whether to receive cash, Shares or other securities or a combination of those things, or a right to elect to have a distribution sold on their behalf, the Depositary may, after consultation with the Company, make that right of election available for exercise by Owners any manner the Depositary considers to be lawful and practical. As a condition of making a distribution election right available to Owners, the Depositary may require satisfactory assurances from the Company that doing so does not require registration of any securities under the Securities Act of 1933.

In the event that the Depositary determines that any distribution received or to be made by the Depositary (including Shares and rights to subscribe therefor) is subject to any tax or other governmental charge that the Depositary is obligated to withhold, the Depositary may sell, by public or private sale, all or a portion of the distributed property (including Shares and rights to subscribe therefor) in the amounts and manner the Depositary deems necessary and practicable to pay any those taxes or charges, and the Depositary shall distribute the net proceeds of that sale, after deduction of those taxes or charges, to the Owners entitled thereto in proportion to the number of American Depositary Shares held by them respectively.

None of the Company, the Depositary or the Custodian shall be liable for the failure by any Holder or Owner to obtain the benefits of credits on the basis of any tax withheld or paid against such Holder's or Owner's tax liability.

13. RIGHTS.

(a) If rights are granted to the Depositary in respect of deposited Shares to purchase additional Shares or other securities, the Company and the Depositary shall endeavor to consult as to the actions, if any, the Depositary should take in connection with that grant of rights. The Depositary may, to the extent deemed by it to be lawful and practical (i) if requested in writing by the Company, grant to all or certain Owners rights to instruct the Depositary to purchase the securities to which the rights relate and deliver those securities or American Depositary Shares representing those securities to Owners, (ii) if requested in writing by the Company, deliver the rights to or to the order of certain Owners, or (iii) sell the rights to the extent practicable and distribute the net proceeds of that sale to Owners entitled to those proceeds. To the extent rights are not exercised, delivered or disposed of under (i), (ii) or (iii) above, the Depositary shall permit the rights to lapse unexercised.

(b) If the Depositary will act under (a)(i) above, the Company and the Depositary will enter into a separate agreement setting forth the conditions and procedures applicable to the particular offering. Upon instruction from an applicable Owner in the form the Depositary specified and upon payment by that Owner to the Depositary of an amount equal to the purchase price of the securities to be received upon the exercise of the rights, the Depositary shall, on behalf of that Owner, exercise the rights and purchase the securities. The purchased securities shall be delivered to, or as instructed by, the Depositary. The Depositary shall (i) deposit the purchased Shares under the Deposit Agreement and deliver American Depositary Shares representing those Shares to that Owner or (ii) deliver or cause the purchased Shares or other securities to be delivered to or to the order of that Owner. The Depositary will not act under (a)(i) above unless the offer and sale of the securities to which the rights relate are registered under the Securities Act of 1933 or the Depositary has received an opinion of United States counsel that is satisfactory to it to the effect that those securities may be sold and delivered to the applicable Owners without registration under the Securities Act of 1933.

(c) If the Depositary will act under (a)(ii) above, the Company and the Depositary will enter into a separate agreement setting forth the conditions and procedures applicable to the particular offering. Upon (i) the request of an applicable Owner to deliver the rights allocable to the American Depositary Shares of that Owner to an account specified by that Owner to which the rights can be delivered and (ii) receipt of such documents as the Company and the Depositary agreed to require to comply with applicable law, the Depositary will deliver those rights as requested by that Owner.

(d) If the Depositary will act under (a)(iii) above, the Depositary will use reasonable efforts to sell the rights in proportion to the number of American Depositary Shares held by the applicable Owners and pay the net proceeds to the Owners otherwise entitled to the rights that were sold, upon an averaged or other practical basis without regard to any distinctions among such Owners because of exchange restrictions or the date of delivery of any American Depositary Shares or otherwise.

(e) Payment or deduction of the fee of the Depositary as provided in Section 5.9 of the Deposit Agreement and payment or deduction of the expenses of the Depositary and any applicable taxes or other governmental charges shall be conditions of any delivery of securities or payment of cash proceeds under Section 4.4 of that Agreement.

(f) The Depositary shall not be responsible for any failure to determine that it may be lawful or feasible to make rights available to or exercise rights on behalf of Owners in general or any Owner in particular, or to sell rights.

## 14. CONVERSION OF FOREIGN CURRENCY.

Whenever the Depositary or the Custodian receives foreign currency, by way of dividends or other distributions or the net proceeds from the sale of securities, property or rights, and if at the time of the receipt thereof the foreign currency so received can in the judgment of the Depositary be converted on a reasonable basis into Dollars and the resulting Dollars transferred to the United States, the Depositary shall convert or cause to be converted by sale or in any other manner that it may determine that foreign currency into Dollars, and those Dollars shall be distributed to the Owners entitled thereto. A cash distribution may be made upon an averaged or other practicable basis without regard to any distinctions among Owners based on exchange restrictions, the date of delivery of any American Depositary Shares or otherwise and shall be net of any expenses of conversion into Dollars incurred by the Depositary as provided in Section 5.9 of the Deposit Agreement.

If a conversion of foreign currency or the repatriation or distribution of Dollars can be effected only with the approval or license of any government or agency thereof, the Depositary may, but will not be required to, file an application for that approval or license.

If the Depositary, after consultation with the Company to the extent practicable, determines that in its judgment any foreign currency received by the Depositary or the Custodian is not convertible on a reasonable basis into Dollars transferable to the United States, or if any approval or license of any government or agency thereof that is required for such conversion is not filed or sought by the Depositary, or if any required approval or license is not obtained within a reasonable period as determined by the Depositary, the Depositary may distribute the foreign currency received by the Depositary to, or in its discretion may hold such foreign currency uninvested and without liability for interest thereon for the respective accounts of, the Owners entitled to receive the same.

If any conversion of foreign currency, in whole or in part, cannot be effected for distribution to some of the Owners entitled thereto, the Depositary may in its discretion make that conversion and distribution in Dollars to the extent practicable and permissible to the Owners entitled thereto and may distribute the balance of the foreign currency

received by the Depositary to, or hold that balance uninvested and without liability for interest thereon for the account of, the Owners entitled thereto.

The Depositary may convert currency itself or through any of its affiliates and, in those cases, acts as principal for its own account and not as agent, advisor, broker or fiduciary on behalf of any other person and earns revenue, including, without limitation, transaction spreads, that it will retain for its own account. The revenue is based on, among other things, the difference between the exchange rate assigned to the currency conversion made under this Deposit Agreement and the rate that the Depositary or its affiliate receives when buying or selling foreign currency for its own account. The Depositary makes no representation that the exchange rate used or obtained in any currency conversion under this Deposit Agreement will be the most favorable rate that could be obtained at the time or that the method by which that rate will be determined will be the most favorable to Owners, subject to the Depositary's obligations under Section 5.3. The methodology used to determine exchange rates used in currency conversions is available upon request.

## 15. RECORD DATES.

Whenever a cash dividend, cash distribution or any other distribution is made on Deposited Securities or rights to purchase Shares or other securities are issued with respect to Deposited Securities (which rights will delivered to or exercised or sold on behalf of Owners in accordance with Section 4.4 of the Deposit Agreement) or the Depositary receives notice that a distribution or issuance of that kind will be made, or whenever the Depositary receives notice that a meeting of holders of Shares will be held in respect of which the Company has requested the Depositary to send a notice under Section 4.7 of the Deposit Agreement, or whenever the Depositary will assess a fee or charge against the Owners, or whenever for any reason the Depositary causes a change in the number of Shares that are represented by each American Depositary Share, or whenever the Depositary otherwise finds it necessary or convenient, the Depositary shall fix a record date, which shall be the same as, or as near as practicable to, any corresponding record date set by the Company with respect to Shares, (a) for the determination of the Owners (i) who shall be entitled to receive the benefit of that dividend or other distribution or those rights, (ii) who shall be entitled to give instructions for the exercise of voting rights at that meeting, (iii) who shall be responsible for that fee or charge or (iv) for any other purpose for which the record date was set, or (b) on or after which each American Depositary Share will represent the changed number of Shares. Subject to the provisions of Sections 4.1 through 4.5 of the Deposit Agreement and to the other terms and conditions of the Deposit Agreement, the Owners on a record date fixed by the Depositary shall be entitled to receive the amount distributable by the Depositary with respect to that dividend or other distribution or those rights or the net proceeds of sale thereof in proportion to the number of American Depositary Shares held by them respectively, to give voting instructions or to a

#### 16. VOTING OF DEPOSITED SHARES.

(a) Upon receipt of notice of any meeting of holders of Shares at which holders of Shares will be entitled to vote, if requested in writing by the Company, the Depositary shall, as soon as practicable thereafter, Disseminate to the Owners a notice, the form of which shall be in the sole discretion of the Depositary, that shall contain (a) the information contained in the notice of meeting received by the Depositary from the Company, (b) a statement that the Owners as of the close of business on a specified record date will be entitled, subject to any applicable provision of French law and of the articles of association or similar documents of the Company, to instruct the Depositary as to the exercise of the voting rights pertaining to the number of Shares represented by their respective American Depositary Shares (c) a statement as to the manner in which those instructions may be given and (d) the last date on which the Depositary will accept instructions (the "Instruction Cutoff Date").

