



A French limited liability company (société anonyme) with share capital of €792,461.10  
Headquarters: Bâtiment Adénine  
60 Avenue Rockefeller  
69008 Lyon  
Lyon Trade and Companies Register 479 560 013

# 2015 REFERENCE DOCUMENT CONTAINING THE ANNUAL FINANCIAL REPORT AND THE MANAGEMENT REPORT



AUTORITÉ  
DES MARCHÉS FINANCIERS

PURSUANT TO ITS GENERAL REGULATION, AND MORE PARTICULARLY TO ARTICLE 212-13, THE *AUTORITÉ DES MARCHÉS FINANCIERS* HAS REGISTERED THIS REFERENCE DOCUMENT APRIL 29, 2016 UNDER NUMBER R.16-039. THIS DOCUMENT MAY BE USED TO SUPPORT A FINANCIAL TRANSACTION ONLY IF COMPLETED BY A TRANSACTION NOTE APPROVED BY THE AMF.

IT WAS PREPARED BY THE ISSUER AND IS THE RESPONSIBILITY OF ITS SIGNATORIES.

PURSUANT TO ARTICLE L. 621-8-1-I OF THE MONETARY AND FINANCIAL CODE, REGISTRATION WAS MADE AFTER THE AMF VERIFIED THAT THE DOCUMENT IS EXHAUSTIVE AND COMPREHENSIBLE AND THAT THE INFORMATION CONTAINED IN IT IS CONSISTENT. IT DOES NOT IMPLY THAT THE *AUTORITÉ DES MARCHÉS FINANCIERS* HAS VERIFIED THE ACCOUNTING AND FINANCIAL INFORMATION PRESENTED HEREIN.

**This document in a free non-binding translation, for information purpose only, of the French language “Document de Référence 2015” as submitted to and registered with the AMF on April 29, 2016 under number R. 16-039. In the event of any ambiguity or conflict between corresponding statements or items contained in this English translation and the original French version, the relevant statements or items of the French version shall prevail. The auditor’s reports apply to the French version of the activity report and the financial statements.**

COPIES OF THIS REFERENCE DOCUMENT ARE AVAILABLE AT NO COST AT THE HEADQUARTERS OF ERYTECH PHARMA, BÂTIMENT ADÉNINE, 60, AVENUE ROCKEFELLER 69008 IN LYON, AS WELL AS ELECTRONICALLY ON THE ERYTECH PHARMA WEBSITE ([WWW.ERYTECH.COM](http://WWW.ERYTECH.COM)).

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## CONCORDANCE TABLE

The concordance table below makes it possible to identify in this reference document:

- the information which forms the annual financial report (article L. 451-1-2 of the French Monetary and Financial Code and article 222-3 of the General Regulation of the AMF), and
- the information which forms the annual management report (article L. 225-100 et seq. of the French Commercial Code).

Annual financial report	Reference Document
1. Certification by the responsible party	See section 1.2
2. Company annual financial statements – French standards	See section 20.2
3. Consolidated annual financial statements – International Financial Reporting Standards (IFRS)	See section 20.1
4. Management report	See index below
5. Chairman’s report on internal audit	See chapter 16
7. Statement pertaining to the statutory auditor’s fees	See section 2.3
8. Statutory auditor’s report on the annual financial statements according to French standards and IFRS standards	See sections 20.3 and 20.4
9. Report by the statutory auditor about the Chairman’s report	See appendix 1
Annual management report	Reference Document
1. Condition of the Company and activity during the past fiscal year	See chapter 6
2. Examination of the financial statements and results – Allocation of results – Review of dividends distributed – Expenses that are not tax-deductible	See chapter 20
3. Information about supplier payment deadlines	See chapter 20
4. Progress made or difficulties encountered	See chapter 6
5. Primary risks and uncertainties faced by the Company – Use of financial instruments by the Company	See chapter 4
6. Research and development activities	See chapters 6 and 11
7. Forecast and outlooks	See chapters 6 and 12
8. Significant events that have occurred since the end of the fiscal year	See chapter 20
9. Employees’ stake in share capital	See chapter 17
10. The Company’s Senior Management	See chapters 14, 15 and 16
11. Information about officers and directors	See chapters 14, 15 and 16
12. Acquisition of significant stakes in companies that have their headquarters in France, or acquisition of control over such companies; sales of such stakes	See chapters 7 and 25
13. Activities of subsidiaries and controlled companies	See chapters 7 and 25
14. Information pertaining to the distribution of capital and cross-holding – Share repurchase program	See sections 18.1 and 21.2
15. Changes in the composition of the share capital that occurred during the fiscal year	See sections 18.1 and 21.1.7
16. Changes in the security – Risk of variation in price	See sections 4.7 and 21.1.8



17. Summary statement of transactions by the executive officers and persons mentioned in article L. 621-18-2 of the monetary and financial code involving shares of the Company conducted during the past fiscal year	See section 15.4
18. Information required by article L. 225-100-3 of the Commercial code	See section 16.3.2
19. Social and environmental information	See section 6.12 and chapter 17
20. Table of five-year results	See section 20.6
21. Delegations relating to capital increases	See section 21.1.5

**NOTE**

In this reference document (the “Reference Document”), the terms “ERYTECH” or “Company” or “Parent Company” mean ERYTECH Pharma, a limited liability company headquartered at 60 Avenue Rockefeller, Bâtiment Adénine, 69008 Lyon, France, registered with the Lyon Trade and Companies Register under number 479 560 013. The term “Group” means the Company and the company ERYTECH Pharma, Inc. headquartered at Riverfront Office Park, One Main Street, Cambridge MA 02142, USA, a subsidiary of the Company.

The Reference Document presents the annual financial statements for the Company, prepared in accordance with accounting standards applicable in France for the financial year ending December 31, 2015, as well as a set of financial statements for the same year, prepared in accordance with the IFRS accounting standards adopted by the European Union. In application of article 28 of regulation (EC) no. 809/2004 of the Commission, the following are included as references in this Reference Document:

- for the financial year ended December 31, 2014, the consolidated financial statements, the corporate financial statements, and the corresponding statutory auditor’s reports, appear in Section 20 of the 2014 Reference Document registered by the AMF on June 4, 2015 under No. R.15-0048;
- for the financial year ended December 31, 2013, the consolidated financial statements, the corporate financial statements, and the corresponding statutory auditor’s report, appear in Section 20 of the 2013 Reference Document registered by the AMF on June 4, 2014 under No. R.14-0038;
- the key financial information and examination of the financial condition and results of the Company shown in Sections 3, 9, and 10 of the 2014 Reference Document registered with the AMF on June 4, 2015 under No. R.15.0048.

The 2013 and 2014 Reference Documents may be consulted on ERYTECH Pharma’s website ([www.erytech.com](http://www.erytech.com)) and that of the AMF ([www.amf-france.org](http://www.amf-france.org)).

Unless stated otherwise, the financial information regarding the Company mentioned in the Reference Document is taken from the IFRS consolidated financial statements. Additionally, the Reference Document contains statements about the Group’s objectives, as well as its areas of focus for development. These statements are at times identified by the use of the future tense, the conditional tense, and forward-looking terms such as “consider,” “plan,” “think,” “has as its objective,” “expects to,” “understand,” “must,” “strive,” “believe,” “estimate,” “wish,” “be able to,” or, as applicable, the negative form of these same terms, or even, any other variation or similar terminology. The reader’s attention is directed to the fact that these objectives and these directions for development depend on circumstances or facts for which the occurrence or completion is uncertain.

A glossary defining certain technical terms referenced in the Reference Document as well as an index of abbreviations used are found in chapter 26.

**WARNING**

The goals and directions for development presented are not historical data and must not be interpreted as being guarantees that the facts and data stated shall occur, that the scenarios have been verified, or that the objectives shall be reached. Inherently, these objectives may not be reached and the statements or information found in the Reference Document could turn out to be erroneous, and the Company shall not be under any obligation in any way whatsoever to provide an update, except as required by applicable regulations and particularly the General Regulation of the French *Autorité des Marchés Financiers* (the “AMF”).

The Reference Document furthermore contains information pertaining to the Group’s activities, as well as the market and industry in which it operates. Some of this information originates from sources external to the Group and has not been verified independently by the Group.

Investors are invited to carefully weigh the risk factors described in chapter 4 - “Risk factors” - of this Reference Document before making their investment decision. The occurrence of all or part of these risks may have a negative impact on the Group’s activities, circumstances, financial results, or the achievement of its objectives. Additionally, other risks that have not yet been identified or considered by the Group to be significant could have the same negative effect and investors could thus lose all or part of their investment.

## 1 RESPONSIBLE PARTIES

### 1.1 Person responsible for the reference document

Gil Beyen  
Chairman and Chief Executive Officer

### 1.2 Certification by the responsible party

“I hereby declare, after having taken all reasonable measures to this effect, that, to my knowledge, the information contained in this Reference Document conforms to reality and does not contain any omissions such as may alter its nature or intent.

I hereby certify that, to my knowledge, the financial statements have been prepared in accordance with applicable accounting standards and fairly present the assets, financial position, and results of operations of the company and all of the companies included in the consolidation, and that the attached management report is an accurate presentation of the changes, results, and financial position of the company and all of the companies included in the consolidation and a description of the main risks and uncertainties that they are facing.

We have obtained a completion letter (*lettre de fin de travaux*) from the statutory auditors, in which they declare that they have audited the information relating to the financial position and the financial statements presented in this Reference Document, and read the Reference Document in its entirety.

The historical financial information presented in this Reference Document has given rise to the statutory auditors’ reports to be found in Chapters 19 and 20.”

April 29, 2016

Gil Beyen



### 1.3 Persons responsible for the financial information

Gil Beyen  
Chairman and Chief Executive Officer

and

Eric Soyer  
Chief Financial and Operating Officer

Tel.: +33 4.78.74.44 38

Fax: +33 4.78.75.56 29

e-mail: [investors@erytech.com](mailto:investors@erytech.com)

## 2 STATUTORY AUDITORS

### 2.1 Statutory Auditors

**KPMG Audit Rhône Alpes Auvergne**, a simplified limited company, Lyon Trade and Companies Register 512 802 828, 51, rue de Saint Cyr - 69338 Lyon Cedex 9, France.

Date of first appointment: June 11, 2010.

Expiration date for term of office: The General Shareholders' Meeting voting on the financial statements for the year ending December 31, 2015.

KPMG SA was the statutory auditor for the period from initial establishment of the Company and up to its replacement by KPMG Audit Rhône Alpes Auvergne on June 11, 2010, upon expiry of its term.

**RSM Rhône Alpes**, Lyon Trade and Companies Register 398 384 198, 2 bis, rue Tête d'Or, Lyon 6, France.

Date of first appointment: June 17, 2014.

Expiration date for term of office: The General Shareholders' Meeting voting on the financial statements for the year ending December 31, 2019.

### 2.2 Deputy Auditors

**KPMG Audit Sud Est**, a simplified limited company, Marseille Trade and Companies Register 512 802 729, 480, avenue du Prado 13269 Marseille Cedex 08, France.

Date of first appointment: June 11, 2010.

Expiration date for term of office: The General Shareholders' Meeting voting on the financial statements for the year ending December 31, 2015.

The deputy statutory auditor from establishment of the Company and up to the expiry of his term on June 11, 2010, was Mr. Pierre Duranel, acting in his own name.

**Pierre-Michel Monneret**, 2 bis, rue Tête d'Or, 69006 Lyon, France.

Date of first appointment: June 17, 2014.

Expiration date for term of office: The General Shareholders' Meeting voting on the financial statements for the year ending December 31, 2019.

## 2.3 Declaration of fees paid to the auditors

The table below presents the auditor fees sustained by the Company in the last two years:

Exercice closing : 01/01/2015 - 31/12/2015

in euros	KPMG Rhône-Alpes Auvergne				RSM Rhône-Alpes			
	Amount (exclVAT)		%		Amount (exclVAT)		%	
	2015	2014	2015	2014	2015	2014	2015	2014
<b>Audit</b>								
Audit engagement; certification, examination of individual and consolidated								
•Parent company	336 067	47 550	93%	82%	59 375	35 450	80%	77%
•Subsidiary								
Directly associated due diligence reviews								
•Parent company	25 000	10 200	7%	18%	15 000	10 650	20%	23%
•Subsidiary								
<i>Subtotal</i>	361 067	57 750	100%	100%	74 375	46 100	100%	100%
<b>Other services</b>								
<input type="checkbox"/> Legal, fiscal, social	None	None			None	None		None
<input type="checkbox"/> Other								
<i>Subtotal</i>	0	0	0%	0%	0	0	0%	0%
<b>TOTAL</b>	<b>361 067</b>	<b>57 750</b>	<b>100%</b>	<b>100 %</b>	<b>74 375</b>	<b>46 100</b>	<b>100%</b>	<b>100%</b>

The other diligence activities and services directly associated with the auditor's mission include:

- fees corresponding to the preparation of auditor certifications relating to expenses incurred within the context of various R&D projects;
- fees relating to the certification of financial statements prepared in accordance with IFRS, IASB and PCAOB audit standards;
- fees relating to the securities note dated November 2015 on the capital increase dated December 2015.

Fees for KPMG Rhône Alpes Auvergne are rising significantly mainly because of their due diligence conducted for the Company's IPO on NASDAQ.

### 3 SELECTED FINANCIAL INFORMATION

The main financial information presented below is extracted from the consolidated financial statements of the ERYTECH Pharma Group, prepared in accordance with IFRS standards, for the financial years ended December 31, 2015, and December 31, 2014, as presented in Section 20.1 of the present Reference Document.

The historical legal financial statements for the Parent Company, prepared in accordance with accounting standards applicable in France, are included in Chapter 20.

This main accounting and operational data should be read alongside the information contained in Chapters 9 “Examination of the Company’s financial position and results,” 10 “Cash position and capital,” and 20 “Financial information concerning the Company’s equity, financial position, and results.”

- **Condensed balance sheet**

as of Dec. 31 in thousands of €	2015	2014
<b>NON-CURRENT ASSETS</b>	<b>1,076</b>	<b>1,080</b>
o/w Intangible assets	61	31
o/w Property, plant and equipment	918	967
o/w Non-current financial assets	97	82
o/w Deferred tax assets	-	-
<b>CURRENT ASSETS</b>	<b>51,929</b>	<b>39,526</b>
o/w Cash and cash equivalents	45,634	36,988
<b>TOTAL ASSETS</b>	<b>53,004</b>	<b>40,607</b>
<b>SHAREHOLDERS’ EQUITY</b>	<b>47,132</b>	<b>35,824</b>
NON-CURRENT LIABILITIES	251	525
CURRENT LIABILITIES	5,621	4,258
<b>TOTAL LIABILITIES AND SHAREHOLDERS’ EQUITY</b>	<b>53,004</b>	<b>40,607</b>

- **Condensed income statement**

as of Dec. 31 in thousands of €	2015	2014
<b>Total operating income</b>	<b>2,929</b>	<b>2,026</b>
o/w revenues	-	-
<b>Operating income/(loss)</b>	<b>(15,583)</b>	<b>(8,948)</b>
<b>Financial income/(loss)</b>	<b>567</b>	<b>68</b>
<b>Net income/(loss)</b>	<b>(15,013)</b>	<b>(8,860)</b>



- **Condensed cash flow statement**

<b>as of Dec. 31 in thousands of €</b>	<b>2015</b>	<b>2014</b>
operating cash flow before change in working capital	(11,962)	(7,325)
Change in working capital	(2,616)	79
<b>Net cash flow used in operating activities</b>	<b>(14,578)</b>	<b>(7,246)</b>
<b>Net cash flow used in investing activities</b>	<b>(284)</b>	<b>(420)</b>
<b>Net cash flow from financing activities</b>	<b>23,524</b>	<b>29,542</b>
o/w Capital increase in cash, net of transaction costs	23,544	29,173
change in other currency cash and cash equivalents	(16)	
<b>Increase / Decrease in cash and cash equivalents</b>	<b>8,646</b>	<b>21 21,87</b>

## 4 RISK FACTORS

Investors are invited to review all information contained in this Reference Document, including the risk factors described in this section. The Company has reviewed the risks and believes that there are no significant risks other than those described in this chapter. These risks are the risks which the Company believes, in the event they occur, could have a material negative impact on the Company, its activity, financial position, results or its development.

### 4.1 Operational risks

#### 4.1.1 Risks related to product development

*The development of the Company's products could be delayed or not be terminated.*

*The marketing approval for ERY-ASP/GRASPA®<sup>1</sup> could be delayed, be subject to "post-MA" studies (these two eventualities may lead to additional costs) or may not be obtained.*

To obtain the regulatory approval required to bring a candidate drug to market, the Company must conduct preclinical and clinical studies to show safety and efficacy. These studies entail high costs. The trend for these costs could be on the rise with the growth of the Company and development of its pipeline of products. If the results of these studies are unsatisfactory or inconclusive, the Company may have to choose between abandoning the program, leading to loss of investment in time and money, or its pursuit, with no guarantee that the additional costs that this would entail would lead to completion.

The Company may choose, or regulatory authorities may compel the Company, to suspend or end clinical trials if the patients are or have been exposed to unexpected and serious risks or to clinical ineffectiveness (loss of opportunity) or request additional scientific information/validations. Deaths and other adverse events could occur during a clinical trial as a result of medical problems that may or may not be related to the treatment subject of the study, and force the Company to delay or interrupt the trial. In light of the results of trials, the Company could also decide to abandon development projects that it initially believed to be promising.