(b) Upon the written request of an Owner of American Depositary Shares, as of the date of the request or, if a record date was specified by the Depositary, as of that record date, received on or before any Instruction Cutoff Date established by the Depositary, the Depositary may, and if the Depositary sent a notice under the preceding paragraph shall, endeavor, in so far as practicable, to vote or cause to be voted the amount of deposited Shares represented by those American Depositary Shares in accordance with the instructions set forth in that request. The Depositary shall not vote or attempt to exercise the right to vote that attaches to the deposited Securities other than in accordance with instructions given by Owners and received by the Depositary.

(c) There can be no assurance that Owners generally or any Owner in particular will receive the notice described in paragraph (a) above in time to enable Owners to give instructions to the Depositary prior to the Instruction Cutoff Date.

(d) In order to give Owners a reasonable opportunity to instruct the Depositary as to the exercise of voting rights relating to Shares, if the Company will request the Depositary to Disseminate a notice under paragraph (a) above, the Company shall give the Depositary notice of the meeting, details concerning the matters to be voted upon and copies of materials to be made available to holders of Shares in connection with the meeting not less than 30 days prior to the meeting date, in which case the Depositary shall upon receipt of the request use its commercially reasonable efforts to distribute to Owners the material described in the first paragraph of Section 4.7 of the Deposit Agreement and carry out the further actions set forth in Section 4.7 of the Deposit Agreement.

Notwithstanding anything in Section 4.7 of the Deposit Agreement to the contrary, the Depositary and the Company may modify, amend or adopt additional procedures from time to time as they determine may be necessary or appropriate.

Without prejudice to the Depositary's rights under Section 2.9, the Depositary will take no action to impair the ability of the Custodian to vote the number of Shares (including the Shares held by the Depositary in registered form) necessary to carry out the instructions of all Owners under this Section 4.7.

# 17. TENDER AND EXCHANGE OFFERS; REDEMPTION, REPLACEMENT OR CANCELLATION OF DEPOSITED SECURITIES.

(a) The Depositary shall not tender any Deposited Securities in response to any voluntary cash tender offer, exchange offer or similar offer made to holders of Deposited Securities (a "<u>Voluntary Offer</u>") except (i) when instructed in writing to do so by an Owner surrendering American Depositary Shares and subject to any conditions or procedures the Depositary may require.

(b) If the Depositary receives a written notice that Deposited Securities have been redeemed for cash or otherwise purchased for cash in a transaction that is mandatory and binding on the Depositary as a holder of those Deposited Securities (a "<u>Redemption</u>"), the Depositary, at the expense of the Company (unless otherwise agreed between the Company and the Depositary), shall (i) if required, surrender Deposited Securities that have been redeemed to the issuer of those securities or its agent on the redemption date, (ii) Disseminate a notice to Owners (A) notifying them of that Redemption, (B) calling for surrender of a corresponding number of American Depositary Shares and (C) notifying them that the called American Depositary Shares have been converted into a right only to receive the money received by the Depositary upon that Redemption and those net proceeds shall be the Deposited Securities to which Owners of those converted American Depositary Shares shall be entitled upon surrenders of those American Depositary Shares in accordance with Section 2.5 or 6.2 of the Depositary Shares in accordance with Section 2.5 or that Agreement (and, for the avoidance of doubt, Owners shall not be entitled to receive that money or other property under Section 4.1 or 4.2 of that Agreement). If the Redemption affects less than all the Depositary Shares will automatically be converted into a right to receive the net proceeds of the Redemption. The Depositary Shares immediately prior to the Redemption, except that the allocations may be adjusted so that no fraction of a converted American Depositary Shares is allocated to any Owner. A Redemption of all or substantially all of the Deposited Securities shall be a Termination Option Event.

(c) If the Depositary is notified of or there occurs any change in nominal value or any subdivision, combination or any other reclassification of the Deposited

Securities or any recapitalization, reorganization, sale of assets substantially as an entirety, merger or consolidation affecting the issuer of the Deposited Securities or to which it is a party that is mandatory and binding on the Depositary as a holder of Deposited Securities and as a result securities or other property have been or will be delivered in exchange, conversion, replacement or in lieu of, Deposited Securities (a "<u>Replacement</u>"), then (i) the Depositary shall, if required surrender the old Deposited Securities affected by that Replacement of Shares and hold, as new Deposited Securities under the Deposit Agreement, the new securities or other property delivered to it in that Replacement. <u>However</u>, the Depositary may elect to sell those new Deposited Securities if in the opinion of the Deposited Securities under the Deposit Agreement because those new Deposited Securities may not be distributed to Owners without registration under the Securities Act of 1933 or for any other reason, at public or private sale, at such places and on such terms as it deems proper and proceed as if those new Deposited Securities had been Redeemed under paragraph (b) above. A Replacement shall be a <u>Termination Option Event</u>.

(d) In the case of a Replacement where the new Deposited Securities will continue to be held under the Deposit Agreement, the Depositary may call for the surrender of outstanding Receipts to be exchanged for new Receipts specifically describing the new Deposited Securities and the number of those new Deposited Securities represented by each American Depositary Share. If the number of Shares represented by each American Depositary Share decreases as a result of a Replacement, the Depositary may, after consultation with the Company to the extent practicable, call for surrender of the American Depositary Shares to be exchanged on a mandatory basis for a lesser number of American Depositary and may sell American Depositary Shares to the extent necessary to avoid distributing fractions of American Depositary Shares in that exchange and distribute the net proceeds of that sale to the Owners entitled to them.

(e) If there are no Deposited Securities with respect to American Depositary Shares, including if the Deposited Securities are cancelled, or the Deposited Securities with respect to American Depositary Shares become apparently worthless, the Depositary may call for surrender of those American Depositary Shares or may cancel those American Depositary Shares, upon notice to Owners, and a <u>Termination Option Event</u> occurs.

#### 18. LIABILITY OF THE COMPANY AND DEPOSITARY.

Neither the Depositary nor the Company nor any of their respective directors, employees, agents or affiliates shall incur any liability to any Owner or Holder, (i) if by reason of any provision of any present or future law or regulation of the United States or any other country, or of any governmental or regulatory authority, or by reason of any provision, present or future, of the articles of association or any similar document of the Company, or by reason of any provision of any securities issued or distributed by the

Company, or any offering or distribution thereof, or by reason of any act of God or war or terrorism or other circumstances beyond its control, the Depositary or the Company is prevented from, forbidden to or delayed in, or could be subject to any civil or criminal penalty on account of doing or performing and therefore does not do or perform, any act or thing that, by the terms of the Deposit Agreement or Deposited Securities, it is provided shall be done or performed, (ii) by reason of any exercise of, or failure to exercise, any discretion provided for in the Deposit Agreement (including any determination by the Depositary to take, or not take, any action that the Deposit Agreement provides the Depositary may take), (iii) for the inability of any Owner or Holder to benefit from any distribution, offering, right or other benefit that is made available to holders of Deposited Securities but is not, under the terms of the Deposit Agreement, made available to Owners or Holders, or (iv) for any special, consequential, indirect or punitive damages for any breach of the terms of the Deposit Agreement. Where, by the terms of a distribution to which Section 4.1, 4.2 or 4.3 of the Deposit Agreement applies, or an offering to which Section 4.4 of the Deposit Agreement applies, that distribution or offering may not be made available to Owners, then the Depositary may not dispose of that distribution or offering on behalf of such Owners and make the net proceeds available to Owners, then the Depositary shall not make that distribution or offering available to Owners, and shall allow any rights, if applicable, to lapse.

Neither the Company nor the Depositary assumes any obligation or shall be subject to any liability under the Deposit Agreement to Owners or Holders, except that they agree to perform their obligations specifically set forth in the Deposit Agreement without negligence or bad faith. The Depositary shall not be subject to any liability with respect to the validity or worth of the Deposited Securities. Neither the Depositary nor the Company shall be under any obligation to appear in, prosecute or defend any action, suit, or other proceeding in respect of any Deposited Securities or in respect of the American Depositary Shares, on behalf of any Owner or Holder or other person. Each of the Depositary and the Company may rely, and shall be protected in relying upon, any written notice, request, direction or other document believed by it to be genuine and to have been signed or presented by the proper party or parties. Neither the Depositary nor the Company, nor any of their respective affiliates (as such term is defined in Regulation C under the Securities Act of 1933) or agents, shall be liable for any action or non-action by it in reliance upon the advice of or information from legal counsel, accountants, any person presenting Shares for deposit, any Owner or Holder, or any other person believed by it in good faith to be competent to give such advice or information. The Depositary shall not be liable for any acts or omissions made by a successor depositary whether in connection with a previous act or omission of the Depositary or in connection with a matter arising wholly after the removal or resignation of the Depositary, provided that in connection with the issue out of which such potential liability arises, the Depositary performed its obligations without negligence or bad faith while it acted as Depositary. The Depositary shall not be liable for the acts or omissions of any securities depository, clearing agency or settlement system in connection with or arising out of book-entry

settlement of American Depositary Shares or Deposited Securities or otherwise. In the absence of bad faith on its part, the Depositary shall not be responsible for any failure to carry out any instructions to vote any of the Deposited Securities or for the manner in which any such vote is cast or the effect of any such vote. Each of the Depositary and the Company may rely, and shall be protected in acting upon, any written notice, request, direction or other document believed by it to be genuine and to have been signed or presented by the proper party or parties. Neither the Company nor the Depositary shall have any duty to make any determination or provide any information as to the tax status of the Company or any liability for any tax consequences that may be incurred by Owners or Holders as a result of owning or holding American Depositary Shares, including without limitation, tax consequences resulting from the Company (or any of its subsidiaries) being treated as a "Passive Foreign Investment Company" ("PFIC") (in each case as defined in the U.S. Internal Revenue Code and the regulations issued thereunder) or otherwise. The Company may have been in the past and may be in the future a PFIC for U.S. Federal income tax purposes. Owners must consult their own tax advisers as to the potential application of the PFIC rules. No disclaimer of liability under the Securities Act of 1933 is intended by any provision of the Deposit Agreement.

#### 19. RESIGNATION AND REMOVAL OF THE DEPOSITARY; APPOINTMENT OF SUCCESSOR CUSTODIAN.

The Depositary may at any time resign as Depositary under the Deposit Agreement by written notice of its election so to do delivered to the Company, to become effective upon the appointment of a successor depositary and its acceptance of such appointment as provided in the Deposit Agreement. The Depositary may at any time be removed by the Company by 120 days' prior written notice of that removal, to become effective upon the later of (i) the 120th day after delivery of the notice to the Depositary and (ii) the appointment of a successor depositary and its acceptance of its appointment as provided in the Deposit Agreement. The Deposit Agreement. The Deposit Agreement. The Deposit Agreement as provided in the Deposit Agreement as provided in the Deposit Agreement.

#### 20. AMENDMENT.

The form of the Receipts and any provisions of the Deposit Agreement may at any time and from time to time be amended by agreement between the Company and the Depositary without the consent of Owners or Holders in any respect which they may deem necessary or desirable. Any amendment that would shall impose or increase any fees or charges (other than taxes and other governmental charges, registration fees, cable, telex or facsimile transmission costs, delivery costs or other such expenses), or that would otherwise prejudice any substantial existing right of Owners, shall, however, not become effective as to outstanding American Depositary Shares until the expiration of 30 days after notice of that amendment has been Disseminated to the Owners of outstanding American Depositary Shares. Every Owner and Holder, at the time any amendment so becomes effective, shall be deemed, by continuing to hold American Depositary Shares

or any interest therein, to consent and agree to that amendment and to be bound by the Deposit Agreement as amended thereby. Upon the effectiveness of an amendment to the form of Receipt, including a change in the number of Shares represented by each American Depositary Share, the Depositary may call for surrender of Receipts to be replaced with new Receipts in the amended form or call for surrender of American Depositary Shares to effect that change of ratio. In no event shall any amendment impair the right of the Owner to surrender American Depositary Shares and receive delivery of the Deposited Securities represented thereby, except in order to comply with mandatory provisions of applicable law.

# 21. TERMINATION OF DEPOSIT AGREEMENT.

(a) The Company may terminate the Deposit Agreement by notice to the Depositary. The Depositary may terminate this Deposit Agreement if (i) at any time 60 days shall have expired after the Depositary delivered to the Company a written resignation notice and a successor depositary has not been appointed and accepted its appointment as provided in Section 5.4 of that Agreement, (ii) an Insolvency Event or Delisting Event occurs with respect to the Company or (iii) a Termination Option Event has occurred or will occur. If a termination of the Depositary Shares then outstanding setting a date for termination (the "Termination Date"), which shall be at least 90 days after the date of that notice, and the Deposit Agreement shall terminate on that Termination Date.

(b) After the Termination Date, the Company shall be discharged from all obligations under the Deposit Agreement except for its obligations to the Depositary under Sections 5.8 and 5.9 of that Agreement.

(c) At any time after the Termination Date, the Depositary may sell the Deposited Securities then held under the Deposit Agreement and may thereafter hold uninvested the net proceeds of any such sale, together with any other cash then held by it hereunder, unsegregated and without liability for interest, for the pro rata benefit of the Owners of American Depositary Shares that remain outstanding, and those Owners will become general creditors of the Depositary with respect to those net proceeds. After making that sale, the Depositary shall be discharged from all obligations under the Deposit Agreement, except (i) to account for the net proceeds and other cash (after deducting, in each case, the fee of the Depositary for the surrender of American Depositary Shares, any expenses for the account of the Owner of such American Depositary Shares in accordance with the terms and conditions of the Deposit Agreement and any applicable taxes or governmental charges) and (ii) for its obligations under Section 5.8 of that Agreement and (iii) to act as provided in the paragraph (d) below.

(d) After the Termination Date, the Depositary shall continue to receive dividends and other distributions pertaining to Deposited Securities (that have not been sold), may sell rights and other property as provided in the Deposit Agreement and shall

deliver Deposited Securities (or sale proceeds) upon surrender of American Depositary Shares (after payment or upon deduction, in each case, of the fee of the Depositary for the surrender of American Depositary Shares, any expenses for the account of the Owner of those American Depositary Shares in accordance with the terms and conditions of the Deposit Agreement and any applicable taxes or governmental charges). <u>However</u>, after the Termination Date, (i) the Depositary may refuse to accept surrenders of American Depositary Shares for the purpose of withdrawal of Deposited Securities (that have not been sold) if in its judgment the requested withdrawal would interfere with its efforts to sell the Deposited Securities, (ii) the Depositary may discontinue the registration of transfers of American Depositary Shares and suspend the distribution of dividends and other distributions on Deposited Securities to the Owners and need not give any further notices or perform any further acts under the Deposit Agreement except as provided in Section 6.2 of that Agreement.

#### 22. DTC DIRECT REGISTRATION SYSTEM AND PROFILE MODIFICATION SYSTEM.

(a) Notwithstanding the provisions of Section 2.4 of the Deposit Agreement, the parties acknowledge that DTC's Direct Registration System ("<u>DRS</u>") and Profile Modification System ("<u>Profile</u>") apply to the American Depositary Shares upon acceptance thereof to DRS by DTC. DRS is the system administered by DTC that facilitates interchange between registered holding of uncertificated securities and holding of security entitlements in those securities through DTC and a DTC participant. Profile is a required feature of DRS that allows a DTC participant, claiming to act on behalf of an Owner of American Depositary Shares, to direct the Depositary to register a transfer of those American Depositary Shares to DTC or its nominee and to deliver those American Depositary Shares to the DTC account of that DTC participant without receipt by the Depositary of prior authorization from the Owner to register that transfer.

(b) In connection with DRS/Profile, the parties acknowledge that the Depositary will not determine whether the DTC participant that is claiming to be acting on behalf of an Owner in requesting registration of transfer and delivery described in paragraph (a) above has the actual authority to act on behalf of that Owner (notwithstanding any requirements under the Uniform Commercial Code). For the avoidance of doubt, the provisions of Sections 5.3 and 5.8 of the Deposit Agreement apply to the matters arising from the use of the DRS/Profile. The parties agree that the Depositary's reliance on and compliance with instructions received by the Depositary through the DRS/Profile system and otherwise in accordance with the Deposit Agreement, shall not constitute negligence or bad faith on the part of the Depositary.