Other factors can have a material adverse effect on the Company's business, prospects, financial position, results of operations and growth:

- Early selection of new products or new areas of development could prove to be less relevant and not lead to the launch of new products;
- Research and development teams may not be able to develop the new products required for the Company's objectives, both for new market penetration and for maintaining current opportunities;
- Co-development with other partners could be more difficult than anticipated and the corresponding launches may be delayed or abandoned;
- New regulatory requirements could delay or jeopardize preclinical and/or clinical development of candidate drugs;
- Patient recruitment in trials could also prove difficult, delay the start of the study, prolong its duration or limit its scope due to a low number of patients;
- Patients included in the trial could, at any time and without justification, stop participating in the trial; if too many patients withdraw, the study could be discontinued due to lack of feasibility;
- Shortages in raw materials impacting the production of clinical batches could delay or interrupt a planned clinical trial or a clinical trial in progress;
- Phase I trials aim, in particular, to show the safety of the candidate drug; negative results in Phase I could lead to discontinuation of the trial program; even in future phases, where Phase I results were positive, tolerance and safety problems or harmful side effects could occur and delay or interrupt the trials; and
- In the event of serious tolerance or toxicity problems, the trials must be interrupted.

<sup>1</sup> The GRASPA® brand has been licensed to Orphan Europe (Recordati Group) to market the product in ALL and AML in Europe and to Teva Group for Israel.

Furthermore, the formulations of the ERY-ASP/GRASPA<sup>®</sup> product used in Europe and in the United States differ, and the regulatory authorities of each jurisdiction may not accept the data from the clinical studies for an alternative formulation of ERY-ASP/GRASPA<sup>®</sup> used in another jurisdiction. This could lead to delays and additional costs in connection with the conduct of additional comparative studies or could require the Company to repeat clinical and non-clinical studies so as to obtain approval in each jurisdiction in which the Company wishes to market ERY-ASP/GRASPA<sup>®</sup>.

Finally, no guarantee can be made as to positive preclinical and clinical results. Favorable results during preclinical studies and preliminary clinical trials are not always confirmed during future clinical trials. In addition, clinical trials can produce safety and efficacy results that, while positive, are not sufficient to obtain marketing approval. Positive results in a clinical trial and/or the grant of marketing approval of a product with a given indication does not presume the efficacy, safe use and MA for another indication, even if the latter may be related or linked by scientific rationale.

#### 4.1.2 Risks relating to the particular nature of the products

***ERY-ASP/GRASPA<sup>®</sup>, ERYTECH's lead product, could present certain risks that exist in relation to blood transfusions.***

ERY-ASP/GRASPA<sup>®</sup> must be intravenously injected in the patient in accordance with the rules for administering red blood cells (transfusion) and, among other things, those regarding donor compatibility (blood type). The red blood cells used during the manufacturing process of ERY-ASP/GRASPA<sup>®</sup> originate from blood donations prepared and tested by blood banks such as the Établissement Français du Sang (EFS), known for their high standards of quality and safety.

However, ERY-ASP/GRASPA<sup>®</sup> could present certain risks that exist in relation to blood transfusions. These risks, while rare, are possible despite having never been observed with ERY-ASP/GRASPA<sup>®</sup> at the time of filing of the Reference Document:

- Risks from transmission of infectious agents:
  - viral;
  - bacterial;
  - parasitic; and
  - prionic.
- Risks from red blood cells:
  - immunological (allergic) risk is the most concerning in terms of its severity and frequency; and
  - risk of post-transfusion graft-versus-host disease and purpura.

In addition, the blood banks follow a strict red blood cell preparation process, approved by health authorities, to detect and reduce possible risks for contamination by infectious agents.

Risks related to molecules encapsulated in red blood cells could be varied and will depend on their known or unknown toxicity. For example, enzymatic biological molecules (such as asparaginase) are immunogenic in humans and promote development of antibodies and allergic reactions, which could lead to anaphylactic shock and death of the patient. The level of knowledge of the risks inherent to encapsulated molecules will be greater for a molecule that has already been granted a marketing approval in France or another country than for a new molecule that has never been used in humans. ERY-ASP/GRASPA<sup>®</sup> uses asparaginase, a product used in Europe since the 1970s, the toxicity of which is well known and documented.

#### 4.1.3 Risk related to the production process

***Production costs may be higher than estimated***

ERYTECH manufactures according to manufacturing best practices applicable to drugs for clinical trials and to specifications approved by the regulatory authority. Only products that meet the standards are released for administration to patients. If a product is found to be non-compliant, ERYTECH would be

required to restart the manufacturing process, which would entail additional costs and may prevent delivery of the product to patients on time.

Other risks 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 cold chain.

These risks, should they occur, could have an adverse effect on the activities, financial position, results of operations, reputation or growth of the Company.

Moreover, a rise in direct/indirect energy rates may increase product manufacturing and logistical costs, therefore having a negative impact on the activities, financial position, results or growth of the Company.

#### 4.1.4 Risks related to production capacity

*The Company's production capacity could be insufficient.*

The Company's production capacity may prove insufficient in the future to meet the growth of its activity. If the Company is forced to increase its production capacity, it could need to make considerable investments that could lead to significant financing needs or to sub-contracting agreements in order to outsource part of the production.

#### 4.1.5 Risk of commercial failure

*The commercial success of the Company's products is not guaranteed.*

At this time, none of the products developed by the Company has received MA. For the development and marketing of products based on its ERYCAPS platform, the Company is confronted with a high level of risk and uncertainty which could slow or suspend the development efforts for its products and negatively affect its activities. Therefore, even if the Company could obtain and maintain regulatory authorizations to market these products, it is possible that:

- The marketing approvals (MA) for its products will not be obtained by the Company in a timely manner so as to gain a competitive advantage in the targeted markets;
- The health authorities will impose restrictions on use that limit the therapeutic value and potential of the product in these targeted markets;
- Health authorities will require that warnings on the use of the product be added to its instructions or packaging and impose more stringent conditions on advertising;
- The Company will not be able to successfully manufacture and market its future products at a price, reimbursement rate or scale allowing it to be profitable ([see also Section 4.4: Regulatory Risks in this Reference Document](#));
- The future products of the Company will lose their competitive advantage and are rendered obsolete by third-party development of other equally or more innovative products ([see also Section 4.2 Strategic Risks in this Reference Document](#)); and
- The future products of the Company are not marketable due to third-party intellectual property rights claims ([see also Section 4.2 Strategic Risks in this Reference Document](#)).

The level of acceptance of each Company product by the market will also depend on the following factors:

- The prescribing physicians' perception of the product's therapeutic benefit;
- The possible occurrence of adverse effects once MA is obtained;
- The ease of integration of the product into the current care process;

- The efficient implementation of a scientific publication strategy; and
- The support of opinion leaders.

These factors could limit or halt product acceptance by the market which would have a material adverse effect on the Company's activities, financial position, results of operations and growth.

#### 4.1.6 Risks related to sales, marketing and distribution resources

*The Company has limited experience in sales, marketing and distribution.*

To date, the Company has not invested in sales, marketing and distribution. The Company will have to develop marketing and sales capability either on its own or with strategic partners.

To market its first product, ERY-ASP/GRASPA<sup>®</sup>, the Company has entered into a partnership with specialists in the sale of orphan drugs, Orphan Europe (Recordati Group) for Europe and Teva Group for Israel ([see also Section 4.1.8](#) and [Chapter 22 in this Reference Document](#)).

For other products and jurisdictions, the Company will choose to market its products:

- by its own means, or
- through a marketing partnership.

In the first case, the Company will have to organize its own sales and marketing infrastructure.

In the second case, it is possible that:

- the Company will not be able to enter into a partnership under economically reasonable conditions; or
- such a partnership will be challenged; or
- the partners will face difficulties or do not implement all means necessary to obtain the expected results pursuant to the agreements concluded with the Company. The partners' budget restrictions or priority given to other development programs, for example, could delay the validation of the potential of the Company's products and their marketing; or
- conflicts could arise between the Company and some of its partners. In particular, the Company cannot guarantee that any of its partners will not design or seek to implement a commercial activity using a competing technology to that of the Company's ([see also Section 4.2.4 on the risks related to competition in this Reference Document](#)).

Such events may have a material adverse effect on the activity, prospects, results of operations, financial position and growth of the Company.

In all cases, it will consequently have to incur additional costs, mobilize management resources, recruit specific personnel, draw on new competencies and take the time required to put in place the appropriate organization and structure to assist the development of the product in accordance with current laws and, more generally, optimize its marketing efforts.

#### 4.1.7 Risks related to its ability to penetrate foreign markets

The future profitability of the Company will depend in part on its ability to market its candidate products on markets inside or outside of the United States and Europe. If the Company markets its candidate products on foreign markets, it will be subject to additional uncertainties and risks such as:

- economic weaknesses, including inflation, or political instabilities in certain economies and markets;
- difficulties in complying with complex and changing foreign regulations on taxation, accounting and legal requirements that often vary from country to country;
- different medical practices and customs in foreign countries that may affect acceptance of the Company's products on the market;
- tariff and trade barriers;

- any other measure of trade protection, import or export licensing requirements or other restrictive measures imposed by the United States or other foreign governments;
- longer accounts receivable collection time;
- longer lead times for shipping;
- compliance with tax, employment, immigration and labor laws for our employees living or traveling abroad;
- uncertainties concerning the workforce in countries where labor unrest is common;
- the language barrier for technical training;
- the reduced protection of intellectual property rights in certain foreign countries, and the resulting prevalence of generic alternatives to the products of the Company;
- fluctuating foreign exchange rates and currency controls;
- differing foreign reimbursement landscapes;
- the uncertain and potentially inadequate reimbursement of our products; and
- the interpretation of contractual provisions governed by foreign laws in the event of a contractual dispute.

Sales of the Company's products abroad may also be adversely affected by the imposition of government controls, political and economic instabilities, trade restrictions and changes in tariffs.

#### 4.1.8 Risk related to dependence on exclusive distributors of GRASPA®

*The marketing of GRASPA® in 38 European countries and in Israel is largely dependent on Orphan Europe (Recordati Group) and Teva Group.*

##### 4.1.8.1 **Teva Group**

The Company has chosen Teva Group (“**Teva**”) as exclusive distributor for GRASPA® in the treatment of ALL in Israel ([see also Chapter 22 in this Reference Document](#)).

A licensing and exclusive distribution agreement has been entered into between the parties as of March 28, 2011.

Although this agreement requires that, every year, Teva reach the minimum sales targets after the launch of GRASPA®, the only recourse that the Company has in the event that Teva fails to reach these targets is the termination of this agreement, which would cost it time and considerable resources either for the development of its own marketing capabilities in Israel or for the conclusion of an agreement with a new suitable distributor, if any exists. The Company cannot guarantee that Teva will succeed in obtaining regulatory authorization to market GRASPA®. The marketing success of GRASPA® in Israel therefore depends on regulatory, marketing and commercial efforts deployed by this distributor as well as its capability to sell the treatments developed by the Company. Any failure on the part of Teva would have adverse consequences for the Company. The Company has limited these risks by putting in place a steering committee to follow up on the development and marketing of products developed by the Company.

##### 4.1.8.2 **Orphan Europe (Recordati Group)**

The Company has chosen Orphan Europe (Recordati Group) as the exclusive distributor of GRASPA® in the treatment of ALL and AML for 38 countries in Europe, including the European Union ([see also Chapter 22 in this Reference Document](#)).

An exclusive licensing and marketing agreement was entered into by the parties on November 23, 2012. The risk resulting from this agreement is the risk of dependence since:

- Orphan Europe (Recordati Group) is the exclusive distributor of GRASPA® for all of Europe. The success of marketing GRASPA® in Europe therefore depends on regulatory, marketing and commercial efforts deployed by this distributor as well as its capacity to sell the treatments developed by the Company. Although this agreement requires a periodic presentation by Orphan Europe on the marketing plans for estimating future sales of GRASPA®, Orphan Europe is not subject to minimum sales requirements and the Company cannot guarantee the success of



- marketing GRASPA® in the event of MA. Any failure on the part of Orphan Europe would have adverse consequences on the Company. The Company has limited these risks by putting in place a steering committee to follow up on the development and marketing of such products developed.
- Milestones payments will be made to the Company: the first payment was made on the date the agreement was signed and others will be made when marketing approval of the treatments developed by the Company is granted and according to the sales levels achieved by Orphan Europe. Consequently, if the Company does not reach these milestones, this will have a material adverse effect on its activities, financial position, results of operations or growth.
  - The termination of the agreement by Orphan Europe in case of a wrongful breach by the Company could result in the payment of significant damages. However, the Company could also terminate the said agreement in the event of serious breach on the part of Orphan Europe, and claim significant damages.
  - The non-compliance of guarantees given by the Company could reduce the milestone payments.

The Company expects that the revenues from its products would be adversely affected by a loss or change of current or future distributors of its products. If the Company decides to terminate any distribution agreement, it will either need to enter into a new agreement with, qualify, train and supply a replacement distributor or supply and service customer accounts in those territories itself. Current or future distributors could irreparably harm relations with current and potential local customers and the reputation of the Company with the biopharmaceutical community in general. In the event that the Company is unable to find alternative distributors or to mobilize its own sales force in the territories in which a distributor operates, the supplying of customers, its reputation and its operating results could be negatively affected.

#### 4.1.9 Risk related to dependency on its most advanced product: ERY-ASP/GRASPA®

*ERY-ASP/GRASPA® is the only product under clinical development, in the process of registration in Europe, and likely to be launched on the market within the next five years.*

ERY-ASP/GRASPA® is, to date, the only Company product under clinical development. In fact, the clinical development of ERY-ASP/GRASPA® is not yet complete.

The development of ERY-ASP/GRASPA® has required and will continue to require the mobilization of numerous Company resources. The future of the Company depends on the successful development of its lead product: ERY-ASP/GRASPA®. Indeed, if the Company does not successfully develop and, ultimately, market ERY-ASP/GRASPA®, and if it does not, in parallel, reduce its dependence on this product, its activities, prospects, financial position, results, and growth could be significantly affected.

The Company considers its dependence on ERY-ASP/GRASPA® to be significant.

#### 4.1.10 Risk of failure in the development of its ERYCAPS platform

The Company is only at an early stage in the development and its ERYCAPS platform has not yet, and may never lead to approved or marketable products. Even if the Company is successful in continuing to build its product pipeline, the potential candidate products that the Company has identified may not be suitable for clinical development for reasons such as their harmful side effects, their limited efficacy or other characteristics that indicate that they are unlikely to be products that will receive marketing approval or be accepted by the market. For example, the FDA has required that the Company implement an additional red blood cell washing step in the manufacture of ERY-ASP to reduce the risk of hemolysis for patients. The use of red blood cells as the basis for its ERYCAPS platform could lead to similar risks affecting the ability of its products to be granted a marketing approval and to be accepted by the market. If the Company fails to develop and market its candidate products based on its ERYCAPS encapsulation technology approach, it may not be able to generate revenues from its products and from its collaborations in the future, which would adversely affect its business and prospects.



#### 4.1.11 Risks related to dependence on key scientific partnerships

*The loss of some scientific partnerships could hinder the growth of the Company.*

The Company currently has and expects to continue to depend on partnerships with public and private research institutions, to conduct an important part of its discovery activities. If one of these partners breached or terminated its agreement with the Company or otherwise failed to work efficiently with the Company, the research, development or marketing of products planned as part of this partnership could be delayed or canceled. In the event a partnership agreement entered into by the Company is terminated or the Company is no longer in a position to renew the partnerships in question under acceptable conditions, the Company's activities may be delayed and even penalized.

#### 4.1.12 Risks of conflict of interest

*A director or a member of the Scientific and Medical Board could be in conflict of interest and harm the Company*

Directors (*see also Sections 14.1 and 16.3.2 of this Reference Document*) are subject to a regulatory and legal framework, including for conflicts of interest. However, no provision can replace the ethical conduct of a director. In addition, in the event of conflict of interest, a director risks losing his/her intellectual independence or objectivity. The occurrence of this risk could have a material adverse effect on the activities, financial position, results of operations, reputation or growth of the Company.

Members of the Scientific and Medical Board (*see also Section 16.3.2 of this Reference Document*) contractually declare their interest(s). The Company consequently assesses the risks, but does not verify the truthfulness of these statements. In the event of omission or of false declaration, a member risks losing his/her intellectual independence or objectivity. The occurrence of this risk could have a material adverse effect on the activities, financial position, results of operations, reputation or growth of the Company.

#### 4.1.13 Risks of dependence on subcontractors and key raw material suppliers

*Access to raw materials and products required to complete clinical trials and to manufacture the Company's products is not guaranteed.*

The Company is supplied, among other things, with:

- Asparaginase (*see also Section 22 of the Reference Document*).
- Red Blood Cell (RBC) Concentrate.

EFS (Établissement Français du Sang) and ARC (American Red Cross) are under contract with ERYTECH to supply the Company for its current clinical trials and as part of temporary approval for use. Blood collection and distribution is managed in France by EFS, a public institution with a monopoly position, and in the United States by the ARC, the only operators in their respective countries responsible for meeting the national need in blood products, which they must supply in sufficient quantity with optimal quality. In the event of a major and/or international crisis impacting blood banks and the practice of blood donation, the Company may no longer be able to procure RBC in a sufficient manner and to satisfy the demand of clinical trials and/or of the markets.

The asparaginase market is a closed market with few international players and multiple marketing exclusivity rights between players and geographical areas. ERYTECH is exclusively supplied by a company (medac) with which it has signed a long-term contract for the supply of asparaginase.

*The Company is dependent on its subcontractors.*

The Company outsources the following:

- the manufacturing of equipment required to operate its manufacturing process (*see also Chapter 22 of the Reference Document*);
- the management of its clinical trials to specialized Contract Research Organizations (CROs);
- the completion of certain research and development studies;
- the shipping of its products.

In the event of failure, bankruptcy or shutdown of, or dispute with these subcontractors and/or key suppliers, the Company could then not be able to enter into new agreements with other contractors under commercially acceptable terms and therefore could not be able to develop, test, manufacture and market its products in the expected time frame and at an acceptable cost. This could have a material adverse effect on the activities, financial position, results of operations or growth of the Company.