# 23. APPOINTMENT OF AGENT FOR SERVICE OF PROCESS; SUBMISSION TO JURISDICTION; JURY TRIAL WAIVER; WAIVER OF IMMUNITIES.

The Company has (i) appointed CorpoMax, Inc., 2915 Ogletown Road, Newark, DE 19713, as the Company's U.S. registered agent upon which process may be served in any suit or proceeding arising out of or relating to the Shares or Deposited Securities, the American Depositary Shares, the Receipts or this Agreement, (ii) consented and submitted to the jurisdiction of any state or federal court in the State of New York in which any such suit or proceeding may be instituted, and (iii) agreed that service of process upon said U.S. registered agent shall be deemed in every respect effective service of process upon the Company in any such suit or proceeding.

EACH PARTY TO THE DEPOSIT AGREEMENT (INCLUDING, FOR AVOIDANCE OF DOUBT, EACH OWNER AND HOLDER) THEREBY IRREVOCABLY WAIVES, TO THE FULLEST EXTENT PERMITTED BY APPLICABLE LAW, ANY RIGHT IT MAY HAVE TO A TRIAL BY JURY IN ANY SUIT, ACTION OR PROCEEDING AGAINST THE COMPANY AND/OR THE DEPOSITARY DIRECTLY OR INDIRECTLY ARISING OUT OF OR RELATING TO THE SHARES OR OTHER DEPOSITED SECURITIES, THE AMERICAN DEPOSITARY SHARES OR THE RECEIPTS, THE DEPOSIT AGREEMENT OR ANY TRANSACTION CONTEMPLATED HEREIN OR THEREIN, OR THE BREACH HEREOF OR THEREOF, INCLUDING WITHOUT LIMITATION ANY QUESTION REGARDING EXISTENCE, VALIDITY OR TERMINATION (WHETHER BASED ON CONTRACT, TORT OR ANY OTHER THEORY).

To the extent that the Company or any of its properties, assets or revenues may have or hereafter become entitled to, or have attributed to it, any right of immunity, on the grounds of sovereignty or otherwise, from any legal action, suit or proceeding, from the giving of any relief in any respect thereof, from setoff or counterclaim, from the jurisdiction of any court, from service of process, from attachment upon or prior to judgment, from attachment in aid of execution or judgment, or other legal process or proceeding for the giving of any relief or for the enforcement of any judgment, in any jurisdiction in which proceedings may at any time be commenced, with respect to its obligations, liabilities or any other matter under or arising out of or in connection with the Shares or Deposited Securities, the American Depositary Shares, the Receipts or the Deposit Agreement, the Company, to the fullest extent permitted by law, hereby irrevocably and unconditionally waives, and agrees not to plead or claim, any such immunity and consents to such relief and enforcement.

#### 24. DISCLOSURE OF INTERESTS.

In order to comply with applicable laws and regulations or the articles of association or similar document of the Company, the Company may from time to time request each Owner and Holder to provide to the Depositary information relating to: (a) the capacity in which it holds American Depositary Shares, (b) the identity of any Holders or other persons or entities then or previously interested in those American Depositary Shares and the nature of those interests and (c) any other matter where

disclosure of such matter is required for that compliance. Each Owner and Holder agrees to provide all information known to it in response to a request made pursuant to this Section. Each Holder consents to the disclosure by the Owner or other Holder through which it holds American Depositary Shares, directly or indirectly, of all information responsive to a request made pursuant to this Section relating to that Holder that is known to that Owner or other Holder. The Depositary agrees to use reasonable efforts, at the Company's expense (unless otherwise agreed between the Company and the Depositary), to comply with written instructions requesting that the Depositary forward any request authorized under this Section to the Owners and to forward to the Company any responses it receives in response to that request.

Each Owner and Holder of American Depositary Shares further agrees to comply with the laws and regulations of the United States and the Republic of France (if and to the extent applicable) with respect to the disclosure requirements regarding beneficial ownership of Shares, all as if the American Depositary Shares were the Shares represented thereby, which is deemed to include, inter alia, requirements to make notifications and filings within the required timeframes to the Company, to the Commision, to the French Autorité des Marchés Financiers and any other authorities in the United States or in the Republic of France. The Company reserves the right to instruct Holders to deliver their American Depositary Shares for cancellation and withdrawal of the Deposited Securities so as to permit the Company to deal directly with the Holder thereof as a holder of Shares and Holders agree to comply with such instructions. The Depositary agrees to cooperate with the Company in its efforts to inform Holders of the Company's exercise of its rights under this paragraph and agrees to consult with, and provide reasonable assistance without risk, liability or expense on the part of the Depositary, to the Company on the manner or manners in which it may enforce such rights with respect to any Holder.

# **COMMERCIAL LEASE BEFORE COMPLETION**

# BY AND BETWEEN THE UNDERSIGNED:

EUROGAL 88 avenue des ternes 75017 PARIS

SAS. With capital of 700,000.00 Euros

*Registered with the Paris Business and Trade Register under No. 401 886 718 Represented by: Alexandre Scappaticci, acting in his capacity and Chief Executive Officer;* 

Hereinafter referred to as the "LESSOR" OF THE FIRST PART;

AND:

ERYTECH PHARMA Adenine résidence biopare 60 avenue Rockefeller 69008 LYON

S.A. (French joint stock company) with capital of 1,712,845.50 Euros

Registered in the Lyon Business and Trade Register under No. 479 560 013

Represented by Gil Beyen, acting in his capacity as Chairman and Chief Executive Officer;

Hereinafter referred to as the "LESSEE" OF THE SECOND PART;

# NOW, THEREFORE, THE FOLLOWING HAS BEEN AGREED:

# **1. PURPOSE OF THE COMMERCIAL LEASE**

The LESSOR hereby leases under a commercial lease to the LESSEE, which agrees, a portion of the building for future completion located at 60 avenue Rockefeller 69008 LYON (Rhône):

A building of offices and laboratories, Lot C, with an surface area of 2,430.02 m<sup>2</sup>, including 317.50 m<sup>2</sup> for a share of common parts, and 158.75 m<sup>2</sup> as a share of pooled spaces, consisting of 3 meeting rooms, 1 dining room equipped with a private kitchen for the LESSEE as well as 40 parking spaces in the sub-basement (hereinafter referred to as the "Leased Premises").

The permit which is the subject hereof must be filed no later than December 15, 2017 and a building permit purged of all appeals must be obtained no later than July 31, 2018.

The detailed plans and specifications of the Leased Premises (materials, services, etc.), particularly the specifications necessary for the LESSEE's activity, are defined in the Schedules to this lease.

In order for the LESSEE, assisted by any advisor it chooses, to be able to monitor the progress in the construction of the Leased Premises and the compliance of the Leased Premises with the characteristics and specifications stipulated in said schedules, the parties agree to respect the following procedure:

- A pre-inspection will be organized the first week of May 2019 during which the LESSEE will be able to make all observations on the condition of the Leased Premises to the LESSOR.
- A second pre-inspection will be organized the third week of May 2019 in order to establish jointly all reservations affecting the Leased Premises, particularly those that may prevent the LESSEE from taking possession on June 1 pursuant to the provisions of Article 2.1 below.

If it appears that the works on the Leased Premises will probably not be completed for June 1, 2019, the parties may defer, by written mutual agreement, the pre-inspections stipulated above, but this delay may not be interpreted as a waiver of any kind of the rights and obligations stipulated in this agreement.

If completion of the work is delayed, the LESSEE may request the organization of an additional pre-inspection 15 days before the planned date of possession, in order to establish jointly the reserves covering the Leased Premises prior to taking possession.

# <u>2. TERM</u>

This lease is granted and accepted as of June 1 2019 for a term of ten full and consecutive years, including nine (9) firm years, to expire on June 30, 2029 on the terms and conditions stipulated in Article L.145-4 of the French Commercial Code. The start of the lease on June 1, 2019 is an essential condition of the LESSEE's commitments.

The LESSEE shall not have the option to terminate this lease before the expiration of the third three-year period as stipulated in Article L.145-4 of the French Commercial Code.

As a result of the preceding, the LESSEE is prohibited from requesting termination of the lease during the period of the first nine years, under penalty of damages.

However, the LESSOR grants the Lessee the possibility of termination at the end of a period of 6 years and 6 months, but the LESSEE must pay to the LESSOR a fixed indemnity of THREE HUNDRED FIFTY THOUSAND EUROS (€350,000).

LESSEE shall have the option to terminate this lease at the expiration of the sixth and ninth year by advising the LESSOR, by bailiff's notice or by registered mail, no later than six months before the expiration of the current period.

If not, if notice is not given before the deadlines stipulated, the LESSEE must either remain in the Leased Premises for a new period of nine (9) years, or pay the rent due until the end of the next three-year period.

Notwithstanding the provisions set forth above, in the absence of notice or a renewal request, the lease will continue by tacit extension for a new period of nine (9) years.

In the event the LESSEE cannot take possession of the Leased Premises for June 1, 2019, because, for example, of non-compliance with the specifications defined in the different schedules or rules of the trade in the construction operations, the absence of administrative authorizations, or because the operation of the Leased Premises in accordance with the intended use of the premises is prevented by non-completion of the works, the effective date of the lease will be postponed until the date possession of the Leased Premises is taken, which will be recorded by the signature of an inventory of the premises, signed by the LESSOR and LESSEE, which expressly indicates that the Lessee agrees to take possession of the Leased Premises as is.

The construction works will be conducted and paid, at its expense, by the LESSOR, so that the Leased Premises defined in Article 1 above are completed, as this is defined by Article R 261-1 of the French Construction and Housing Code, and in accordance with the plans and descriptions below attached hereto, allowing the premises to be available to the LESSEE for its activity, no later than June 1, 2019, except in an event of force majeure or a legitimate cause for suspension of the completion deadline, as described below (hereinafter the "Legitimate causes for suspension").

For the application of this clause, the following will be considered Legitimate Causes for the suspension of the completion deadline:

- Disturbances resulting from hostilities, revolutions, riots, violent demonstrations, civil wars, insurrections, disasters, seismic tremors, falling aircraft, as long as such events occur after the signing of this agreement and they have effectively resulted in a delay in the progress of the work;
- Days of delay as the result of a general strike;
- Administrative or judicial orders to suspend the work on the Leased Premise, unless the origin of the order is faults or negligence attributable to the LESSOR;
- Delays attributable to the companies using networks (electricity, water, natural gas) when such delays are not chargeable to the fault or negligence of the LESSOR;
- Work delay on the Leased Premises resulting from fires, flood and construction accidents, to the extent that such delays are not chargeable to the fault or negligence of the LESSOR;
- Delays resulting from any operations resulting from the accidental discovery during excavation work of archeological remains on the site on which the Leased Premises are being built.

In any event, the LESSOR shall exert its best efforts to limit as much as possible the period of suspension imposed on the LESSEE and, for this purpose, shall implement the resources necessary. LESSOR shall immediately inform the LESSEE of its suspension and projected duration so that the LESSEE can, to the extent possible, take the measures necessary to limit the consequences of the delay in the availability of the Leased Premises.

If an event of force majeure or a Legitimate Cause of suspension of completion time occurs, the date the LESSOR makes the Leased Premises available will be extended by a period equal to the period during which the event in question has prevented the continuation of the work on the Leased Premises. The LESSOR agrees to keep the LESSEE informed of any event of force majeure or Legitimate Cause of suspension of completion time within a period of fortyeight (48) hours. The LESSOR will also notify in writing, as soon as possible, the new date of availability anticipated by the LESSOR because of the extension of the deadline for the LESSOR to make the Leased Premises available.

The LESSOR is informed that the date of June 1, 2019 for the availability of the Leased Premises to the LESSEE is an essential condition of its commitment. In the event the Leased Premises are not available to the LESSEE and completed on the date of June 1, 2019, except in an event of force majeure, the LESSOR must pay the LESSEE a daily indemnity in an amount equal to the contractual daily rent due as of June 1, 2019 plus 20% on a *prorated basis*, all fees and taxes arising from this lease, which constitute a fixed penalty to indemnify the LESSEE for the increased occupancy indemnity that it will be forced to pay (and exclusively for this purpose).

In all cases, the LESSOR shall not under any circumstance be liable to the LESSEE for any penalties and indemnities other than those stipulated in the aforementioned article of this lease.

In any event, if the delay in the availability of the Leased Premises for the LESSEE is greater than six (6) months from June 1, 2019, the LESSEE may, at its discretion, waive this lease, which will therefore not enter into force and effect.

# **3. USE OF THE LEASED PREMISES**

The LESSEE may use the premises only for offices and laboratory in accordance with the corporate purpose of the Company, and excluding any other activity, even related or complementary use, or any other use.

LESSEE must maintain this contractual intended use in the Leased Premises, excluding any other use of any kind, magnitude and duration, under penalty of immediate termination of this lease at the discretion of the LESSOR.

# 4 RENT

This lease is granted and accepted in consideration for an annual rent excluding tax/charges of: THREE HUNDRED SEVENTY THOUSAND THREE HUNDRED FIFTY-THREE EUROS AND THIRTY-SIX CENTS (€370,353.36).

This rent is payable in advance, on the first day of each quarter as of the date the LESSEE takes possession of the Leased Premises.

- In addition to the rent, the LESSEE shall reimburse the LESSOR for the following charges, prorated on its share of leased area:
- Private charges,
  - Cleaning of common sections and shared spaces;
  - Supply of toilet paper, towels, hand soap, etc.;

- Maintenance of the gate and garage doors;
- Elevator maintenance;
- Elevator telephone lines;
- Rental of garbage bins;
- Garbage collection;
- The heat and air conditioning and fire equipment maintenance contract;
- Electricity and water use by the common sections;
- Smoke ejection contract;
- The fees of the manager other than those related to management of rents;
- Other light maintenance (change consumables);
- Maintenance of electrical and sanitary equipment;
- Surveillance system by a custodial company;
- Property insurance;
- Maintenance of green spaces;
- Clean of outside and sub-basement parking areas;
- Snow removal;
- Exterior lighting.

Finally, the Lessee will also reimburse its share of the property tax calculated and prorated on the basis of the Leased Premises.

This list is complete.

All other charges shall be paid by the LESSOR.

Conditions for payment of charges

The LESSEE must pay to the LESSOR, or to its manager, quarterly provisions on the first day of the first month of each calendar quarter as of the date of effective possession of the Leased Premises.

This provision shall be called on the basis of a provision amount before tax of  $\leq 35 / m^2 / year$ , i.e. the sum of  $\leq 85,050.70$ .

The accounts shall be established on December 31 of each calendar year, and divided among the occupants; the first accounts will be established on December 31, 2019.

As a result, the LESSEE undertakes to pay to the LESSOR, or to its manager, on demand by the LESSOR, the total for its shares, under conditions defined above, as well as the adjustment that results from the closed accounts.

Information and valuation of the charges and taxes owed by the LESSEE

Pursuant to the regulations in force, the following is attached to this lease:

- A precise inventory of the categories of charges related to the lease and reinvoiced to LESSEE and the distribution of those charges among the different lots, prorated on the basis of the areas occupied, as they appear in the statement of accounts for the last full year (APPENDIX No. 1);
- A summary statement of the work performed over the leased entity for the previous three years (APPENDIX No. 2);
- A provisional budget for the work to be performed until the end of the first three-year period (**APPENDIX No. 3**).

During the lease, the Lessor must inform the tenants of any element that could change the distribution of the charges among the tenants, and must communicate to the Lessee, at each three-year expiration date, the documents described above, i.e.: a summary statement of the charges reinvoiced to the LESSEE; a summary state of the work performed during the previous three years; and, finally, a provisional statements of the work planned over the next three years.

The rent and all incidental charges are understood to exclude VAT; the LESSEE agrees to pay the amount of the VAT to the LESSOR on an invoice, as well as the amount of all other new or additional duties or tax legally owed by the Lessee or a replacement for the property tax, at the legal rate in effect on the date of each invoice. The rent and related charges will be indicated in an invoice established and sent one month before the date for payment to the LESSEE at the address indicated by the Lessee and will contain the order number indicated by the LESSEE. The LESSEE agrees to provide the LESSOR with the information, immediately at LESSOR's demand. The invoices shall be paid within thirty (30) days end of month from the date of issue of the invoice. If payment of an invoice is late, the penalty interest shall be three times the legal interest rate.

# **5. REVISION OF THE RENT**

The amount of the rent as set is indexed annually to the index of commercial rents (ILC) published by INSEE, including in the event of a renewal of this lease.

The contractual rent shall be automatically revised every year on the effective date of the lease; it is expressly agreed that any discount on rent granted by the LESSOR shall not be included when calculating the indexed rent.

Therefore, subject to a postponement of the effective date of the leased under the conditions stipulated in Article 2 of this agreement, as of June 1, 2019, the rent shall be indexed annually on the basis of the changes in the quarterly index of commercial rents published by INSEE.

Thus, if the lease cannot take effect on June 1, 2019, the indexing shall take effect as of the date of possession of the Leased Premises as defined in Article 2.

The base index is the latest index published on the effective date of the lease and the revision index is the one for the same quarter the following year.

The comparison index used to calculate the indexing from one year will become the base index for the indexing of the following year, and so on from year to year.

As the indexing clause applies automatically, the fact that the rent is not immediately adjusted shall not result in any forfeiture of the right of the parties to claim subsequent application of the index effective retroactively.

The variation in the index may never have the effect of reducing the rent below the initial rent as defined in Article 4.