In addition, the contracts that the Company entered into with these companies usually contain limitation of liability clauses in their favor, meaning that the Company will not have recourse to full compensation for potential losses likely to be incurred by the Company in the event of failure.

To reduce its dependence on these companies, the Company's contracts provide for, where possible, an extended notice period before any termination or shutdown of activity in order to have sufficient time to find a new qualified contractor.

Where possible, the Company also has alternate suppliers as part of its purchasing policy, and undergoes follow-up with its contractors through audits managed by the Company Quality Assurance department. In addition, the Company contractors generally have agreed to precise specifications. However, the Company cannot guarantee these contractors will follow the Company's instructions.

If products supplied and manufactured by third parties do not comply with regulatory standards, penalties may be imposed on the Company. These eventualities may include fines, injunctions, a refusal by regulatory authorities to allow the Company to pursue its clinical trials, delays, suspension or withdrawal of approvals, seizure or recall of its products and criminal prosecution; all such measures could have a considerable adverse impact on the Company's business.

In the event the Company is forced to change key suppliers or subcontractors, it will be asked to show that the change has had no impact on the quality of the manufactured products. Such verification could be costly, time-consuming and could require the attention of the Company's most qualified personnel. In order to show absence of impact due to such change, the Company could be required to conduct animal studies or other clinical studies. Some changes are subject to approval by regulatory authorities. If the change is refused, the Company could be compelled to find another supplier/subcontractor which could delay the production, development or marketing of products and increase the manufacturing costs of these products.

#### **4.1.14 Risks relating to health, safety, and the environment**

##### ***The Company is exposed to risks related to hazardous substance handling.***

The Company's research and development activities expose it to chemical and biological risks and require it to take and follow preventive measures according to current legislation.

During company preclinical research and development programs and tests, the Company uses hazardous materials, such as compressed gases, and biological material, blood not only from donors but also from patients (*see also Section 4.1.2, Risks related to the particular nature of products from technology in this Reference Document*), solvents and other chemical products that could be genotoxic.

There are therefore health risks related to the handling of these hazardous materials by the Company employees and/or subcontractors. Consequently, the Company is subject to environmental and safety legislation and regulations governing use, storage, handling, emission and hazardous materials disposal, including of chemical and biological products. While the Company considers that the safety measures

meet the standards set out by current legislation and regulations and allow its employees and subcontractors to work under good conditions, the risk of accidental contamination or of occupational diseases related to hazardous material handling cannot be completely eliminated.

Although the Company has not identified any major environmental risks related to its activities, in the event of an accident the Company could be held responsible for all resulting damages and the incurred liability could exceed the limits of the insurance policies taken out by the Company or even not be covered by such policies.

Moreover, compliance with environmental, health and safety regulations imposes on the Company additional costs, and the Company may have to incur significant expenses to comply with future environmental legislation and regulations.

## 4.2 Strategic risks

### 4.2.1 Risk related to key personnel

***The Company could lose key partners and not be able to attract new qualified personnel.***

The Company's success depends in large part on the actions and efforts by its executive officers and personnel in key positions. In the event that the Company is not able to keep its executive officers and scientists, its research and development (preclinical as well as clinical) could be delayed, and the implementation of its strategy could be negatively affected. As the Company progresses in its programs and extends the scope of its activities, it could have to recruit new employees with competencies in areas such as clinical trials, regulatory matters, reimbursement procedures, sales and marketing. As part of recruiting and retaining qualified personnel, the Company is confronted with intense competition from other companies in the sector, universities and public and private research institutions, as well as other organizations. Under these circumstances, the Company cannot guarantee its ability to recruit and/or retain its qualified personnel under conditions that are acceptable from an economic point of view. The delay in recruiting or the loss of a key employee could prevent the Company from reaching its overall objectives and consequently have a negative impact on its activities, results of operations, financial position and prospects.

Moreover, the loss or disability of one or more members of Management could lead to material adverse effects on the activities, financial position and overall growth of the Company. While the Company benefits from a "Key Persons" insurance policy (*described in Section 4.9 of the 2014 Reference Document*) for Gil Beyen, this policy could prove insufficient to compensate for any damages suffered.

### 4.2.2 Risks related to key objectives not being reached

***The Company might not reach its contractual objectives as set out under certain partnerships and partnership agreements.***

The Company is bound to academic and commercial partners through financial agreements for research programs or by commercial development agreements. The payment of royalties or public funding under these agreements are conditioned to the respect of certain commercial, industrial, proof of concept and others objectives.

Consequently, not reaching these objectives will have a material adverse effect on the Company's activities, financial position, results of operations or growth.

In particular, since the founding of the Company in October 2004 and until December 31, 2015, BPI France has awarded the Company €2,275,783 in non-repayable grants and €878,607 in conditional advances. If the Company fails to meet its contractual obligations under the applicable research program financing agreements, and especially if the Company loses its exclusive right for the commercial development of its candidate products, it may be required to repay early the conditional advances of a

total amount of €570,857 at December 31, 2015. Such early repayment could have a negative impact on the Company's ability to finance its research and development projects, in which case it will have to find other sources of financing that may not be available under reasonable economic terms or may not be available at all.

#### 4.2.3 Risks related to the management of internal growth

*The development of the Company will depend on its ability to manage its growth.*

As part of its development strategy, the Company will need to recruit additional personnel and develop its operational capabilities, which could excessively mobilize its internal resources. To do so, the Company will need to:

- train, manage, motivate and retain an increasing number of employees;
- anticipate the expenses related to this growth and associated financing needs;
- increase or transfer its production division and its premises;
- accurately project demand for Company products and revenues that could be generated; and
- develop its information systems.

If the Company fails to manage its development or if it encounters unexpected difficulties in its development, this could have a material adverse effect on its activities, financial situation, results of operations or growth.

#### 4.2.4 Risks related to competition

*Direct or indirect competitive solutions could hinder the growth of the Company and render its products obsolete.*

The markets in which the Company operates are well-defined, very competitive and progress rapidly. The Company competes with larger companies that have more industrial and marketing experience and which have access to clearly greater resources.

Consequently, the Company cannot guarantee that its drugs will:

- reach the target markets more rapidly than those of its competitors;
- be competitive compared to other developed products or products under development that turn out to be safer, more effective or less expensive;
- adapt rapidly enough to new emerging and developing technologies and scientific breakthroughs;
- be accepted by medical centers, physicians and patients in lieu of existing treatments; and
- be effectively competitive compared to other products treating the same indications.

Finally, the Company cannot guarantee that its partners and/or employees will not prefer, in the short, medium or long term, to join or work for competitors.

Such events could have a material adverse effect on the activities, results of operations, financial position and growth prospects of the Company.

It is likely that new developments will continue in the pharmaceutical industry and in public and private research institutions. In addition to developing safer, more effective and less expensive products than those developed by the Company, its competitors could manufacture and market their products under better conditions. Accordingly, the Company cannot exclude the possibility that companies and other public and private organizations that are currently competing in the same space, merge or enter into partnerships or other types of alliances, consequently becoming more aggressive competitors. Moreover, rapid technological developments by these competitors could render the Company's candidate drugs or its potential products obsolete before the Company is able to make a profit on the research, development and marketing costs for its products.

To the Company's knowledge, new forms of asparaginase are under development as well as other products that could be used in the treatment of acute leukemia ([see also Section 6.4.7 The current market for L-asparaginase in this Reference Document](#)).

Even if the Company's products are marketed successfully, market recognition could be delayed and the Company may not be able to offset its costs with its potential revenues. In order to gain market acceptance for its products over existing ones, the Company will have to commit to significant marketing as well as investment efforts. To date, the Company has not undertaken significant marketing activities and has few financial and human resources available for such purposes.

#### 4.2.5 Risks related to confidentiality of Company information and knowledge

***The Company may not be able to protect the confidentiality of its information and/or know-how.***

As part of current or future partnership agreements between the Company and individuals as well as other public or private entities, subcontractors or third parties, information and/or products may be provided to them in order to conduct tests or other services. In such case, the Company requires the signing of a confidentiality agreement. In fact, the proprietary non-patented and/or non-patentable technology, processes, know-how and data are considered trade secrets that the Company attempts to protect through such confidentiality agreements.

There is no guarantee that such confidentiality agreements will ensure the intended protection or will not be breached, and that the Company has appropriate solutions against such breaches, or that its trade secrets will not be disclosed to or be developed by its competitors.

More specifically, the Company has no control over the conditions under which third parties with which it contracts, use themselves other third parties, and protect its confidential information.

The occurrence of this risk could have a material adverse effect on the activities, prospects, financial position, results of operations and growth of the Company.

#### 4.2.6 Risks related to the use of information systems

***ERYTECH could be the target of cyber-attacks.***

In order to maintain the security of its information systems and their users, the Company standardized rules governing their use (information technology charter, internal control procedures) to outline the main precautions and guidelines of use that each user must follow when using Company information systems.

However, the Company cannot guarantee that the users will follow these rules and that these rules are sufficient to avoid cyber-attacks, loss of sensitive data, discontinuity of operations and claims against the Company. These risks, should they occur, could have an adverse effect on the activities, financial position, results of operations, reputation or growth of the Company.

#### 4.2.7 Risks related to industrial espionage

***ERYTECH could be a target of industrial espionage.***

Given its highly technological and innovative activity and advanced research and development projects that could confer it a competitive advantage in its market, the Company is exposed to an industrial espionage risk.

Disclosure or theft of its scientific research content would deprive the Company of potential revenue sources and affect its activities.

Such a situation, should it occur, is likely to have an adverse effect on the Company, its activities, financial position, results of operations or growth.

#### 4.2.8 Specific risks related to the use of technologies owned by third parties

***The Company cannot guarantee the intellectual property of technologies owned by third parties and that it uses.***

The Company has signed agreements with researchers working for public and/or private entities ([see Chapter 22 of this Reference Document](#)). The agreements signed with these entities contain clauses pertaining to intellectual property rights and confidentiality commitments.

It cannot be guaranteed that those agreements will ensure the intended protection or that they will be respected by the Company's co-contracting parties. The Company also relies on the commercial licensing terms which it will obtain, if applicable, for the results of the experiments covered by such agreements.

Finally, the Company cannot guarantee that entities with which it has contracted, have at their disposal all the rights to use the technologies and that they will be able to grant the Company licenses for such rights.

When the Company is granted a patent license from third parties ([see Chapter 22 of this Reference Document](#)), the Company undertakes to comply with certain conditions to maintain its rights on the patent. In addition, the Company relies on the patent being protected and enforced.

The conditions for maintaining rights on the technology could include elements such as carrying out development efforts to transform the patent into a commercial product, payment of licensing fees while carrying out predefined steps and payment of annual licensing fees based on sales revenue generated as a result of the patent.

Any failure on the part of the Company could lead to loss of patent exclusivity. If the Company loses its rights to the patent obtained under license or if it cannot obtain new similar rights under reasonable terms, this could constitute an obstacle to development, manufacture and sale of its products.

#### 4.2.9 Risks related to intellectual property

***The protection offered by patents and other intellectual property rights is uncertain. The Company may not be able to maintain adequate protection of its intellectual property rights and thereby lose its technological and competitive advantage. Part of the Company's activity could depend on or infringe upon patents and/or other intellectual property rights owned by third parties. The exclusive nature conferred by intellectual property rights could be circumvented by the Company's third parties/competitors.***

The Company's success depends on its ability to obtain, maintain and enforce its patents and other intellectual property rights. If one or more brands or patents covering a technology, the manufacturing process or a product were to be invalidated or found unenforceable, the development and marketing of such a technology or product could be directly affected or interrupted.

In the pharmaceutical industry in which the Company operates, patent law varies according to the country and is in constant evolution. There is therefore much uncertainty in this area. Consequently, the Company cannot guarantee that:

- its patents will be the basis for commercially viable products;
- its pending patent applications will lead to patent grants;
- its patent applications, even if they are granted, will not be challenged, invalidated or found unenforceable;
- the scope of protection offered by patents will be sufficient to protect the Company from its competitors;



- the products will not infringe on third-party intellectual property rights or patents and that the Company will not be forced to defend itself against such allegations made by third parties;
- third parties will not be granted patents or file patent applications for the Company's products before the Company is granted such patents or files such applications; or
- third parties will not be granted or will not file patent applications or use any other intellectual property rights that, even if they do not infringe on those of the Company, limit its growth.

Intellectual property litigation is often long, costly and complex. Some of the Company's competitors have access to greater resources and could be more able to conduct such proceedings. A court judgment against the Company could seriously affect its ability to continue its activities and, more particularly, could force the Company to:

- cease the sale or use of its products;
- acquire the right to use the intellectual property under costly terms; or
- change the design, delay the launch or even abandon some of its products.

Patent applications in Europe and in the United States are not generally published until 18 months after the priority date on the application and, moreover, in the United States, some applications are not published before the patent is granted. In addition, in the United States, while the laws changed in 2012, the notion of the right to the patent for all patent applications before March 2013 is related to the notion of first-to-invent which is based on the date the invention was conceived, while in other countries, the right to the patent is attributed to the first to file the patent application. The new laws in the United States provide that the right henceforth belongs to the first inventor who files according to the new rules. As a result, the Company cannot guarantee that third parties will not be in a position to be considered as first inventor or first inventor to file an invention covered by its patents and its pending patent applications in the United States. In such circumstances, the Company could have to sign licensing agreements with third parties (provided that such licenses are available), modify some of its activities or manufacturing processes, or develop or acquire different technologies.

The Company is confronted with similar risks for its trademarks.

The Company also relies on its technology, manufacturing processes, knowledge and non-patented confidential data that it protects through confidentiality agreements signed by its employees, consultants and some of its subcontractors. The Company cannot guarantee that these agreements will always be respected, that the Company has recourse in the event of a breach of such agreements or that the confidential information in question will not be disclosed to third parties or independently developed by competitors. The Company also cannot guarantee that, despite the implementation of measures, a consultant or employee will not claim rights on an invention discovered as part of a Company project.

The occurrence of any one of these situations regarding any patent or intellectual property right of the Company could have a material adverse effect on the activities, financial position, results of operations or development of the Company.

***The Company will not seek to protect its intellectual property rights in all countries throughout the world and it may not be able to obtain good enforcement of those rights even in countries where it attempts to protect them.***

The filing, processing and defense of patents associated with the candidate drugs of the Company in all countries and jurisdictions worldwide would be extremely expensive and its intellectual property rights in certain territories outside the European Union and the United States could be less extensive than within Europe and the United States if such rights are obtained in the United States or in Europe.

Furthermore, the laws of certain foreign countries do not protect intellectual property rights in the same way as European Union law and US federal and state laws do. Therefore, the Company may not be able to prevent third parties from using its inventions in territories other than the United States or the European Union or from selling or importing products manufactured on the basis of its inventions in Europe and in the United States or other jurisdictions.



The legal deadlines for patent protection applications in each foreign jurisdiction are based on the priority dates of each of the Company's patent applications. Competitors may use the Company's technologies in jurisdictions where it does not apply for and does not obtain patent protection in order to develop their own products and may even export illegal products to territories where it has patent protection but where enforcement is not as fundamental as in Europe or the United States. Such products could compete with the Company's products, and patents or any other intellectual property right may not be effective or sufficient to prevent such competition. Even if the Company applies for and obtains patents issued in certain particular jurisdictions, such patent claims or other intellectual property rights may not be effective or sufficient to prevent third parties from engaging in such competition.

The legislation of certain foreign countries does not protect intellectual property rights in the same way as the legislation of the European Union and the United States does. Many companies have encountered serious problems in the protection and defense of intellectual property rights in certain foreign jurisdictions. The legal systems of certain countries, particularly developing countries, are not favorable to the enforcement of patents and other intellectual property protections, especially those involving biopharmaceutical products and biotechnologies. It may therefore be difficult for the Company to prevent infringement of its patents, even if it obtains them, or misappropriation of its other intellectual property rights.

For example, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. Furthermore, many countries limit the enforceability of patents against third parties, particularly government agencies or government sponsors. In such countries, patents may be of limited benefit or no benefit at all. Patent protection should be considered country by country, which is a burdensome and time-consuming process, with uncertain results.

Therefore, it is possible that the Company will not apply for patent protection in certain countries and therefore would not be able to benefit from patent protection in those countries.

Litigation initiated for the enforcement of the Company's patent rights in foreign jurisdictions could result in substantial expenses and divert its efforts and attention from other aspects of its business, as well as result in the invalidity or a strict interpretation of its patents, prevent its patent applications from succeeding and enable third parties to make claims against it. It is possible that the Company may not prevail in any litigation that it undertakes and that the damages that it would be awarded, if any, would not be commercially significant. Moreover, changes in law and in the rulings of the courts in Europe, the United States and other countries may affect its ability to obtain adequate protection for its technology and for enforcement of its intellectual property. Therefore, the efforts made by the Company for worldwide enforcement of its intellectual property rights may prove unsuitable for obtaining significant commercial benefit deriving from the intellectual property that it develops or licenses.

### 4.3 Legal risks

***The liability of the Company and/or its subsidiary may be incurred where any harm is caused by one of its products.***

The use or misuse of the Company's products during feasibility studies and clinical trials, as well as the sale, promotion, or the use of future related products risk exposing the Company and/or its subsidiary to liability actions.

Complaints can be filed and legal action taken against the Company and/or its subsidiary by patients, regulatory authorities, pharmaceutical companies, or other third parties using or selling the Company's products. The Company cannot guarantee that its current insurance policies are sufficient to protect the Company and/or its subsidiary against such proceedings. If the Company and/or its subsidiary, its subcontractors, or its other partners are found liable (even in the case of proceedings that do not lead to conviction) or if it is impossible to obtain or maintain appropriate insurance policies at an acceptable price or to obtain other protection, this could significantly affect the development and, in the future, the

marketing of the Company's products and have a significant negative effect on the activities, financial position, results, reputation, and growth of the Company.