If the publication of the index of commercial rents used to revise the rent ends, without replacement, by law or regulations, by a new index with a multiplier coefficient, or if said index is or becomes inapplicable, for any reason, the closest existing applicable index shall be applied, for one or more products and/or raw materials, and/or if the parties cannot agree on this closest index with a period of three months after the date on which one of the two parties has proposed a replacement index in writing to the other party, this index shall be determined by an expert designated by mutual agreement of the parties or, if they cannot agree, by order of the Chief Judge of the District Court (Tribunal de Grande Instance) with jurisdiction for the location of the leased premises, issue on a motion by the more diligent party.

If the designated expert does not want to or cannot determine the replacement index within the three-month period stipulated above, another expert shall be designated under the conditions set forth above (agreement of the parties or, if they cannot agree, by order).

The expert so designated shall not be required to respect any formality and must indicated its choice of the replacement index within three months after the date on which he was petitioned, via registered letter sent to each of the parties to this agreement.

The registered letter by which the expert announced the new index chosen, as set by law, shall be automatically attached to the lease and to all subsequent amendments thereto in order to form, with these documents, the agreement of the parties and shall be executed as such.

The costs and fees of the expert and for his designation shall be paid in equal parts by the LESSOR and the LESSEE.

# 6. SECURITIES

### 6.1 Security deposit

In order to guarantee the performance of its obligations under this agreement, the LESSEE is paying today to the LESSOR, which acknowledges the payment and gives LESSEE a receipt, the sum of NINETY-TWO THOUSAND FIVE HUNDRED EIGHTY-EIGHT EUROS AND THIRTY FOUR CENTS (€92,588.34) representing three months rent excluding charges and taxes.

The LESSOR may freely dispose of this sum until the expiration of this agreement, the date on which this sum shall be returned to the LESSEE, subject to complete performance by LESSEE of its obligations under this lease and the payment of all amounts it may owe to the LESSOR when it leaves, or for which the LESSOR may be responsible because of the LESSEE for any reason.

By express agreement, this sum shall not bear any interest.

If this lease is termination as a result of LESSEE's failure to perform any of its obligations, the security deposit shall inure to the LESSOR up to the amount of the damages for which the LESSEE may potentially be responsible.

If there are changes in the rent, the amount of the security deposit must be automatically increased so that it always represents three months rent excluding taxes and charges.

In the event that the LESSEE enters court-ordered receivership or liquidation, if the administrator or liquidator does not exercise the option to continue the lease agreement, the LESSOR may defer the return of the security deposit until there has been a ruling on damages pursuant to Article L.621-28 section 5 of the French Commercial Code.

Moreover, and again in the event of court-order receivership or liquidation of the LESSEE, it is expressly agreed by the parties that the LESSOR shall be free to assign the security deposit to the payment of the amounts owed by the LESSEE prior to its court-ordered receivership or liquidation and declared by the LESSOR on the basis of Article L621-43 of the French Commercial Code.

Pursuant to the provisions of Article L.145-16-1 of the Commercial Code, the LESSOR must inform the guarantor of any failure to pay rent by the LESSEE within one-month from the date on which the sum should have been paid by the LESSEE.

# 7. OBLIGATIONS AND CONDITIONS

This lease is moreover granted and accepted subject to the ordinary and lawful charges and conditions, and to customary usage in such matters to the extent not inconsistent with the following terms and conditions, which the parties undertake to perform.

# 7.1 COMMERCIAL USE

#### 7.1.1. Condition of the Premises

The TENANT shall take the leased premises in the same condition as found when taking possession.

A report on the condition of the premises shall be made jointly by the parties on the effective date of the present lease; it shall be made by an officer of the court so empowered by the lessor with the expenses shared between the TENANT and the LESSOR.

In the event that the TENANT refrains from participating in the report, the premises will be deemed to have been leased as indicated in the record of condition determined by the officer of the court.

#### 7.1.2. Furnishings

The TENANT undertakes to keep the premises always leased and normally furnished with furniture, equipment, and goods of sufficient value to meet at all times the payment of rent and ancillary charges as well as the performance of the clauses and obligations arising from this lease.

#### 7.1.3. Operating Conditions

- The TENANT undertakes to keep the leased premises in a constant state of actual and normal operation, except for the weekly and annual closings.
- The TENANT shall not affix any plaque, sign, awning, or installation whatsoever on the exterior of the Leased Premises without the prior written
  consent of the LESSOR, and subject to strict compliance with all regulations in force. Notwithstanding the above, it is agreed that the TENANT may
  display a sign indicating its company name, as well as its logo.

#### 7.1.4. Authorizations

The contractual use stipulated above does not imply any warranty on the part of the LESSOR as to compliance with any administrative condition or authorization that may be necessary, on any grounds whatsoever, for the performance of the TENANT's business.

The TENANT shall therefore take personal responsibility for its expenses, risks, and perils in obtaining any necessary authorization, as well as for the payment of any sum, charge, fee, tax, or levy whatsoever pertaining to the activities performed in the Leased Premises and to the use of the premises.

It is also agreed that, in the event that the local government or any authority whatsoever may happen to require, at any time, a modification of the premises covered by this lease, and even if such requirement may constitute a case of force majeure, all expenses and consequences whatsoever deriving from this modification shall be borne in full by the LESSOR, which shall be liable for them unless such requirement is directly linked to the Tenant's business.

During the course of the lease as well as any eventual renewals, the TENANT will be responsible for all the works to bring the premises into conformity with the regulations in force that are imposed by any authority whatsoever, by virtue of its business.

It must comply with any official order announced to such effect so that the LESSOR may never be disturbed or sought out, this in express derogation of the provisions of Article 1719 of the French Civil Code.

In the event of expropriation in the public interest, the TENANT cannot make any claim against the Lessor as all rights are reserved against the party requiring the expropriation.

# 8 MAINTENANCE—REPAIRS—WORKS

#### 8.1.1 Maintenance—Major Repairs

- Throughout the term of the lease, the TENANT undertakes to keep the Leased Premises in a good state of repair and maintenance as well as to carry
  out, as the case may be, any repairs except those provided for by Article 606 of the French Civil Code, which remain the responsibility of the LESSOR.
- The Tenant accepts that, if it has not itself carried out all works for which it is responsible, the LESSOR undertakes, thirty days after sending a registered letter with acknowledgement of receipt that has remained ineffective, and except in the event of emergency, to carry out such services and works itself instead, with the TENANT undertaking to reimburse it for the actual cost thereof, including all fees and expenses relating thereto, within fifteen days of a statement that is to be sent to it by the LESSOR.

#### 8.1.2 Works by the TENANT

The TENANT shall not make any change to the layout of the Leased Premises, whether interior or exterior, affecting the structural work without the prior express agreement of the LESSOR.

Any embellishments, improvements, repairs, or other works carried out by the TENANT in the Leased Premises, with the LESSOR's authorization, shall automatically and without formality become the property of the LESSOR upon departure from the premises without compensation of any kind unless otherwise agreed to in writing by the parties prior to the commencement of the works.

#### 8.1.3 Informing of the Lessor

The TENANT must immediately inform the LESSOR of any damage that may occur in the Leased Premises, even if no apparent damage so results, under penalty of becoming personally liable for reimbursing it for the amount of the direct or indirect harm resulting for the LESSOR from such casualty and from a delay in declaring it to the insurers.

#### 8.1.4 Works by the Lessor

The LESSOR expressly reserves the right to carry out, during the course of the lease, any repairs or any work that may prove necessary without the TENANT being able to claim any compensation or reduction in rent.

In the event that such works exceeds 21 (TWENTY-ONE) days, the Parties shall apply Article 1724 of the French Civil Code:

"If, during the course of the lease, the leased object needs urgent repairs that cannot be deferred until its end, the lessee must tolerate them, whatever inconvenience they may cause to him, even though for the duration thereof he may be deprived of a portion of the leased object.

However, if such repairs last more than twenty-one days, the price of the lease will be reduced in proportion to the time and the portion of the leased object of which he is deprived.

If the repairs are of such nature as to render uninhabitable what is necessary for the accommodation of the lessee and his family, he will be able to have the lease cancelled."

The parties must take all measures to ensure that such works can be carried out without delay and in accordance with the rules of the trade.

## 8.2 TAXES, FEES, AND EXPENSES

The TENANT undertakes to satisfy all city, police, and road charges or other national, regional, departmental, municipal, or other fees, whatever the nature of such obligations may be, so that the LESSOR may never be disturbed in this regard, and, in particular, to pay any personal and personal property contribution, rental tax, territorial economic contribution, and, more generally, any other taxes and fees for which the LESSOR may be liable for any reason whatsoever, particularly the real property tax, which will be re-invoiced to it by the LESSOR in proportion to the leased surface area, payable quarterly in advance and the balance thirty (30) days from the end of the month following receipt of the invoice.