## 4.4 Regulatory risks

### 4.4.1 Risks related to the regulatory environment

#### *Obtaining prior marketing approvals is uncertain.*

At this time, none of the Company products, including its most advanced product, ERY-ASP/GRASPA<sup>®</sup>, has received marketing approval from any regulatory authority. The Company cannot be assured that it will receive the necessary approvals to market any of its products. The Company as well as its products are subject to extensive and very stringent laws and regulations and to controls from regulatory authorities such as the Agence Nationale de Sécurité du Médicament et des Produits de Santé (ANSM) in France, the Food and Drug Administration (FDA) in the United States and the European Medicines Agency (EMA) in Europe. The applicable regulatory requirements are known, but subject to change. Any failure to comply with such requirements can lead to sanctions including fines, rulings, civil penalties, refusal of marketing approval, delays, suspension or withdrawal of approvals, seizure or recall of products, restriction of use and criminal prosecution.

To obtain marketing approval for any of its products, the Company must show, through many long and costly clinical trials with uncertain outcomes, that use of its products is safe and effective in humans. The Company's inability to follow its development schedule or to conduct clinical trials for its products within expected time limits could have a material adverse effect on its activities, financial position, results of operations or growth.

The Company's ability to obtain marketing approval for its products will depend on many factors, including the following:

- the opportunity to continue the development of its products that, with the exception of ERY-ASP/GRASPA<sup>®</sup>, are currently in early clinical stages, or to move products currently under pre-clinical development into a clinical stage;
- the Company alone or with its potential partners being able to successfully conduct clinical trials within stated time limits and with the resources and under the conditions originally set out;
- the Company's trials showing the safety and efficacy of its products as well as a positive risk/benefit for the patient;
- the Company obtaining clinical results that are more promising than those of its competitors;
- the results of clinical trials, although positive, not meeting the applicable regulatory criteria;
- the Company's inability to submit to the competent regulatory authority in its respective jurisdiction the results of clinical trials conducted in another jurisdiction or for other candidate drugs;
- the Company being required to conduct additional clinical trials requested by regulatory authorities;
- the Company's competitors announcing clinical trial results that causes the amendment of evaluation criteria used by relevant regulatory authorities;
- the ability of the Company to obtain the clinical trial approvals in relevant jurisdictions within the timelines set out in the development plan; and
- the ability of the Company to respond (among other things, within the required timelines) to questions by the competent authorities during the marketing approval process.

In addition, the Company's products that have already been approved could prove unsafe and be withdrawn from the market, or produce effects over time other than those expected, which could limit or render impossible their marketing.

To obtain marketing approval for its products in a given jurisdiction, the Company must show that they meet the quality, safety and efficacy criteria defined by the relevant authorities for the intended indications.

If the Company is not granted marketing approval of a product in a given jurisdiction, it will not be able to sell the product in question for the intended indication in that jurisdiction. In addition, a refusal of marketing approval in one of the Company's key jurisdictions could have a negative influence on the authority in charge of granting marketing approvals in another key jurisdiction.

Accordingly, if the Company is not granted marketing approval for its products in a given jurisdiction, this will have a material adverse effect on its activities, financial position, results of operations or growth.

***It is possible that the Company may not obtain data exclusivity for GRASPA®***

The Company considers that GRASPA® contains a “new active substance” that has not been approved previously in the European Union. If that proves to be the case, the Company will benefit from data exclusivity for a period of eight years following the granting of the MA, plus an additional two-year market exclusivity period. Data exclusivity refers to the period during which another company cannot use the data that the Company submitted in support of its MA application. This exclusivity prevents certain types of pharmaceutical products, such as generic, hybrid or bio-similar drugs, from obtaining an MA from the European Medicines Agency (EMA) during the data exclusivity period. The additional market exclusivity period refers to the period during which generic, hybrid or bio-similar drugs cannot be sold even if they have been granted an MA. Should the EMA decide that the active substance in GRASPA® is not a new active substance, anyone applying for an MA for a generic or bio-similar product can file an MA application using the Company's data. This would consequently undermine the protection granted by GRASPA® data exclusivity, as well as market exclusivity. However, if the Company retains “orphan drug” status for GRASPA® at the time that it obtains the MA, the Company will still benefit from a market exclusivity for a period of 10 years.

***It is possible that the Company may not benefit from market exclusivity connected with the orphan drug status for GRASPA®, ERY-ASP, or its other drug candidates or in other indications.***

The Company has obtained the orphan drug status for GRASPA® in the treatment of ALL, AML, and pancreatic cancer from the EMA in Europe as well as for ERY-ASP for the same indications from the FDA in the United States. Additionally, the Company may apply for orphan drug status for some of its other products or for other indications.

In general, any drug designated as orphan that obtains an MA in Europe or the United States is eligible for market exclusivity in the orphan indication concerned, depending on the case, for 10 years in the European Union and 7 years in the United States. During that period, the regulatory authorities in Europe and the United States refrain from granting an MA for a similar drug. No other directly competitive drug may therefore be marketed during that period. Nonetheless, even after granting a drug orphan status, the regulatory authorities can withdraw that status if they decide that it does not meet the designation criteria. The exclusivity period in Europe may be reduced to 6 years in certain conditions or be withdrawn in certain cases, such as the manufacturer's inability to ensure sufficient quantities of the drug to meet patient needs. In this respect, when reviewing the MA application in Europe, the EMA will reassess in particular whether GRASPA® still meets the designation criteria that apply in the European Union. If the EMA decides that GRASPA® no longer meets those criteria, particularly because it does not offer a significant advantage over existing treatment, it may withdraw the orphan drug status before granting the MA.

The relevant regulatory authorities may also grant an MA to a product that is a direct competitor in the same indication if it decides that the new competitor is clinically superior in terms of safety or efficacy or makes a major contribution to patient care.

Furthermore, should the Company's competitors succeed in obtaining marketing exclusivity for their orphan drugs in the same indications as those targeted by the Company's drug candidates, this could prevent the Company from obtaining an MA for a significant period of time.

Should such events occur, they could have a material adverse effect on the Company's activities, operating results, financial position and growth prospects.

***Marketing conditions may become less favorable to the Company.***

While it is becoming increasingly difficult to obtain marketing approvals for the reasons mentioned above, government authorities are seeking to facilitate the entry of generic drugs into the market of products already being sold by the implementation of new regulations aimed at modifying patent law and the rules on the exclusivity of data in the main markets.

To the extent that these new regulations may lead to an increase in the costs of obtaining and maintaining product marketing approvals or may limit the economic value of a new product for its inventor, the growth prospects for the pharmaceutical industry and for the Company may diminish.

#### **4.4.2 Risks related to regulations for the collection of human samples**

***The collection of human samples is strictly regulated.***

ERYTECH and its partners comply with the regulations on the collection of human samples. Those regulations require, in some cases, patient consent, confidentiality of the patient's identity, approval of clinical tests by (hospital) ethics boards and/or other supervisory boards and, in some cases, grant of certain regulatory approvals.

If ERYTECH and its partners failed in its obligation to comply with such regulations or if the relevant regulations were to be amended unfavorably, research projects and activities and growth at ERYTECH as well as its related schedule could be penalized.

#### **4.4.3 Risks related to changes in health care reimbursement policies**

***The conditions for determining the price and reimbursement rate of Company products constitute a key factor in the commercial success of the Company.***

The commercial success of the Company will depend, in part, on the level of reimbursement of its products by public health agencies, private insurers and managed healthcare organizations or any other organization.

No guarantee exists relative to the terms of reimbursement which will be applied on the Company's products or to the sufficiency of such reimbursement.

If the Company's products are not granted a reasonable level of reimbursement, their market acceptance could be adversely affected.

Moreover, the legislative and regulatory measures implemented to control or reduce health costs or to reform healthcare programs could mean lower sale prices for Company tests and products. A low price for the relevant products will limit the Company's ability to generate sales revenues in line with expectations, as currently estimated by the Company.

#### **4.4.4 Risks related to the regulatory status of the Company**

***The upholding of the status required to manufacture and market Company products is uncertain.***

To date, the Company has the regulated status of "Etablissement Pharmaceutique de Fabrication" and of "Etablissement Pharmaceutique d'Exploitation." There is no guarantee that the Company or its partners will retain those designations to manufacture and market any of its products. The Company as well as its products are subject to extensive and very stringent laws and regulations and to controls from

regulatory authorities such as the ANSM, the FDA and the EMA. The applicable regulatory requirements are known, but subject to change. The Company must show that it meets the quality and safety criteria defined by relevant authorities.

Any failure to comply with such requirements can lead to sanctions including fines, rulings, civil penalties, refusal of marketing approval, delays, suspension or withdrawal of approvals, seizure or recall of products, restriction of use and criminal prosecution.

If the Company or its partners fail to maintain such status, it or they will not be able to manufacture and/or sell the relevant product in the jurisdiction concerned; this would have a material adverse effect on the Company's activities, financial position, results of operations or growth.

## 4.5 Financial risks

### 4.5.1 Risks related to historical and forecast losses

*The Group has a history of operating losses, losses that could persist.*

The Group has recorded accounting and tax losses since the beginning of its activities in 2004. As of December 31, 2015, the cumulative losses amounted, respectively, to €59 million under IFRS. These operating losses are principally due to investments in research expenditures and development costs for conducting preclinical studies and clinical trials. The Group anticipates substantial new operating losses for the coming years as its research and development activities, pre-clinical studies, and clinical trials are pursued. At the time of filing of this Reference Document, neither ERY-ASP/GRASPA® nor any other of its products have generated sales revenue.

The Group's profitability will depend on its ability to successfully develop, produce, and market its products. The Group's own financial resources will be generated, in the near future, from the first sales of ERY-ASP/GRASPA® and from payments made by partners within the context of established distribution or licensing agreements related to the development of new products and/or use of the research platform.

Additional funding through public subsidies or from private associations is also possible. The Group does not anticipate revenue from the sale of products other than ERY-ASP/GRASPA® in the medium term. In the event of the absence or delay of marketing approval for this product, the Company may not sell any product in the short, medium or long term.

*Refer to Section 20 of this Reference Document.*

### 4.5.2 Risks related to uncertain additional funding

*The Group may need to strengthen its equity base or use additional funding to ensure its growth.*

As the final phases of product development in the biotechnology and biopharmaceutical industry require increasing investments, the financial needs of the Group will continue to increase as the Group invests in the development of existing and new products. However, the Group believes that its self-financing capacities will be sufficient to cover its financing needs for the next 24 months. These financing needs, other than committed fixed costs, concern clinical trials that the Group has planned to conduct (please refer to Chapter 6 of this Reference Document) as well as expenses involved in research programs assisted by BPI France (please refer to Section 20.1 of this Reference Document). However, the Group may be required to raise additional funds sooner, by reason of various factors, such as:

- unexpected opportunities to develop new promising products or acquire technologies or other activities;
- higher costs and slower progress than anticipated by the Group for the development of new products and for obtaining the indispensable marketing approvals;
- costs incurred by the Group to file, maintain, and enforce patents and other intellectual property rights;



- costs incurred by the Group to respond to technological and market developments, to enter into and maintain partnership agreements, and to ensure the effective manufacturing and marketing of its products; and
- the inability of the Group to establish partnership agreements within the projected time frame.

At the date of this Reference Document, the Group conducted a specific review of its liquidity risk and believes that it is not exposed to a liquidity risk for the next 24 months given the cash and cash equivalents available as at December 31, 2015; these amount to €45.6 million.

It is possible that the Company may fail to obtain additional capital when it is needed, or that such capital may not be available on financial terms acceptable to the Company. If the necessary funds are not available, the Company may need to:

- delay, reduce or eliminate the number or extent of its preclinical and clinical trials program;
- grant licenses on its technologies to partners or third parties; or
- sign new cooperation agreements under conditions that are less favorable to the Company than those it could have obtained under different circumstances.

Moreover, if the Company raises capital by issuing new shares, its shareholders' stakes could be diluted. Debt financing, to the extent that it may be available, could also generate restrictive conditions on the Company and its shareholders.

If one or more of these risks materializes it could have a material adverse effect on the Company, its business, its financial position, its results of operations, its development and its prospects.

#### 4.5.3 Risk of major financial crisis

The Group could be linked to major events related to the economic environment and external to its activities or existence. A systemic financial risk with a non-negligible probability of major disruption can cause serious deterioration - if not paralysis - of the financial system as a whole for an entire economic sector, over a vast geographical area or even on a global scale.

A crisis of this magnitude would have a material adverse effect on its financial position, results of operations, and growth.

#### 4.5.4 Risk of dilution

As part of its incentive policy for its executive officers, directors and employees, the Group has issued or allocated warrants. The exercise of all dilutive instruments granted but not yet exercised based on share capital of €792,461.10 would lead to a 4.93% dilution (*see Chapter 21.1.4 of this Reference Document*). In the future, the Group could proceed with the issue or allocation of new financial instruments giving access to Group share capital.

Any additional allocation or issue of shares or other financial instruments giving access to capital would lead to potentially significant dilution for the Group's shareholders.

## 4.6 Social and fiscal risks

### 4.6.1 Risks related to research tax credit

The Group benefits from public funding to which all innovative companies have access, in particular the research tax credit (crédit d'impôt-recherche - "CIR"). The research expenditures that are eligible for the research tax credit include wages and salaries, consumer goods, services subcontracted to approved research organizations (public or private) and intellectual property costs.

Only the research projects (and related expenses) that meet the eligibility criteria for the research tax credit in accordance with article 244c B of the General Tax Code are entitled to the research tax credit scheme.

Due to its inherent nature, its corporate purpose, and its pipeline of pre-clinical and clinical projects, the Group is confident in its eligibility for the research tax credit program. Moreover, in 2013, the Group's authorization from the French Ministry of Research and Higher Education was renewed.

Last, the Group has been audited by the tax authorities with respect to the research tax credit for 2010, 2011, and 2012, the risk being thus extinguished for these years, as well as for previous years, due to the lapse of the limitation period.

The Group believes that any financial consequences of future tax audits could jeopardize and/or halt the growth of the Group.

#### 4.6.2 Risks related to tax fluctuations for drugs

The deficit of certain national drug cost-sharing and coverage programs has led to and could lead to governments in certain countries imposing taxes on drug company activities. The introduction of such taxes or their increase could have a negative impact on the activities and profitability of the Group.

#### 4.6.3 Risks associated with changes in tax or labor legislation

There are many tax risks related to changes in fiscal or labor legislation. If the risk of deliberate violation of a tax law (legal or illegality risk) is ruled out, the risks could be current or long term; they could originate externally or internally, and could be related to persons, operating processes, technology, or business tax management procedures.

Taxation also constitutes an aspect of market risk as an element of cost and pricing.

##### *US risk*

The French – US tax authorities and/or tax agreements could jeopardize the agreements between the Company and its subsidiary. The Group, however, is not specifically affected by this risk, in the absence of any special new tax aspects existing at the present time.

##### *Transaction risk*

Each transaction is subject to taxation. The more complex a transaction is, the more tax uncertainty and, consequently, tax risks, it could generate. The more uncommon or unusual the transaction is, the more it is exposed to specific risks.

The Group, however, is currently not specifically affected by this risk with regard to the present situation.

##### *Situation risk*

Fiscal risk depends on its impact and its probability of occurrence. The probability of occurrence depends on the action or reaction of the tax authorities in response to a situation. As such, this probability is high when a company finds itself in certain situations motivating a tax audit, such as a company generating VAT (Value-Added Tax) and CIT tax credits, namely, during initial claims for restitution.

The Group, however, is not specifically affected by this risk, in the absence of any special new tax aspects existing at the present time.

##### *Operational risk*

Generally, repetitive operations do not tolerate uncertainty since uncertainty that relies on common activities can have consequences in terms of high risks. Operational risks involve all departments and persons concerned with tax aspects, and not only its corporate tax department (supply, transportation, inventory records, personnel, treasury and finances, commercial, invoicing, delivery, shipping, investment, accounting, etc.).

The Group does not consider itself to be affected by this risk, as it monitors the proper training of and documentation by persons involved and good communication between the parties involved in operations having a direct fiscal impact.

*Risks related to retroactivity of the law*

A good fiscal compliance strategy involves staying informed and taking into account the administrative doctrine or, even better, obtaining authorization or approval for fiscal administration on the chosen approach for the resolution of a tax problem. The risk is even greater since fiscal as well as social legislation could be retroactive and incur additional costs for the Group (for example, tax aspects relating to the BSPCE).

The Group does not consider that its current tax situation is particularly subject to a risk of assessed back taxes.

*Accounting risks*

Accounting, as a consolidation, synthesis and tax base instrument, constitutes the main foundation for tax audits and, consequently, for tax litigation. Accounting also embodies the choices of the directors that have a fiscal consequence (allocation theory, tax credit, choice of accounting policies, etc...). Accounting therefore appears to be the tool for formalizing the options deemed to offer an opportunity for the company. Efficient processes for entry and allocation, analysis and cost accounting and accounting-tax alignment are to reduce fiscal accounting risks. The Group does not believe that its accounting structure bears any risk at the present time, aside from the work performed by the audit committee.

*Management risks*

Few companies document and formalize their management of fiscal risk. In this case, the main risk lies in the fact that fiscal risk management is the responsibility of the executive officers in charge of it. If these persons leave the company, there is the risk of a difficult succession and especially loss of the ability to seize opportunities during the search for successors. Recourse to external advisers as well as internal expertise offers a certain level of stability and continuity and, at least, assistance for an easier succession.

However, the Group believes that it is not specifically affected by this risk at the present time, primarily due to its use of external advisors.

*Risk to reputation*

A serious fiscal failure can affect the reputation of a company, its executive officers, its personnel and its auditors.

Given the aforementioned aspects of risk exposure, the Group does not believe that it is exposed to any particular risk to its reputation at the present time.

## **4.7 Market Risk**

### **4.7.1 Liquidity risk**

The Group has been structurally loss generating since its creation. The net cash flows associated with the Group's operating activities were respectively -€15 million at December 31, 2015, and -€7.2 million at December 31, 2014.

Historically, the Group has financed its growth by strengthening its shareholders' equity in the form of capital increases and the issue of convertible bonds. The capital increase associated with its introduction on the stock market in May 2013, as well as the operation renewed in 2014 and 2015, enables the Group to ensure its business continuity through to June 30, 2018.



The remaining contractual maturities of financial liabilities are broken down as follows (including interest payments):

in €k	2015			
	Book value	Contractual cash flow		
		Total	< 1 year	1 ≥ 5 years
Borrowing				
Conditional advances	563	(570)	(507)	(63)
Financial debt relating to leases	144	(149)	(59)	(91)
Convertible bonds				
Bank overdrafts				
Trade and related payables	3,672	(3,672)	(3,672)	
<b>Total</b>	<b>4,380</b>	<b>(4,392)</b>	<b>(4,238)</b>	<b>(153)</b>

in €k	2014			
	Book value	Contractual cash flow		
		Total	< 1 year	1 ≥ 5 years
Borrowing				
Conditional advances	549	(580)	(258)	(323)
Financial debt relating to leases	220	(230)	(81)	(149)
Convertible bonds		-		
Bank overdrafts		-		
Trade and related payables	2,085	(2,085)	(2,085)	
<b>Total</b>	<b>2,854</b>	<b>(2,895)</b>	<b>(2,423)</b>	<b>(472)</b>

The Company has conducted a specific review of its liquidity risk and considers that it is capable of meeting its upcoming payment deadlines. The net cash available at December 31, 2015, totals €45.6 million.

#### 4.7.2 Exchange rate risk

The Group uses the euro as its reference currency within the scope of its disclosures and financial communications. However, a significant portion, in the amount of 15% of its operating expenses, is denominated in US dollars (agency office in Boston, collaborations 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 around tests and clinical projects in the United States).

The Group is exposed to "operational" risk in its more regular activities in the United States.

To date, the Group has not opted to use active hedging techniques, and has not made recourse to derivative instruments to this end. Unfavorable exchange rate fluctuations between the euro and the dollar that are difficult to predict could affect the financial position of the Company.

This dependency will increase, as the Group will perform clinical trials in the USA and, in the longer term, sell on this market.

Expenses in US Dollars totaled \$3,149,196 during the 2015 financial year.

However, the EUR/USD rate fell considerably at the period end, reaching \$1.0887 per €1 at December 31, 2015.

The impact of “operational” risk is reflected in a currency translation gain of €72,715 for the 2015 financial year. At the end of the 2015 financial year, the Group held \$152 k (€141 k) in cash and cash equivalents.

The exchange rate differences are not significant for the periods presented.

#### 4.7.3 Interest rate risk

The Group has little exposure to interest rate risk. Such exposure would involve monetary fund investments in foreign currencies and term deposit accounts. The change in interest rates has a direct impact on the rate of return on investment and cash flows generated.

The Group has no borrowings or credit. The repayment of conditional advances from BPI France is not subject to interest rate risk.

### 4.8 Volatility risk

The price of the Company’s shares could be affected by significant volatility. Aside from occurrence of the risks described in this section, the market price of the Company’s shares could be significantly affected by a number of factors that would impact the Group, its competitors, or general economic conditions and the biotechnology sector.

The following factors could have a significant influence on the share price:

- negative changes in market conditions related to the Group’s sector of activity;
- announcements by the Group, its competitors, or other companies with similar activities and/or announcements regarding the biotechnology market, including those concerning financial and operational performance or the scientific results of these companies;
- changes in the forecasts or outlook for the Group or its competitors from one period to another;
- changes in patents or intellectual property rights of the Group or those of its competitors;
- changes in international political, economic, and monetary context and especially unfavorable changes in the regulatory environment applicable in the countries or the markets specific to the Group’s sector of activity or to the Group itself;
- announcements regarding changes in the Group’s ownership structure;
- announcements regarding changes in the Group’s management team; and
- announcements regarding the Group’s asset perimeter (acquisitions, disposals, etc.).

Furthermore, stock markets have seen significant fluctuations that have not always been due to the results and outlook of the companies whose shares are traded on them. Such market fluctuations as well as economic environment could therefore also significantly affect the market price of the Company’s shares.

### 4.9 Insurance and risk coverage

The Company has implemented a coverage policy of main insurable risks that it considers compatible with its cash flow requirements and activities.

The total premiums paid for all the Company’s insurance policies amounted to €79,775.33 for the financial year ended December 31, 2015, and €45,818 for the financial year ended December 31, 2014.

The Company has subscribed to several insurance policies, including the following:

<b>Policy</b>	<b>Insurer</b>	<b>Risks covered</b>	<b>Main characteristics</b>	<b>Expiration Date</b>
Key person	April	Death for Mr. Gil Beyen.	Limit of liability of €500,000 per person.	Renewable by tacit agreement on January 1 of every year.
Premises and liability	Chubb	Insured activities: - Development of a new generation of drugs for serious diseases, orphan indications or patient sub-populations in areas of hematology, cancer and metabolic diseases - Encapsulation of therapeutic molecules in red blood cells - Development of a therapeutic pipeline of innovative solutions based on its proprietary technology and its expertise in the physical properties of erythrocytes	All damages including physical injury: €7,500,000 per claim with sub-limits outlined in the contract  Criminal Defense - Recourse: €30,000 per dispute	Renewable by tacit agreement on January 1 of every year.
Property and Casualty Business	COVEA RISKS	Address of risk: 60 Avenue Rockefeller 69008 Lyon, France	Fire and related risks Water damage: Equipment - furniture - personal belongings: guaranteed up to €2,016,198  Natural disasters Electrical damage Recovery by neighbors and third parties Broken glass Theft Equipment breakdown Computer and office automation all risks  Other events cover Automatic insurance on investment Resulting costs and losses Business interruption/material damage, equipment breakdown and electrical damage Inaccessibility	Renewable by tacit agreement on January 1 of every year.

<b>Policy</b>	<b>Insurer</b>	<b>Risks covered</b>	<b>Main characteristics</b>	<b>Expiration Date</b>
Civil Liability for Executive Officers and Corporate Officers	Chubb	Civil liability for executive officers.	Extensions: Claim of misconduct Claim against legal entity Crisis management costs  Maximum aggregate amount per insurance period: €5,000,000 with sub-limits set out in contract  Territory covered: Global coverage	Renewable by tacit agreement on January 1 of every year.
Transported Goods	Chubb	Merchandise consists of: - ERY-ASP/GRASPA® - ENHOXY®  Guaranteed worldwide Excluding shipments to/from the following countries: Afghanistan, Birma, Irak, Iran, Cuba, North Korea, Sudan and any country at war	Ground and air transport  Additional guarantees: Packing and packaging Loading and unloading Undelivered packages Merchandise return and reshipment Controlled temperature Disposal  Exclusions: rust, oxidation, various scratches, disturbed content	Renewable by tacit agreement on January 1 of every year.
Automobile	COVEA FLEET	All employees on assignments for a total of 3,000 km maximum per year.	Automobile liability Criminal defense and claim All accidental damages, theft and attempted theft, fire Broken glass Luggage and personal belongings Physical injury - driver	Renewable by tacit agreement on January 1 of every year.
Business travel	Chubb	Travel by 5 employees on behalf of the subscriber.	Personal injury Assistance Business travel Personal safety	Renewable by tacit agreement on January 1 of every year.
Clinical trials	HDI Gerling	Covers liability of the Company as a sponsor of biomedical research. The amount of guarantees subscribed for the trials depends on the number of trials, their location and the number of patients involved in the trial.	Fixed amount per patient and per protocol based on each clinical trial program.	—
Clinical trials	CHUBB	Covers liability of the Company as a sponsor of biomedical research in the United States	Maximum aggregate amount per insurance period: \$10,000,000	—

Given that the Company has no sales revenues, it has not yet subscribed to insurance policies covering risks of operating losses.

The Company cannot guarantee that it will always be in a position to maintain, and in some cases, obtain similar insurance coverage at an acceptable price, which could lead it to accept more expensive insurance policies and to assume a higher level of risk particularly as the Company grows. Moreover, the occurrence of one or more important disasters, even if they are covered by these insurance policies, can seriously affect the activity of the Company and its financial position due to the interruption of its activities, which could result from such a disaster, reimbursement delays from the insurance companies in the event policy limits are exceeded and finally due to increased premiums that would result.

The occurrence of one or more of these risks could have a significant material adverse effect on the activity, outlook, financial position, results or growth of the Company.

Given the Company's outlook, namely current and future activities in the United States, as described in Section 6.4.14 of this Reference Document, the Company anticipates that its insurance premiums could increase while remaining insignificant compared to its research and development expenses, its annual losses and the value of its assets.

#### **4.10 Exceptional events and litigation**

In the course of its normal activities, the Group is not involved in any legal proceedings. To the Group's knowledge, there is no litigation or arbitration or pre-litigation having recently had or that will have in the future a significant influence on the financial position, results, activity and capital of the Group.

In January 2016, the Company settled the dispute with BPI France regarding the GR-SIL subsidy in the amount of €81 k as well as a residual repayable advance in the amount of €23 k, by repaying both of them. This dispute was the subject of a provision in the amount of €81 k for the financial year ended December 31, 2015 (see Note 7.9 in the Notes to the IFRS financial statements in Section 20.1 "Financial statements prepared in accordance with IFRS standards for the year ended December 31, 2015").

The tax audit begun in fiscal 2015 was completed in February 2016 without any major reassessment by the tax authorities. The Company therefore hopes to receive in the next few months the research tax credit owed for 2014 in the amount of €1,525,000 and has now already received other tax refunds.

## **5 INFORMATION ABOUT THE COMPANY**

### **5.1 History and evolution of the Company**

#### **5.1.1 Company name, trade name, and headquarters of the Company**

The corporate name of the Company is ERYTECH Pharma S.A.

The company's headquarters are located at Bâtiment Adénine, 60 Avenue Rockefeller, 69008 Lyon, France

The Company's telephone number is +33 (0)4.78.74.44.38

The Company's website can be found at the following address: [www.ERYTECH.com](http://www.ERYTECH.com)

#### **5.1.2 Location and registration number of the Company**

The Company is registered with the Lyon Trade and Companies Register under number 479 560 013.

The Company's professional activity code (APE) is 7211Z and its computerized identification code (SIRET) is 479 560 013 000 19.

#### **5.1.3 Date of establishment, duration, and transformation of the Company**

ERYTECH was incorporated in the form of a French simplified limited company, pursuant to a private deed stipulated in Lyon dated October 26, 2004. ERYTECH was transformed into a French limited liability company with an Executive Board and a Board of Supervisors following a decision by the Company's Extraordinary General Meeting of September 29, 2005. At the General Meeting of April 2, 2013, the Company amended its mode of governance, subject to the Company's initial public offering, so as to implement a Board of Directors instead of the Executive Board and the Board of Supervisors.

The term of the Company was set at 99 years from the date of its registration with the Trade and Companies Register, except in case of early dissolution or extension.

#### **5.1.4 Legal form of the Company and applicable laws**

The Company is a French limited liability company subject to the provisions of the French Commercial Code.

#### **5.1.5 Financial year**

The fiscal year, having a term of 12 months, begins on January 1 and ends on December 31 of each year.

#### **5.1.6 History**

ERYTECH's two co-founders, Dr. Yann Godfrin (Biomedical Engineer from the University of Compiègne, Doctorate in Life and Health Sciences from the University of Nantes, Master's degree in Strategy and Methods for Clinical Development – University of Lyon) and Mr. Pierre-Olivier Goineau (Master's and DEA [Advanced Studies Degree] in Management Sciences, Master's in Management for Pharmaceutical Industries – IAE Lyon), met in 2003, through the Lyon biotechnology entrepreneurs' network, BioTuesday.

At that time, Dr. Yann Godfrin was Chairman and R&D Director of Hemoxymed Europe, a subsidiary of Hemoxymed Inc based in the United States, a company developing technologies involving red blood cells. He had previously worked as a consultant with BioAlliance (FR0010095596 – BIO) and as a Development Engineer at Hémosystem (systems for detecting contamination in blood products).

Mr. Pierre-Olivier Goineau was, at the same time, a senior consultant for strategy at KPMG Enterprises, the national standard-setter in the “health and life sciences” sector. Previously, he had been the majority partner in his own finance and development consulting company targeting international projects.

Both wished to create a company specialized in the development of therapeutic products for orphan indications.

Convinced of their complementary nature, they decided to combine their skills and abilities in biology, technology, preclinical and clinical development for Dr. Yann Godfrin, and management, strategic positioning and marketing, public and private finance for Mr. Pierre-Olivier Goineau.

## 2004

ERYTECH began activity in March as part of the Créalys incubator, one of the best-known in the domain of life sciences in France, with the financial support of Conseil Régional Rhône-Alpes. An initial R&D collaboration was entered into with Centre Léon Bérard in Lyon, a reputable cancer-fighting research center in Europe. The “ERYTECH Pharma” project was awarded a prize by the French Ministry of Research in the category of Creation and received a €40,000 grant. In August, the Company filed its first patent involving encapsulation technology.

ERYTECH was established in October and started operations in the BioParc Lyon-Laennec business incubator. The co-founders made initial rounds with Business Angels. The Company also has surrounded itself with external scientific experts.

ERYTECH obtained the status of Young Innovative Company.

## 2005

ERYTECH won a prize from the French Ministry of Research in the “Development” category and received a €450,000 subsidy. Additionally, it obtained significant initial financial support from the Agence Nationale de la Recherche [National Agency for Research] and from the Cancéropole Lyon Rhône-Alpes Auvergne[Cancer Center of Rhône-Alpes Auvergne].

In October, the AFSSAPS (which later became the ANSM - the French National Agency of Medicine and Health Product Safety) authorized the conducting of ERYTECH’s first clinical trial: a Phase I/II trial involving the treatment of Acute Lymphoblastic Leukemia with GRASPA®.

Emboldened by this initial success, the Company raised €750,000 from its shareholders, Cap Décisif, Amorce Rhône Alpes, and two new business angels from the health sector.

Two new patents associated with new candidate-products were filed.

## 2006

ERYTECH began opening clinical investigation centers to conduct its first trial involving leukemia: more than 20 centers would be opened throughout France bringing together most of the French opinion leaders treating children and adult patients suffering from acute lymphoblastic leukemia.

The European Medicines Agency (EMA) classified ERYTECH’s medicinal product GRASPA® as its first Orphan Drug Designation (ODD) in the treatment of acute lymphoblastic leukemia and gave it “SME” status.

ERYTECH received a significant subsidy of €450,000 from BPI France to finance the development of GRASPA®.

The Company accelerated its development by raising €12 million in funds from its historic shareholders, AGF Private Equity (which became IDInvest Partners), Auriga Partners, and Axa Private Equity.



**2007**

2007 was a year of structuring, organization, and team building to prepare for future challenges:

The Company acquired space in a new building in the Bioparc Laennec site in Lyon and started work on its production unit in order to master its technology on an industrial scale and its production costs.

The team was enriched with a Medical Director, a Regulatory Director, a Quality Assurance Director, and increased its number of researchers; at the end of the year it would have 14 people.

The Belgian health authorities gave approval to treat patients in Belgium as part of the Phase I/II trial already authorized in France.

At the same time, the work by the R&D department was allowing new candidate products to be identified.

**2008**Europe:

At the start of the year, ERYTECH included its last patient in the Phase I/II clinical trial started in 2006.

The Lyon production unit was completed at the end of the year and reached the most demanding regulatory criteria. This unit is capable of production for both clinical trials and commercial uses.

The Company received new support from the Agence Nationale de la Recherche and the Cancéropôle Lyon Rhône Alpes (CLARA). BPI France also confirmed its commitment to the Company through a repayable aid of €735,000 to finance clinical Phase I for GRASPA® in pancreatic cancer.

United States:

Very promising results from the study were presented orally at the American Society of Hematology's (ASH) Annual Meeting in San Francisco. ERYTECH presented its scientific results in New York and Las Vegas.

**2009**Europe:

ERYTECH's production unit, after an audit and inspection by AFSSAPS (which became ANSM), obtained the classification as a "Pharmaceutical Facility" validating its level of health safety in accordance with the EMA rules.

Shortly afterward, ISO 9001:2008 certification was delivered by SGS to ERYTECH, validating the quality control organization implemented in all departments in accordance with the policy of excellence sought by the executive officers.

The results from the Phase I/II clinical trial allowed ERYTECH to pursue its clinical development and obtain the authorizations to start two new clinical phases from the AFSSAPS (now the ANSM) for the treatment of acute lymphoblastic leukemia (ALL):

A Phase II clinical trial for first-line treatment of adult patients over 55 years of age;

A Phase II/III clinical trial for treatment of child and adult patients under 55 years of age who have relapsed.

ERYTECH also obtained authorization from the AFSSAPS to initiate a Phase I clinical trial to test GRASPA® among patients suffering from pancreatic cancer. The European Medicines Agency granted a second Orphan Drug Designation to GRASPA® for pancreatic cancer.

The Ministry of Research granted new financial assistance to the Company in the form of a grant awarded by the ANR.

ERYTECH filed its 10th patent.

United States:

ERYTECH found space within the Philadelphia Science Center, one of the largest health clusters in the United States. Shortly thereafter, the Company signed two agreements with the American Red Cross which is the largest blood bank in the world:

An agreement to provide Red Blood Cells coming from American donors;

A subcontracting agreement providing that premises of cGMP based in Philadelphia would be provided, in accordance with FDA regulations and personnel dedicated to produce GRASPA® in the United States.