The TENANT must so substantiate upon first written request, and in particular at least eight days before departing from the premises for any reason and at any time whatsoever, and before any removal of furnishings and goods.

The cost of any modification, change, or arrangement of piping, devices, or other installations made necessary by virtue of the TENANT's business or regulatory measures subsequent to the making of the present lease, and which are to be settled by the LESSOR, shall be reimbursed by the TENANT to the LESSOR upon substantiation.

# 9. INSURANCE

#### 9.1. Lessor's Insurance

The LESSOR shall cover the financial consequences of any civil liability it may incur as owner.

The LESSOR shall cover the Leased Premises as well as all of the amenities and facilities of a real property nature with which the Leased Premises are to be equipped when the lease takes effect, particularly against the risks of fire, explosions, storms, and water damage.

In this regard, the TENANT undertakes to notify the LESSOR by registered letter as to any cause of aggravating risks (in particular when the height of storage is greater than 7 m) that may result from the creation of its business or any modification of its activity, as well as to bear any additional premiums that may thus result for the lessor.

# 9.2. Tenant's Insurance

The TENANT shall cover, with insurance companies of known solvency, the financial consequences of the civil liabilities that it may incur as a result:

- of its character as tenant and/or occupant
- of its activities,

particularly regarding the LESSOR as well as the neighbors and third parties in general.

The TENANT shall cover, with insurance companies of known solvency, its own property and such adaptations as it may make, in particular against the risks of fire, explosions and implosions of all kinds, and other damage, including those in response to attacks or vandalism, riots, civil commotion, acts of terrorism or sabotage, smoke, whatever the origin or cause thereof, lightning strikes, electrical accidents affecting electrical power supply installations, the fall of or impact from all or part of air navigation devices or spacecraft, or falling objects, meteorites, crossing of the sound barrier, land vehicle impact, storms and natural events, weather phenomena and natural disasters, damage from water and other liquids, claims by neighbors and third parties, glass breakage, loss of use, and operational and professional civil liability.

# 9.3. Waiver of Recourse

In the event of claim the LESSOR waives, and shall have its insurers waive, any recourse that may pertain thereto against the TENANT and its insurers or other occupants of the premises pertaining to the TENANT.

The TENANT's insurance policy must include waiver by its insurance company of any recourse against the finance LESSOR, the LESSOR's agents, and the insurers of the aforementioned entities, for the portion of the loss or damage for which the latter could be liable for any reason whatsoever.

The TENANT expressly waives all recourse and actions whatsoever against the aforementioned entities by reason of the damage referred to above or by reason of deprivation of enjoyment of the leased premises resulting from such damage, even in the event of full or partial loss of its business.

The TENANT must maintain and renew such insurance throughout the term of the lease, regularly pay the premiums and charges, and substantiate all of this to the Lessee at its first request, and for the first time at the time of the signing hereof.

In addition, the TENANT undertakes to inform the LESSOR of any modification made to the aforementioned insurance policies as well as their cancellation for any reason whatsoever within a period of 15 days preceding the effectiveness of such cancellation.

If the business done by the TENANT directly gives rise to insurance premium surcharges, whether for the owner or for the neighbors or co-tenants, the TENANT must reimburse the amounts of such surcharges to those involved.

Notwithstanding the aforegoing, the TENANT shall not be entitled to invoke the LESSOR's liability, except in the event of major deficiency on the part of the LESSOR, in the following eventualities:

- In the event of theft, burglary, or other wrongful acts and, generally, disturbances caused by third parties or co-tenants in the Leased Premises or appurtenances of the real property to which the Leased Premises pertain;
- In the event of interruption in the service of the facilities of the real property to which the Leased Premises pertain;
- In the event of an accident that may occur as a result of the installation of such services in the Leased Premises;
- In the event that the Leased Premises are flooded or penetrated by river water or other waters.

The TENANT shall be personally responsible for the above eventualities and generally for all other acts of God and unforeseen eventualities with the exception of its entitlement to recourse beyond the LESSOR.

For further assurance, the TENANT must obtain all insurance policies necessary so that the LESSOR's liability is entirely eliminated.

9.4. The LESSOR and the TENANT undertake to inform their respective insurers of all of the provisions of the present article.

**9.5.** The TENANT alone shall bear the consequences of neighborhood disturbances caused by it and for which the Lessor suffers blame.

**9.6.** The TENANT must follow the recommendations as to prevention provided both by its own insurer for operational risks as well as by the LESSOR's insurer for the protection of the Leased Premises or of the Real Property, relating in particular to the following points:

- Checking of fire extinguishers. Indeed, in application of Article R.4227-29 of the French Labor Code, each establishment must have fire extinguishers numbering one 6-liter water-type extinguisher per 200 m<sup>2</sup>, with a minimum of one per floor, in addition to an extinguisher adapted to the risks.
- Smoke vents.
- Fire doors.
- Electrical installations. Indeed, in accordance with Article R.4226-16 of the French Labor Code, electrical installations must be checked by an approved inspection body annually.
- Thermographic verification.
- Sprinkler installations.

# 10. SUBLET—ASSIGNMENT—SUBSTITUTION OF TENANT

The LESSEE may not sublet all or any part the Leased Premises. The LESSEE may not assign use of the Leased Premises for any purpose whatsoever or in any manner whatsoever, even without consideration or on a temporary basis, without the approval of the LESSOR.

The LESSEE may not, without the prior consent of the LESSOR contribute or assign his right to this lease, as the LESSOR must become a party to any such agreement.

# **11. INSPECTION AND RESTITUTION OF THE PREMISES**

The LESSEE undertakes to allow the LESSOR, its representatives, architects, contractors and workers, enter the leased premises during business hours to check their condition, take any precautionary measures, carry out any work and show them with a view to their rental or sale. The LESSEE must receive 48 hours advance notice for such access to the premises.

At the end of the lease, the LESSEE must inform the LESSOR of the date the premises will be abandoned fifteen days prior to leaving, and give the LESSOR the LESSEE'S new address.

Before moving, the LESSEE must, prior to any removal of furniture or equipment, even partial, have paid up all rental periods and fees and justify with invoices, the payment of all charges incumbent upon the LESSEE, both for all past years and for the current year.

The LESSEE must, at the latest on the day of the expiration of the lease, return the leased premises in good repair and properly maintained. The condition of the premises will be subject to an inspection and inventory, upon completion of which the LESSEE will return the keys to the LESSOR. The LESSEE will also restore all floors, walls and ceilings to good condition. In case the LESSEE is not present on the day and hour fixed by the LESSOR for the inventory of fixtures, the inspection will be carried out by a bailiff, and all expenses corresponding to this inspection shall be borne by the LESSEE.

In the event that the LESSEE has not fulfilled the repair obligations under the present lease, the LESSOR shall be entitled to prepare a description of the condition of the premises and to submit an estimate of work required to restore them, and to address them to the LESSEE by registered letter with acknowledgment of receipt.

It will be the LESSEE'S responsibility to state whether or not it intends to dispute the nature of the work required by the LESSOR and sum for such work within fifteen (15) days: should the LESSEE fail to respond within this period, the quote(s) and the repair work planned by the LESSOR will be considered approved and the LESSOR may have it carried out by the companies of his choice, at the expense of the LESSEE, including the costs for any general contractor to supervise the work, if required.

If the LESSEE declares his intention to execute the work, the LESSEE undertakes to employ qualified companies.

In addition, if this works requires closing down the premises beyond the date planned for their return, a daily charge will be due in an amount equal to the contractual daily rent due at the end of the lease, plus 20% on a *pro rata* basis, of all charges and taxes arising from this lease.

# 12. INDIVISIBILITY—TOLERANCE—MODIFICATIONS

The parties expressly agree that the Leased Premises form an indivisible whole.

This lease is declared indivisible and to the sole benefit of the Lessor. In the case of shared tenancy under the effect of this lease via assignment or death, the co-tenants' obligation shall be deemed indivisible and binding both for the payment of rent and fees and for the execution of the terms and conditions of the lease.

Such co-tenants will also be responsible for the costs of service provided for in Article 877 of the Civil Code under the same conditions.

#### **13. TERMINATION AND PENALTY CLAUSES**

Failure to pay the rent or other charge on the exact date of the end of a rental period or part of a rental period, or any breach of any of the terms and conditions of this lease by the LESSEE, will result in the lease being terminated ipso jure and without formality. This will hold true if a notice to pay or a summons to execute containing a statement by the LESSOR of its intention to make use of this clause remains wholly or partially without effect after one month from receiving such notice, even should payment or execution be made subsequent to the expiration of the above-mentioned period.