This major step prepared the way for conducting clinical trials in the United States and considerably strengthened the visibility of ERYTECH's actions among American companies.

**2010**Europe:

ERYTECH continued its three clinical trials in parallel. The Company finished at the end of the year and ahead of schedule, the recruitment of the last patient for its Phase II trial with treatment by GRASPA® of patients older than 55 years of age suffering from acute lymphoblastic leukemia.

The Company employed 36 people at the end of 2010.

United States:

The FDA granted Orphan Drug Designation status to GRASPA® for the treatment of acute lymphoblastic leukemia, offering advantages comparable to the European designation on American soil.

The Company signed an R&D partnership agreement with the MD Anderson Cancer Center in Houston to develop a companion test that would make it possible to detect patients suffering from cancer who could be treated with GRASPA®.

**2011**Europe:

ERYTECH recruited its last Phase I patient for pancreatic cancer.

The Company formed a joint venture with the Teva Group (a NASDAQ-listed company as TLV:TEVA) to market GRASPA® in Israel ([See also chapters 6 and 22 of the Reference Document](#)).

ERYTECH signed a long-term contract to provide asparaginase with the German pharmaceutical laboratory medac GmbH.

ERYTECH was selected by several international Conferences on Hematology to orally present promising preclinical results from a new proposed product for the treatment of sickle cell anemia.

United States:

ERYTECH filed an IND application with the FDA to start a Phase I clinical trial with GRASPA® to provide therapy as first-line treatment of adult patients, over 40 years of age, suffering from Acute Lymphoblastic Leukemia, in which the principal investigator was Professor Richard Larson (Chicago), Chairman of the Adult Leukemia group within the CALGB (the largest cooperative group treating leukemia and cancer in the United States).

**2012**

Gil Beyen became a consultant to the Company then Chairman of the Supervisory Board in August. Gil Beyen was the co-founder and CEO of TiGenix N.V. (NYSE Euronext Brussels: TIG), a European cellular therapy company with an approved product and advanced clinical trials.

Europe:

The Company has received assistance totaling €7 million, including €4.9 million in repayable advances and €2.1 million in grants (refer to Section 22.1 for the terms of this contract), which shall be paid progressively between 2012 and 2019 in keeping with development within the context of the TEDAC project, a research and development project focused on developing therapies for radiation/chemotherapy-resistant cancers, in association with other companies and entities (Diaxonhit, Inserm, University of Paris-Diderot, and the AP-HP [Public Assistance-Paris Hospitals]).

Over time, the goal is to offer a solution including a test predicting response to treatment, one or more suitable enzyme therapies, as well as a test to monitor therapeutic efficacy.

ERYTECH's production unit obtained the designation of "Operating Facility."

The Company received a favorable opinion from the Committee for Orphan Medicinal Products of the EMA (European Medicines Agency) concerning the orphan drug designation of its experimental product ENHOXY® for the treatment of sickle cell anemia.

The Company signed a partnership agreement with Orphan Europe (Recordati group) for the development and marketing of GRASPA® in 38 European countries for the treatment of children and adults suffering from acute lymphoblastic leukemia and acute myeloid leukemia (AML) ([See also chapters 6 and 22 of the Reference Document](#)).

United States:

Dialog with the FDA continued for the purpose of starting a clinical trial involving acute lymphoblastic leukemia with ERY-ASP.

**2013**

On April 30, 2013, the Company was listed on the regulated market NYSE Euronext Paris, compartment C, raising €17.7 million (excluding issue costs).

On May 6, 2013, the Company changed its method of governance, with a view to establishing a Board of Directors in place of the Executive Board and Supervisory Board, and appointed Gil Beyen as Chief Executive Officer, formerly Chairman of the Supervisory Board.

Europe:

The committee of independent experts (the Data Safety Monitoring Board or DSMB) in charge of monitoring the Phase II/III clinical trial of ERY-ASP/GRASPA® in adults and children experiencing a relapse of ALL met and delivered a favorable opinion concerning the conduct of this Phase III clinical trial following the original protocol with a total pool of 80 patients.

The European Union granted ERY-ASP/GRASPA® orphan drug designation for AML.

The Company received the authorization from ANSM (French Medicine Agency) to start a Phase IIb clinical trial in AML. The first patient was enrolled in March.

The DSMB in charge of monitoring the Phase IIb clinical study of ERY-ASP/GRASPA® in AML delivered a favorable opinion concerning the conduct of this clinical trial following an evaluation of the product's tolerance in 30 initial patients.

United States:

The FDA granted ERYTECH the right to start a Phase Ib clinical study with ERY-ASP in ALL.

The USPTO (United States Patent and Trademark Office) delivered the patent protecting ERYTECH's technology, granting it exclusivity until 2029 with the potential for extension into 2034.

Internationally, the company filed two new patent applications.

**2014**Europe:

The Company announced the launch of a Phase II study in pancreatic cancer with its ERY-ASP product.

ERYTECH received approval from several European countries for its AML study, thus enabling it to broaden the recruitment of patients, and the DSMB issued a second positive opinion following an analysis of tolerance in 60 patients.

The Company announced the addition of a new candidate drug to its oncology portfolio: “Affameur de tumeurs” [Tumor starvation inducer] ERY-MET.

The Company announced positive results for its Phase III clinical trial with ERY-ASP/GRASPA® in the treatment of ALL.

USA:

The main centers of patient recruitment for the Phase I/II study are open (Chicago, Duke, Columbus) and the first patients have been treated.

The Company has obtained the issue of a new patent in the United States, in the area of asparaginase.

On the financial level, the Company:

- welcomed new shareholders following a reclassification with European institutional and American investors specialized in the field of healthcare;
- successfully raised thirty million euros to extend its therapeutic indications in oncology and accelerate its clinical developments.

**2015**

On January 9, 2015, the Company established a Level 1 American Depositary Receipt (“ADR”) program on the American over-the-counter (“OTC”) market, for which the Bank of New York Mellon is the custodian. Each American Depositary Share represents one ERYTECH Pharma share as traded on Euronext Paris.

The Company announced a change in its management team with the resignation of Pierre-Olivier Goineau, co-founder and Deputy Chief Executive Officer, on January 11, 2015.

On March 24, 2015, the Company presented three of its abstracts at the annual conference of the American Association for Cancer Research (AACR) held in Philadelphia (USA), from April 18 to 22, 2015; this included the oral presentation of the complete results of Phase III of GRASPA® in ALL and an update on Phase IIb in AML.

The Company has strengthened its patent portfolio in the United States:

- with a newly issued patent protecting the use of ERY-ASP for the treatment of pancreatic cancer (currently in Phase II clinical trial); and
- extension of the protection duration by one and a half years on its active ingredient patent entitled “Lysis/Resealing Process for Preparing Erythrocytes.”

On March 26, 2015, the Company announced the appointment to its Board of Directors of Luc Dochez as an independent director.

On May 5, 2015, the Company announced a positive opinion from the DSMB regarding its Expanded Access Program in Acute Lymphoblastic Leukemia.

On June 1, 2015, the Company presented the complete results of Phase III of GRASPA® in ALL and an update on Phase IIb in AML at the ASCO conference.

On June 22, 2015, the Company announced two positive opinions for the tolerance of the product ERY-ASP for the first cohort of patients with acute lymphoblastic leukemia (ALL) treated in the Phase I study

in the United States and for the first three patients treated in combination with Folfox in the Phase II pancreatic cancer study.

On July 15, the Company announced that it was strengthening its management team with the appointment of Dr. Iman El Hariry as Chief Medical Officer.

On July 20, 2015, the Company received a positive opinion from the DSMB regarding tolerance for the product ERY-ASP in the Phase II pancreatic cancer study, after treatment of the first 24 patients.

On September 1, 2015, Mr. Eric Soyer was appointed Chief Financial and Operating Officer.

On September 14, 2015, the Company submitted a centralized application for a marketing authorization (MA) to the European Medicines Agency (EMA) for GRASPA<sup>®</sup> for the treatment of patients with Acute Lymphoblastic Leukemia (ALL).

On September 28, 2015, the Company announced that it had expanded its portfolio of patients in the United States with a new issued patent, and the extension of the period of protection of its original patent entitled “Medication for the Treatment of Cancer of the Pancreas” issued in the United States.

On December 3, 2015, the Company announced the successful completion of a private placement of common shares of approximately €25.4 million (excluding issue costs) from European and US investors.

On December 8, 2015, the Company announced the presentation of additional data from the pivotal Phase 2/3 study with GRASPA<sup>®</sup>, in addition to the data that already supported the potential benefit of GRASPA<sup>®</sup> in combination with chemotherapy in the treatment of Acute Lymphoblastic Leukemia (ALL).

## **2016**

Mr. Godfrin, co-founder of ERYTECH Pharma S.A. and Deputy Chief Executive Officer, submitted his resignation to the Group at the meeting of the Parent Company’s Board of Directors on January 10, 2016.

On March 15, 2016, the Company announced it had received from the United States Patent and Trademark Office (USPTO) a notice of acceptance of its patent application number 12/672.094 entitled “Composition and Therapeutic Anti-tumour Vaccine.”

## 5.2 Investments

### 5.2.1 Principal investments made since 2014

Because all clinical research and development costs are booked as charges until obtaining marketing approval, the principal investments in the last two fiscal years essentially pertain to the current production site, the Pharmaceutical Facility, and the R&D laboratory, and to a lesser degree, office and computer equipment. In 2015, the Company also incurred capital expenditure on office refurbishment after taking over an additional story to set up the “Quality Control” laboratory.

<b>as of Dec. 31 in € thousands</b>	<b>2015</b>	<b>2014</b>
Asset acquisitions		
- Intangible assets	(49)	(26)
- Tangible assets (property, plant & equipment)	(220)	(396)
- Financial assets	(15)	(0)
Asset disposals		
- Intangible assets	-	-
- Tangible assets (property, plant & equipment)	-	-
- Financial assets	-	1
Subsidies collected	-	-
Impact of changes in scope	-	-
<b>Net cash flow from investing activities</b>	<b>(284)</b>	<b>(420)</b>

### 5.2.2 Principal investments currently being made

No significant investments have been made since January 1, 2016. The investments correspond mainly to the transfer of assets in progress (office refurbishment not finished at December 31, 2015) to property, plant and equipment.

### 5.2.3 Principal investments planned

As of the date of this Reference Document, the Company is not currently planning to make any significant investments in forthcoming years for which the Company’s oversight bodies have made firm commitments.

## 6 OVERVIEW OF BUSINESS ACTIVITIES

### 6.1 General overview

ERYTECH was founded in 2004 to develop and market innovative therapies for acute leukemia and other cancers for which medical needs remain unmet. The innovative approach by ERYTECH consists of acting on the tumor's environment and "starving" it, so that the cancerous cells no longer have access to the growth factors that are necessary for them to live and proliferate.

ERYTECH lead product ERY-ASP, named GRASPA®<sup>2</sup> in Europe and Israel, is positioned in the treatment of acute leukemia, a cancer of the blood and bone marrow, the proliferation of which is rapid and requires urgent treatment. The two most frequent forms are Acute Lymphoblastic Leukemia (ALL) and Acute Myeloid Leukemia (AML), depending on the cells at the origin of the disease. Each year, approximately 50,000 patients are diagnosed with acute leukemia in Europe and the United States.

ERY-ASP/GRASPA® has convincing clinical results obtained in several clinical trials. Based on these clinical trials, the Company submitted to the EMA, in September 2015, a marketing authorization application (MAA) for ALL in Europe. If this marketing authorization is issued, the Company hopes to be able to begin marketing the product in 2017.

ERY-ASP, developed on the basis of ERYTECH's proprietary technology, consists of an enzyme, the L-asparaginase encapsulated in red blood cells. L-asparaginase is an essential weapon in the treatment of acute leukemia. The enzyme has the property of being able to stop the supply of asparagine to leukemic cells, a naturally occurring substance in the blood that is essential for their growth. The existing treatments, based on free form L-asparaginase, causing the death of cancer cells, have demonstrated their effectiveness in children with ALL; approximately 90% of those having received treatment enter remission and have a high probability of recovery. However, their use is considerably limited by their serious side effects (for example, allergic and immune reactions, coagulation problems, pancreatitis). Clinicians cannot administer them to most adult and older patients, who often cannot tolerate free form asparaginase.

Worldwide sales of the three forms of existing treatments based on L-asparaginase are estimated at approximately \$300 million.<sup>3</sup> Other leukemia patients, i.e., adults and older adults with ALL as well as children allergic to free form asparaginase, and nearly all patients with AML (more than 80% of patients with acute leukemia) have little or no access to these drugs because they are often too weak to tolerate them.

Through the encapsulation of asparaginase in red blood cells using ERYTECH's proprietary technology, ERY-ASP is uniquely positioned to provide a solution to the significant unmet medical needs of these fragile patients. The red cell membrane prevents interactions between the body and L-asparaginase, thereby protecting the body from the side effects of L-asparaginase and simultaneously preventing the immune system from eliminating L-asparaginase, and thus from reducing its efficacy. Encapsulated L-asparaginase fully achieves its goal of destroying asparagine circulating in the blood because it is absorbed inside the red blood cell through a natural phenomenon. The red blood cell acts as a bioreactor circulating in the blood and destroys asparagine which could feed leukemic cells.

ERY-ASP has the potential to become a reference drug in the treatment of acute leukemias: ERY-ASP allows fragile patients who currently do not have the possibility, due to their state of general health and induced side effects, to be treated with free-form L-asparaginase, and who have as a result smaller chances of survival. For patients who are unable to receive the current treatments based on L-asparaginase, ERY-ASP aims to provide an effective alternative with a considerably improved tolerance profile.

<sup>2</sup> GRASPA® is the brand name approved in Europe for ERY-ASP. It has been licensed to Orphan Europe (Recordati Group) for marketing of the product in ALL and AML in Europe and to TEVA for marketing the product in ALL in Israel.

<sup>3</sup> Source: Jazz Pharmaceuticals et ERYTECH



ERYTECH has completed its clinical studies in Europe for GRASPA® for ALL and has compelling results in terms of efficacy and tolerance in: (a) the results of a Phase I/II study in children and adults with a relapse of ALL, (b) the results of a Phase II study performed on patients over 55 years of age with ALL, and (c) the positive results of a Phase II/III study (in adults and children in relapse). These studies support the application for Marketing Approval (MA) at the European level, which was filed by the Company with the EMA in September 2015. If this MA is issued, the Company hopes to be able to begin marketing the product in 2017.

In November 2012, ERYTECH signed a marketing and exclusive licensing agreement with Orphan Europe, a subsidiary of Recordati Group specialized in orphan drugs, a leading European pharmaceutical group, to distribute ERY-ASP under the brand name GRASPA®, in 38 European countries. With the establishment of this partnership, GRASPA® may be commercialized efficiently as soon as the necessary approvals are obtained in all European countries; pursuant to this agreement ERYTECH will receive a substantial part of the profits. ERYTECH has also signed a marketing and exclusive licensing agreement with Abic Marketing Limited, a subsidiary of Teva Group (hereinafter “Teva”), to distribute GRASPA® in Israel.

The Company has a production unit based in Lyon qualified as an “Etablissement Pharmaceutique” and “Etablissement Exploitant”, which makes it possible to serve the European and Israeli markets.

ERYTECH is developing possible new indications for ERY-ASP outside the field of leukemia. Initial pre-clinical and clinical results suggest that ERY-ASP could also be effective against certain solid tumors for which therapeutic options are currently limited. ERYTECH launched a Phase II study of pancreatic cancer in 2014, the primary results of which should be presented in the second half of 2016. In addition to the existing candidate-products which are intended to starve tumors through the use of red blood cell-encapsulated enzymes, ERYTECH is exploring other uses of its ERYCAPS technological platform in order to develop vaccines against cancer and enzyme replacement therapies.

Further, the Company has a pipeline of potential products targeting orphan diseases that constitute medium and long-term sources of growth for the company and/or partnership options. In the longer term, the ERYTECH technology can be used to encapsulate various molecules or active ingredients inside red blood cells and could help develop new drugs, particularly in cancer treatment, with much better efficacy and toxicity profiles, consequently improving patient survival and quality of life.

## 6.2 Strategy of the Group

The Company’s objective is to become the leading biopharmaceutical company in the development, production and marketing of innovative therapies based on its red blood cell-encapsulation platform, ERYCAPS, in order to treat rare forms of cancer and other orphan diseases. The key elements of our strategy to achieve this objective are as follows:

- **Completing the development and obtaining the marketing approvals in Europe for GRASPA® in the treatment of ALL**

In September 2015, the Company submitted an application for a MA to the EMA for GRASPA® as a treatment, in combination with chemotherapy, for adult and pediatric ALL patients in relapse, and for the treatment of adult and pediatric ALL patients with hypersensitivity to asparagine.

The Company is aiming at obtaining marketing approval in Europe by late 2016 / early 2017 and launching marketing in 2017. Orphan Europe (Recordati Group) will be responsible for the marketing launch of GRASPA® in Europe. The Company will also seek to expand the potential indications of GRASPA® for the treatment of ALL in Europe by transforming its current Expanded Access Program (EAP) into a global pivotal trial for double-allergic patients and by conducting a global, randomized pivotal trial of GRASPA® as a first-line ALL treatment.

- **Progressing rapidly in the clinical development of ERY-ASP for other indications**

The Company is planning to finalize its ongoing Phase II clinical trials of ERY-ASP for the treatment of pancreatic cancer and AML in 2016 and 2017, respectively, and to launch and finalize other clinical studies for other types of cancer. In addition, the Company is also preparing to launch Phase II/III clinical trials of ERY-ASP for the treatment of certain forms of non-Hodgkin lymphoma (NHL), such as Natural Killer T-cell lymphoma (NKTCL).

- **Obtaining approvals to market and sell ERY-ASP in the United States**

The objective of the Company is to rapidly obtain MA for ERY-ASP in the United States first for the treatment of double-allergic ALL patients and, subsequently, for a larger population of ALL patients, based on the results of its current global pivotal clinical trials. The Company has begun clinical trials of ERY-ASP in the United States for the treatment of adults with ALL, and has also planned to seek regulatory approval to market ERY-ASP in the United States for other indications, including AML and solid tumors. The Company has retained all rights to commercialize its candidate products in the United States. Although it believes it is in a position to market its candidates itself, if approved in the United States, thanks to a targeted sales force, the Company may consider collaborations with third parties for the distribution and marketing of the approved products.

- **Leveraging the ERYCAPS platform to develop new, innovative drugs targeting rare forms of cancer and other orphan diseases**

In addition to L-asparaginase, the active ingredient in ERY-ASP, the Company intends to leverage the broad scope of application of its ERYCAPS platform in order to develop new candidate drugs that use other therapeutic drug substances. On the basis of its preclinical research, the Company has identified two other enzymes, methionine- $\gamma$ -lyase (MGL) and arginine deiminase (ADI), which can be encapsulated in red blood cells in order to induce tumor starvation. The Company plans to launch a Phase I clinical trial in Europe to evaluate the safety of administering encapsulated MGL to cancer patients. The Company is also planning to expand its product pipeline and include other therapeutic approaches, such as cancer vaccination and enzyme replacement therapies. In order to support this strategy, the Company intends to continue to seek robust worldwide intellectual property protection for its platform technology and the resulting drug candidates.

- **Exploring opportunities for collaboration and licensing agreements**

The Company will seek to maximize the value of its proprietary technology platform through the combination of in-house development and carefully selected partnership opportunities. In certain cases, the Company may decide to continue the development and market activities by strengthening its in-house capacities and, in the cases where it will be more appropriate, it will evaluate and pursue collaboration agreements with third parties for the development and marketing of its drug candidates for specific indications and territories. The Company believes that it will benefit in this regard from the experience acquired during the negotiations of the exclusive distribution contracts with Orphan Europe (Recordati Group) and TEVA for ALL and AML respectively in Europe and Israel. The Company may also explore other opportunities for co-development or licensing its platform technology to third parties or via the creation of spin-off companies.

### 6.3 Advantages and strengths of the Group

ERYTECH has all necessary strengths to establish itself as a mature biotechnology company with revenues from partnership agreements for the distribution of a drug to the doorstep of the market and a pipeline of promising products and indications:

- **ERYCAPS, a proprietary platform that offers a unique positioning to respond to an unmet medical need**

In order to respond to the unmet medical need of fragile patients suffering from acute leukemia, the Company has developed an innovative technology platform known as ERYCAPS designed to use red blood cells in order to boost the efficacy of the administration of active ingredients with a lower risk of side effects, by trapping these active ingredients within red blood using the principles of reversible hypotonic and hypertonic osmotic stress. This platform technology uses red blood cells from different donors with specific blood groups which are compatible with the blood group of the patients that will be receiving the treatment. The Company is supplied by blood banks with transfusion-grade, standard packed red blood cells. The red blood cells are submitted to osmotic stress in order to open and close the pores at the surface of the cells and thus allow the therapeutic compounds to be added and trapped within the cell. This encapsulation process (as described in Section 6.4.1) offers many advantages over therapeutic compounds in free form. By protecting the therapeutic compound against detection by the organism's immune system, the encapsulation is designed to reduce potential allergic reactions and allow the therapeutic compound to remain in the body longer. The cellular membrane also protects the body against the direct toxicity of the active ingredient, which should have the effect of reducing the incidence of side effects. In the case of L-asparaginase, it has been demonstrated that encapsulation extends the half-life of L-asparaginase in free form by a period ranging from one to approximately thirty days, which should reduce the number of injections necessary during treatment as well as the overall dose. The Company believes that these properties make ERY-ASP a promising treatment for patients who cannot tolerate the administration of current treatments based on free form L-asparaginase.

The Company believes that its ERYCAPS platform technology is an innovative approach offering a number of key advantages:

A longer period of activity.

A reduced risk of side effects.

High reproducibility with a rapid turnaround on commercial scale.

Stability and ease of administration.

Broad scope of application.

- **An initial target market with high potential: Acute leukemia**

ERYTECH is positioned as a treatment for acute leukemia, which are most common forms of leukemia, and account for about 50,000 new cases diagnosed per year in Europe and the United States.<sup>4</sup> Medical needs are considerable given this cancer's very poor prognosis for most patients. Children with ALL, who account for approximately 12% of new cases of acute leukemia, have a 5-year survival rate of over 90% due to L-asparaginase-based treatment.<sup>5</sup> All other patients, adults and older adults, and relapsed patients typically cannot tolerate this treatment, despite efforts over decades to adapt it. Adult and older adult patients with ALL have a 5-year survival rate of 15% to 30%,<sup>6</sup> one of the lowest rates of all cancers. Existing asparaginase-based treatments generate sales estimated at approximately \$300 million,<sup>7</sup> largely in children. However, the existing forms of treatment based on L-asparaginase actually target only a limited number of patients with acute leukemia, and the Company believes that a large number of other patients could benefit from a perfected L-asparaginase-based treatment.

- **Convincing clinical results ERY-ASP (GRASPA®): Efficacy and tolerance**

ERYTECH has completed three clinical studies in Europe, in which 100 patients with ALL were treated with GRASPA®. ERYTECH filed application for regulatory market approval with the European Medicines Agency (EMA) to market GRASPA® on the market for ALL in September 2015, based on

<sup>4</sup> Source: American Cancer Society, RARE Cancer Europe, 2014

<sup>5</sup> Source: American Cancer Society, RARE Cancer Europe, 2014

<sup>6</sup> Source: American Cancer Society, RARE Cancer Europe, 2014

<sup>7</sup> Source: Sales and estimates. Jazz Pharmaceuticals 2014 / Baxalta 2015

those three studies (including one Phase I/II and one Phase II/III study) in adult and pediatric patients with ALL in relapse and one Phase II study carried out in patients aged over 55. The first study, in children and adults with ALL in relapse, demonstrated good tolerance of the product and identified the appropriate dose. It also demonstrated that an injection of GRASPA® can result in the same depletion of asparagine as up to 8 injections of the free form L-asparaginase. It was followed by a Phase II/III study in the same type of patients. The analysis of the data from the clinical trial, named GRASPIVOTALL or GRASPALL2009-06, after one year of follow-up shows that the trial is convincingly achieving its primary objectives and its secondary objectives confirm a favorable clinical efficacy of GRASPA®. The study also shows favorable results in patients with histories of allergies to L-asparaginase. The third study is a Phase II study in ALL patients aged over 55 years as the first line of treatment. The study showed that, in this category of fragile patients who often cannot be treated with L-asparaginase in induction, GRASPA® was well-tolerated and resulted in complete remission for 70% of patients completing their induction.

In 2013, ERYTECH began a Phase IIb clinical trial in AML, the results of which, if positive, will allow the indication of GRASPA® to be extended to these patients once the drug is on the market, an Expanded Access Program (EAP) for ALL in France, and a Phase I study, again on ALL, in the United States.

- **Strong marketing partnerships: Orphan Europe (Recordati Group) and the Teva Group**

ERYTECH has entered into two major partnerships for the marketing of GRASPA® in 38 European countries with Orphan Europe (Recordati Group) and in Israel with Teva. Due to the innovative nature of GRASPA®, its ability to respond to unmet medical needs, and its progress in clinical development, ERYTECH was able to obtain favorable terms, particularly with regard to the sharing of future revenues (representing up to 45% of the net sale price). Both partners have recognized sales capacities and can effectively promote GRASPA® in their respective territories. In particular, through its subsidiary Orphan Europe, Recordati is a specialist in orphan diseases and will work with ERYTECH on the regulatory approach to optimize the marketing of GRASPA®. The agreement with Orphan Europe (Recordati Group) provides, among other things, for the payment of €5 million on signing, sharing in the development costs for GRASPA® in AML, and future payments of up to €37.5 million, subject to the achievement of regulatory and sales milestones. ERYTECH will receive a payment for product delivered, and royalties on the sales made by Orphan Europe (Recordati Group) with GRASPA®, for a total of up to 45% of the net sale price.

Separately, another Recordati Group company has subscribed to convertible bonds issued by the Company and that were converted into an equity stake in the Company's share capital worth €5 million at the time of the initial public offering.

- **Favorable conditions for market access: The orphan drug designation, current medical practice and expected medical needs**

ERY-ASP/GRASPA® has obtained orphan drug designation in ALL, AML, and pancreatic cancer in Europe from the EMA, and in the United States from the FDA. ERYTECH will therefore be able to take advantage of research subsidies, tax credits, and a marketing procedure with shorter lead times and reduced costs, and will benefit from exclusive marketing after obtaining the marketing approval for the product for 7 and 10 years, in the United States and Europe, respectively. L-asparaginase-based treatment has been included in almost all European and American chemotherapy protocols since the 1970s for pediatric ALL patients. ERY-ASP/GRASPA® will be incorporated in or added to current medical regimens. As a result, ERYTECH anticipates a rapid adoption of ERY-ASP/GRASPA®. Moreover, these same clinicians treat AML patients and, for this indication, ERY-ASP/GRASPA+ will capitalize on the clinical experience of these prescribers. The marketing of ERY-ASP/GRASPA® will require reasonable promotional and sales resources, given the specialized positioning of the drug (clearly identified and relatively few prescribers, hospital treatment or special care center).

- **Proprietary and industrialized technology: regulated status of “Etablissement Pharmaceutique” and “Etablissement Exploitant”**

ERYTECH’s encapsulation technology is internationally protected by 13 patent families filed both on the processes and on the products. ERYTECH has successfully developed a process to produce loaded erythrocytes in a reproducible, reliable and economical way on a large scale, regardless of the initial characteristic and origin of the red cells used. More than 500 bags of ERY-ASP have already been produced and transfused in five clinical trials conducted by ERYTECH. ERYTECH’s production unit operates according to the highest standards of pharmaceutical production, quality and traceability. The Company has obtained the regulated status of “Etablissement Pharmaceutique” and “Etablissement Exploitant” from ANSM to produce ERY-ASP/GRASPA® for the European and Israeli markets. The current production capacity is sufficient to meet the needs of the various clinical trials scheduled and for approximately the first two years of commercialization in Europe.

- **Opportunity to develop ERY-ASP in the United States: Launch of the clinical program**

The US market is virtually equivalent to that of Europe in terms of number of patients with acute leukemia and is the natural progression in the development of ERY-ASP. A Phase I clinical trial in adult patients with ALL is in progress, after having obtained authorization for this study from the US Food and Drug Administration (FDA). The Company is relying on studies already conducted in Europe and will also rely on the other studies that will be launched in the United States in order to obtain regulatory approvals for ALL treatment and for other indications like AML and solid tumors. The Company retains all rights to commercialize its candidate products in the United States. Even though the Company believes that it is able to market its product candidates itself, once the marketing approval in the United States has been issued, through a small and, targeted sales force, it may consider agreements with third parties for the distribution and sale of its approval products. Moreover, ERYTECH has established a close partnership with the American Red Cross of Pennsylvania (Philadelphia, USA) to produce, under the Company’s supervision, the batches needed for clinical studies.

- **A promising pipeline: Solid tumors and other orphan diseases**

Asparagine has been shown to also be an essential nutriment for several other types of cancer. In partnership with the MD Anderson Cancer Centre (Houston, USA), one of the most renowned hospitals in the world for the treatment of cancer, ERYTECH analyzed various types of solid tumors and determined that asparaginase could effectively combat solid tumors and lymphomas. The first milestone for developing ERY-ASP for solid tumors was achieved with a positive Phase I study in patients with pancreatic cancer, which demonstrated good tolerance of the product even at high doses. The next step is the initiation of a Phase II study, for which the first patients were recruited in 2014. The Company hopes to be able to present the first results of this study in 2016. ERYTECH is also preparing to launch Phase II/III clinical studies on non-Hodgkin lymphomas.

The efficacy of the technology to induce tumor starvation has been demonstrated mainly with L-asparaginase, but it is possible to encapsulate other enzymes that starve tumors in red blood cells, such as methionine- $\gamma$ -lyase (MGL) and arginine-deiminase (ADI). In the TEDAC program, we are developing them as new drug candidates ERY-MET and ERY-ADI.

In addition, the ERYTECH technology platform is versatile and can encapsulate other enzymes and molecules, and opens possibilities to develop cancer vaccines and enzyme replacement therapies, for example.

We have used our ERYCAPS platform to develop a pipeline of drug candidates to treat rare forms of cancer and other orphan drugs. The following table shows our pipeline of product:



Mode of action	Product/Candidate/Program	Drug/ Substance	Indication	Discovery	Pre-clinical	Phase 1	Phase 2	Phase 3/Pivotal	MAA	Status / Milestones	Commercial rights	
Tumor starvation	ERY-ASP (GRASPA®)	Asparaginase	ALL	EU							Submitted MAA in October 2015; regulatory approval expected by end of 2016 early 2017	RECORDATI Europe TEVA
				US							Expected to complete Phase 1 clinical trial in 2016 and initiate global pivotal trials	Israel (initially in ALL only)
			AML	EU then EU/US							Ongoing Phase 2b clinical trial; third DSMB completed; primary results expected in 2017	erytech RoW
			Pancreatic cancer	EU then EU/US							Ongoing Phase 2 clinical trial; primary results expected in 2016	erytech
		NH-lymphoma	Global							Expected to initiate clinical trials in 2016 (expected to be Phase 2 based on safety data from other trials)	erytech	
		ERY-MET	Methionine-γ-lyase	TBD							Expected to initiate Phase 1 clinical trial in 2016	erytech
	ERY-ADI	Arginine deiminase	TBD							Continue preclinical development	erytech	
Immuno-therapy	ERY-VAX	Tumor antigens	TBD							Continue preclinical development	erytech	
Enzyme replacement	ERY-ERT	Therapeutic enzymes	TBD							Continue preclinical development	erytech	

- **Strong scientific and medical support: 7 leading world experts**

With its scientific and medical board, ERYTECH is surrounded by world-renowned American and European experts, particularly in the fields of oncology and leukemia. In addition to their active role in optimizing ERYTECH's strategy, their opinion in the scientific and medical communities will help promote the adoption of ERY-ASP/GRASPA® in hospitals and special care centers.

- **An experienced and highly complementary team**

ERYTECH is led by Gil Beyen, Chief Executive Officer of the Company, who brings strong expertise in international development and pharmaceutical partnerships, Iman El-Hariry, Chief Medical Officer and oncologist with more than 15 years of experience in product development in the pharmaceutical industry, Jérôme Bailly, Deputy Chief Executive Officer, Chief Pharmacist and Director of Pharmaceutical Operations, who is a Doctor of Pharmacy and holds a degree in chemical engineering with a concentration in pharmaceutical engineering, and Eric Soyer, Chief Financial Officer and Chief Operating Officer, who has more than 20 years of experience in management positions in the financial and operational departments of public and private, new and established companies. The Company relies on a talented team of 45 professionals with diverse, complementary backgrounds and skill sets that are fully in line with ERYTECH's development objectives.

- **The pharmaceutical industry's strong and growing interest in orphan drugs**

The interest of pharmaceutical companies in orphan and rare diseases has grown steadily since the mid-2000s and the last decade has been the most productive for the development of these drugs. Several major international pharmaceutical companies such as Pfizer, GSK and Sanofi, and many mid-size pharmaceutical groups such as Recordati, Swedish Orphan Biovitrum and Shire have created specialized divisions for orphan and rare diseases and/or made them a major strategic focus. Consequently, transactions in this area in the form of acquisitions or partnership agreements have multiplied. In particular, there have been 4 transactions finalized or in progress in the L-asparaginase market: Shire's project for a hostile takeover of Baxalta for \$30 billion, the acquisition of OPI (France) by EUSA (UK) for €110 million in 2007, the acquisition of a portfolio of products from Enzon (US) by Sigma Tau (Italy) for \$327 million in 2009, and the acquisition of EUSA by Jazz Pharmaceuticals (US) for \$700 million in 2012. In this context, ERYTECH's objective is to create significant strategic value with ERY-ASP/GRASPA® and its technological platform.

## 6.4 ERYTECH's encapsulation technology

### 6.4.1 The innovative approach to encapsulate therapeutic enzymes

ERYTECH's proprietary technology is based on the encapsulation of therapeutic molecules in red blood cells, also called erythrocytes. The administration of red blood cells is completely managed and controlled by the hospital staff. In addition, it is a biocompatible carrier with a long half-life in the body of approximately one month and its elimination by the cells of the reticuloendothelial system is well known.

Because the red cell membrane protects its contents from the external environment, i.e. the body, and vice versa:

- the encapsulated molecule is protected from the body's defense reactions or interactions with it, which can lead to inactivation, degradation or to its rapid elimination; and
- the body is protected against attack from its contents, and as a result, there are fewer side effects.

This results in an increase of the therapeutic index (toxicity offset by efficacy). For example, in the case of asparaginase, for a given level of efficacy, patients receive a dose 10 times lower when it is encapsulated using ERYTECH's technology.

ERYTECH's technology can transform the red blood cell into a cellular bioreactor. The red blood cell has the natural property of being able to absorb certain amino acids freely circulating in the blood. The therapeutic enzyme encapsulated in the red blood cell can interact and break down the amino acid targeted.