In the event that the LESSEE refuses to evacuate the Leased Premises, the LESSEE may be evicted without delay with a simple summary order delivered by the Judge of the competent Regional Court or by any other court ruling issuing the order and shall be provisionally enforceable, notwithstanding any opposition or appeal.

In addition, and without prejudice to this termination clause, the LESSEE formally undertakes to comply with the following two penalty clauses:

1) Failing payment of rent or fees at the end of a single rental period, the amounts due will be automatically increased by 10% within eight days of the sending of a registered letter with acknowledgment of receipt by the LESSOR indicating that failing payment in time, this increase will be applied. In addition, the sums due will bear interest from the due date at the rate of 10% per annum, subject to the application by the LESSOR of the termination clause.

In addition, the LESSEE shall reimburse costs and fees incurred for the recovery of said sums to the LESSOR, without prejudice to the legal application of Article 700 of the Code of Civil Procedure.

2) If the LESSEE, who is stripped of all occupancy rights does not abandon the premises and resists an eviction order or succeeds in delaying departure, it must pay compensation of double the daily contractual rent until the premises are fully liberated and the keys have been returned, in addition to any incidental expenses.

This amount is intended to compensate the LESSOR for damages caused by the abusive occupation of the rented premises that impede the exercise of the LESSOR'S rights.

In the event of cancellation or eviction, rent paid in advance, if any, will remain the property of the LESSOR as compensation, without prejudice to further damages and the application of Article 1760 of the Civil Code, notwithstanding eviction.

# 14. REPORT OF NATURAL, TECHNOLOGICAL AND MINING RISKS

The LESSOR states that the area in which the leased building is located is not in an earthquake zone as defined by decree or in a zone covered by a technological or natural risks prevention plan as stipulated in Article L125-5 and R125-23 to R125-27 of the Environment Code.

The LESSOR informs the LESSEE that the leased building has not been awarded any compensation as a consequence of a natural or technological disaster.

This report of natural and technological risks cannot be submitted until the lease takes effect on June 1, 2019.

#### **15. ENERGY PERFORMANCE DIAGNOSTIC**

Notwithstanding article L 134-3-1 of the Construction and Housing Code, as the building is under construction, the energy performance diagnosis referred to in article L134-1 of the Construction Code and of the dwelling cannot be submitted until the lease takes effect on June 1, 2019.

### 16. COSTS—ELECTION OF DOMICILE—RECORDING

Pursuant to Article 10-1 a of Law No. 69-1168 dated December 26, 1969, this deed is exempt from recording formalities.

For the execution hereof, the Lessee elects domicile in the Leased Premises, the Lessor in his headquarters listed to above.

# **17. SPECIAL PROVISIONS**

Notwithstanding the foregoing and in order to support the development of the LESSEE, the LESSOR exempts the LESSEE from payment of six (6) months rent between June 1 and November 30, 2019.

As from the conclusion of this agreement, the LESSEE will have the option of a thirty-six (36) month lease of the second floor of building B, involving a surface area of 635.23 sq m including 81.5 sq m of common area and 40.08 sq m of shared space, under the same terms and conditions as the present lease.

### **18. APPENDICES**

- Appendix 1: List of charges
- Appendix 2 : Summary of work
- Appendix 3 : Estimated budget
- Appendix 4: ERNT DPE risks and energy diagnostics
- Appendix 5: Plans of the Leased Premises
- Appendix 6: Kbis certificate of incorporation

# **19. APPLICABLE LAW—COMPETENT JURISDICTION**

Any dispute to which the present lease could give rise, in particular regarding its validity, its interpretation or its execution, will be subject to the exclusive competence of the Regional Court in which the Leased Premises are located.

Done in two copies, In Lyon, on December 06, 2017

THE LESSOR EUROGAL SCAPPATICCI /s/ Alexandre Scappaticci Chief Executive Officer

#### THE LESSEE ERYTECH PHARMA

/s/ Gil Beyen Chairman and Chief Executive Officer

# Certification by the Principal Executive Officer pursuant to Securities Exchange Act Rules 13a-14(a) and 15d-14(a) as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002

I, Gil Beyen, certify that:

- 1. I have reviewed this annual report on Form 20-F of ERYTECH Pharma S.A. (the "Company");
- 2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
- 3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the Company as of, and for, the periods presented in this report;
- 4. The Company's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the Company and have:
  - (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the Company, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
  - (b) Evaluated the effectiveness of the Company's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
  - (c) Disclosed in this report any change in the Company's internal control over financial reporting that occurred during the period covered by the annual report that has materially affected, or is reasonably likely to materially affect, the Company's internal control over financial reporting; and
- 5. The Company's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the Company's auditors and the audit committee of the Company's board of directors (or persons performing the equivalent functions):
  - (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the Company's ability to record, process, summarize and report financial information; and
  - (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the Company's internal control over financial reporting.

Date: April 24, 2018

/s/ Gil Beyen

Name: Gil Beyen

Title: Chief Executive Officer (Principal Executive Officer)

# Certification by the Principal Financial Officer pursuant to Securities Exchange Act Rules 13a-14(a) and 15d-14(a) as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002

I, Eric Soyer, certify that:

- 1. I have reviewed this annual report on Form 20-F of ERYTECH Pharma S.A. (the "Company");
- 2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
- 3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the Company as of, and for, the periods presented in this report;
- 4. The Company's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the Company and have:
  - (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the Company, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
  - (b) Evaluated the effectiveness of the Company's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
  - (c) Disclosed in this report any change in the Company's internal control over financial reporting that occurred during the period covered by the annual report that has materially affected, or is reasonably likely to materially affect, the Company's internal control over financial reporting; and
- 5. The Company's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the Company's auditors and the audit committee of the Company's board of directors (or persons performing the equivalent functions):
  - (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the Company's ability to record, process, summarize and report financial information; and
  - (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the Company's internal control over financial reporting.

Date: April 24, 2018

/s/ Eric Soyer

Name: Eric Soyer Title: Chief Financial Officer and Chief Operating Officer (Principal Financial Officer)

#### Certification by the Principal Executive Officer and Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002

Pursuant to the requirement set forth in Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. §1350), Gil Beyen, Chief Executive Officer of ERYTECH Pharma S.A. (the "Company"), and Eric Soyer, Chief Financial Officer and Chief Operating Officer of the Company, each hereby certifies that, to the best of his knowledge:

- (1) The Company's Annual Report on Form 20-F for the year ended December 31, 2017, to which this Certification is attached as Exhibit 13.1 (the "Report") fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended; and
- (2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: April 24, 2018

/s/ Gil Beyen

Name: Gil Beyen Title: Chief Executive Officer (Principal Executive Officer)

/s/ Eric Soyer

Name: Eric Soyer Title: Chief Financial Officer and Chief Operating Officer (Principal Financial Officer)



**Consent of Independent Registered Public Accounting Firm** 

KPMG Audit 51 rue de Saint-Cyr CS 60409 69338 Lyon Cedex 9 France Téléphone : Télécopie : Site internet : +33 (0)4 37 84 78 00 +33 (0)4 37 84 78 09 www.kpmg.fr

The Board of Directors,

Erytech Pharma S.A.

We consent to the incorporation by reference in the registration statement (no. 333-222673) on Form S-8 of Erytech Pharma S.A. of our report dated April 23, 2018, with respect to the consolidated statements of financial position of Erytech Pharma S.A. and its subsidiary as of December 31, 2017 2016 and 2015, and the related consolidated statements of income (loss), comprehensive income (loss), changes in shareholders' equity and cash flows for each of the years in the three-year period ended December 31, 2017, and the related notes (collectively, the "consolidated financial statements"), which report appears in the Annual Report on Form 20-F of Erytech Pharma S.A for the year ended December 31, 2017.

Lyon, April 24, 2018

KPMG Audit Département de KPMG S.A.

/s/ Sara Righenzi de Villers

Sara Righenzi de Villers Partner

KPMG 8.A., soděté française membre du rěseau KPMG constitué de cabinets indépendants adhérents de KPMG international Cooperative, une entité de droit suisse. 
 Siège social :

 Société anonyme d'expertise
 KPMG 8.A.

 comptable et de commissariat
 Tour Egito

 aux comptes à directoire d'
 zavenue Gambetta

 conseil de surveillance.
 S2066 Paris la Défense Codex

 insorte au Tableau de l'Oxire
 Capital : 5 497 100 €

 à Paris sous le n° 14-30080101
 Code APE 65202

 et à la Compagnie Réglonale
 775 726 417

 des Commissaires aux Comptes
 FR 77 775 726 417