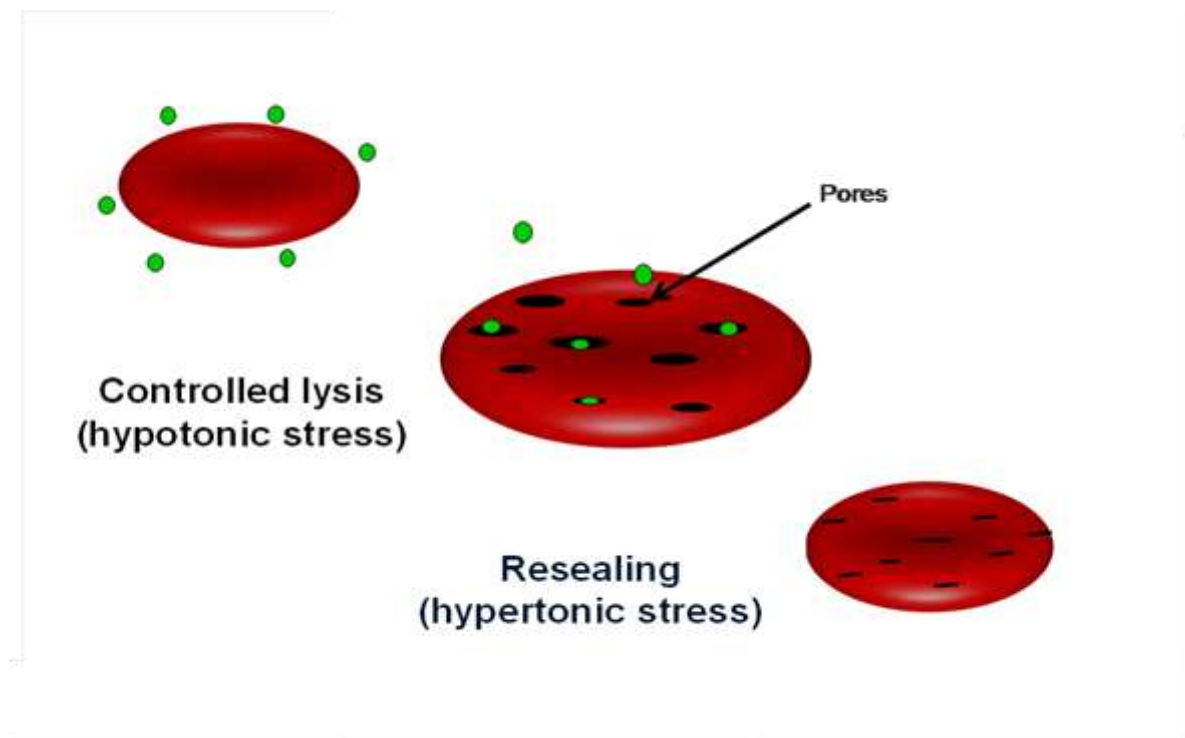
In addition, on the basis of the Company's preclinical studies and the first clinical experience in blood oncology, the Company believes that a variety of other therapeutic molecules can be encapsulated in red blood cells in order to starve cancer cells, both in blood cancers or in solid tumors, and develop cancer vaccines and enzyme replacement therapies (see Section 6.11 Other ERYCAPS development projects).

#### 6.4.2 Automated and strong industrialized encapsulation process

The ERYCAPS platform uses the Company's proprietary technology to trap active ingredients within red blood cells using the principles of reversible hypotonic and hypertonic osmotic stress. To allow therapeutic compounds to enter the red blood cells, the cells are subjected to a hypotonic solution that causes them to swell and the pores of the cellular membrane to dilate until they reach a critical volume when the membrane is distended to the point of becoming permeable to macromolecules. Pores form on the surface of the membrane allowing molecules to enter the erythrocyte. As soon as the desired concentration level of molecules is reached within the red blood cells, the cells are plunged into a hypertonic solution to restore their isotonicity. This procedure draws water outside the cell, thus closing the pores, and makes the membrane impermeable to the macromolecules. Only permeability to very small elements (less than 200 Daltons) is retained. The molecule is thus permanently encapsulated.

The capacity of a red blood cell to dilate, known by the term osmotic fragility, is not uniform and varies depending on the batch of red blood cells. When the Company receives a package of red blood cells from a blood bank, it identifies the key hematological parameters, including the osmotic fragility of the blood sample. Depending on the osmotic fragility measures, the Company is able to calculate the specific amount of osmotic pressure to apply in order to obtain the desired concentration of active substances to be encapsulated, which ensures that quantifiable levels of active substances can be captured in each production batch. This procedure thus reduces the variations in the amount of active substances in each production batch.

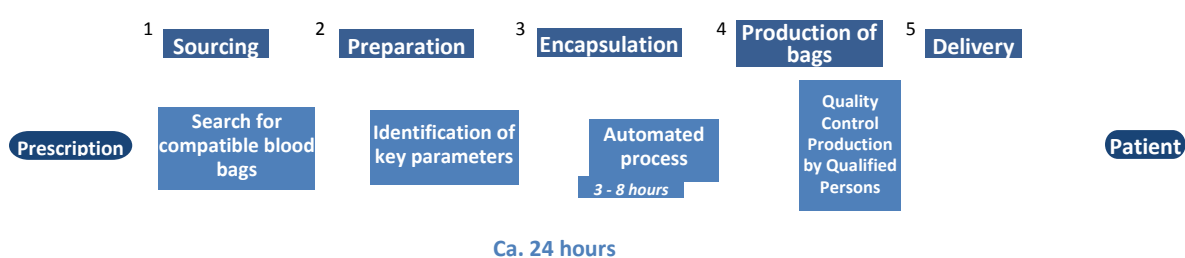
Principle of the encapsulation process



The osmotic fragility of one sample of red blood cells to another varies. Thus, the membrane distension capacity and therefore the encapsulation capacity varies. However, osmotic fragility variation may be offset by hypotonic lysis parameters. Thus, variations in the amount of the product encapsulated are reduced. This is the core of the ERYTECH patented process (see Chapter 11 of this Reference Document).

ERYTECH has successfully developed this encapsulation process to produce loaded erythrocytes in a reproducible, reliable and economical way on a large scale, regardless of the initial characteristic and origin of the red cells used. The delivery of ERY-ASP, the first product developed by ERY-TECH on the basis of the ERYCAPS technology, to patients which includes the phase to encapsulate L-asparaginase in the red blood cells, generally takes approximately 24 hours from the end of production until shipping of the product to the hospital. More than 500 bags of ERY-ASP/GRASPA® have already been produced and transfused during the five clinical trials conducted by ERYTECH.

An automated and industrialized encapsulation process



Specifically, the major competitive advantages of the production process are:

- its speed: the fully automated preparation of the product requires only 3 hours;
- its stability: 72 hours (at a temperature of 2-8°C) and 6 hours (at ambient temperature). This allows hospital personnel to perform the necessary blood transfusions at an optimal time and to retain control of the treatment administration procedure. On the basis of the stability studies the Company has performed, it believes that it is able to extend the shelf life of ERY-ASP to at least 5 days;
- reproducibility: consistent quality loaded erythrocytes are produced, regardless of the initial characteristics and the origin of the red blood cells used. Various control steps ensure the quality of the product before release by the head pharmacist;
- its safety: supply of transfusion-quality red blood cells from blood banks operating in accordance with the highest quality standards and quality control processes strengthened at each stage of production.

The ERYTECH production unit is based in Lyon and there are 12 employees dedicated to the production. Production meets the highest pharmaceutical production standards (cGMP) and is ISO 9001 certified. In particular, product batches are fully traceable from blood collection and separation of red blood cells performed by the blood banks that supply ERYTECH to the patient. The Company has the regulated status of “Etablissement Pharmaceutique” and “Etablissement Exploitant” status, which allows it to operate on the European market.

### 6.4.3 Organized production in the United States for future clinical trials

In anticipation of clinical trials in the United States, ERYTECH has deployed a qualified production unit in Philadelphia in partnership with the American Red Cross (ARC). The American Red Cross (ARC) is the leading blood bank in the world. It is a federal agency located in all states in the United States of America and its primary activity is collecting, classifying and distributing bags of red blood cells for transfusion.

The ARC is the service provider for the production of GMP (Good Manufacturing Practice) batches of ERY-ASP for clinical trials. The ARC also provides the raw material, the bag of red blood cells. Since ERYTECH's analytical method and process were the subject of an industrial transfer, the operations performed at the U.S. site are similar to those at the French site in compliance with FDA regulations. ERYTECH oversees production and controls for this unit jointly with the ARC.

This agreement with the ARC does not include any transfer of rights to technology or to ERY-ASP, and allows ERYTECH to produce the quantities needed for clinical trials planned in the United States.

## 6.5 Acute leukemia: A significant unmet medical need

### 6.5.1 Bone marrow cancer

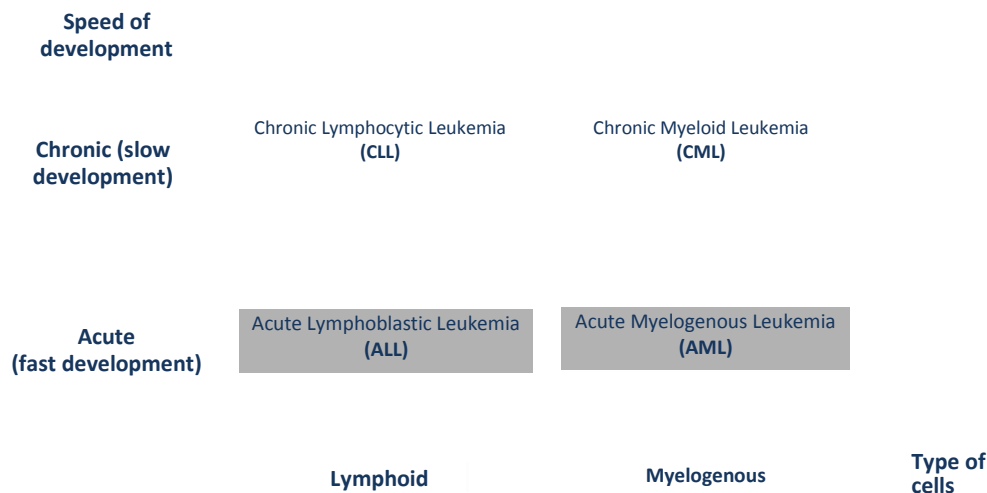
Leukemia is a cancer of the bone marrow cells, sometimes referred to as blood cancer. Leukemia is characterized by an abnormal and excessive proliferation of white blood cell precursors which, left untreated, invade the bone marrow and then the blood.

Leukemia is categorized according to its speed of development and the type of cells that proliferate: Acute leukemia (AL) is characterized by the rapid proliferation of abnormal cells in the bone marrow and requires urgent treatment. Chronic leukemia (CL) has a slow proliferation with a clinical tolerance of cancer cells and a development that may take place over months or years.

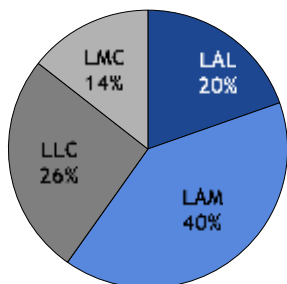
The cancer cell lineage can be either lymphoid precursors (which, in their normal state, participate in the defense of the body and form white blood cells) at the onset of lymphoblastic leukemia, or it can be myeloid cells for myeloid leukemia.

By combining these two criteria as shown in the diagram below, there are four types of leukemia. ERYTECH is focused exclusively on acute lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML), which are quickly life-threatening for patients.

The 4 categories of leukemia



## Breakdown of cases of leukemia by cell type



Source: PETRI Study

### 6.5.2 An increasing number of patients worldwide

Each year, approximately 50,000 patients are diagnosed with acute leukemia in Europe and the United States.

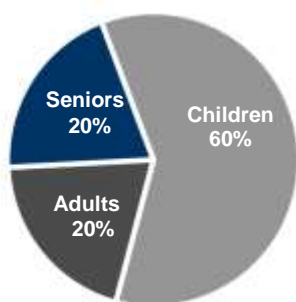
Around 6,000 new cases of ALL are diagnosed in the United States<sup>8</sup> and at least as many in Europe, which equals, with an age-adjusted incidence estimated at about 2 new cases per 100,000 people each year<sup>9</sup>.

AML has an age-adjusted incidence approximately twice as high, which is around 4 new cases for 100,000 people each year, representing approximately 17,000 new cases in Europe<sup>10</sup> and 20,000 in the United States<sup>11</sup>.

As shown in the following diagram, the majority of ALL patients are children. The remaining ALL patients are divided evenly between adults (18-55 years old) and older adults (>55 years old).

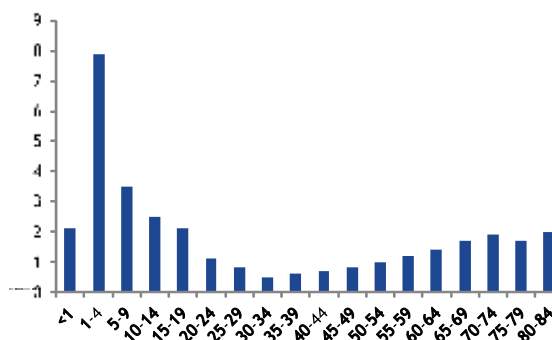
Breakdown of ALL patients by age and disease incidence according to age

Breakdown by patient type  
*Breakdown by patient type*



Source: U.S. NIH – NCI - SEER Cancer Statistics

Incidence according to age  
*Incidence according to age*



Source SEER Cancer Statistics 1975-2007

Source SEER Cancer Statistics 1975-2007

<sup>8</sup> Siegal et al., CA Cancer J Clin, 2013.

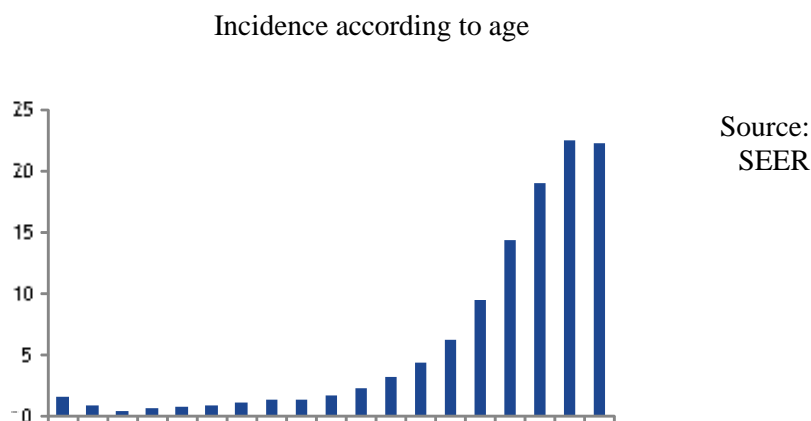
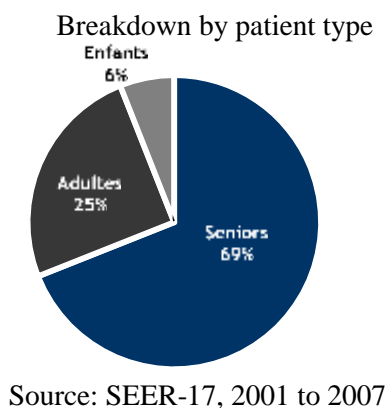
<sup>9</sup> Dorez et al., Blood 2010; SEER Cancer Statistics.

<sup>10</sup> Rodrigues-Abreu et al., Annals of Oncology, 2007.

<sup>11</sup> Siegal et al., CA Cancer J Clin, 2013 RARE Cancer, American Cancer Society.

AML is, however, a form of leukemia that affects mainly adults and older adults, and marginally children as shown in the following chart. The median age at diagnosis is 67. Because of their age and often multiple diseases, these patients are particularly difficult for clinicians to treat.

Breakdown of AML patients by age and disease incidence according to age



(Surveillance, Epidemiology and End Results) Cancer Statistics Review, 1975-2008. National Cancer Institute; 2011.

The exact causes of leukemia are not completely known, but different studies<sup>12</sup> have shown that the following conditions increase the risks:

- radiation;
- benzene, formaldehyde and dioxins;
- tobacco;
- anticancer chemotherapy;
- some genetic disorders.

The incidence of the disease is relatively stable and tends to increase with the aging of the population.

### 6.5.3 A lower 5-year survival rate for adults and older adults

With the development of new drugs and therapies, the prognosis for certain cancers has improved significantly, such as breast cancer, prostate cancer, ALL in children and thyroid cancer. There is still a large number of cancers with a poor prognosis, such as pancreatic, liver, esophageal or lung cancer. Among the cancers with the worst prognoses are ALL and AML in adults and older adults.

The 5-year survival rates for ALL vary significantly between young patients (children and young adults) which today achieve a 5-year survival rate of around 90%<sup>13</sup>, and older patients (adults and older adults), who have a low 5-year survival rate (15%-30%).

The development of treatment protocols and new drugs has led to steady improvement in the remission rate and chance of long-term survival. The protocols and drugs used successfully in children, in particular L-asparaginase, are often not transposable in older subjects due to their low tolerance for intensive chemotherapy because of their general health.

Especially for these patients as a priority, clinicians have a great need for new treatments with a better safety profile. ERYTECH is developing a new product ERY-ASP/GRASPA® to respond to this need.

<sup>12</sup> Rodriguez-Abreu et al., Annals of Oncology, 2007.

<sup>13</sup> Source: Cancer Statistics Review 1975-2005.%).

In AML, because of the damaging effects of induction treatments, the mortality rate from high intensity chemotherapies varies from 5% to 15% in young patients with AML and from 20% to 50% in elderly patients. Because of the aggressive nature of the treatment, a significant percentage of patients over 65 opt for palliative care only, which highlights the unmet medical need for effective and safe treatments for AML.

## 6.6 L-asparaginase: a decisive drug in the treatment of acute leukemia

### 6.6.1 Current treatment of patients with acute leukemia

The current treatment of patients with leukemia is based on chemotherapy combining several drugs according to various regimens, as is the case for the vast majority of cancers.

Treatment protocols for ALL are clearly established in all European countries and the United States depending on the patient's age, medical history and the specific characteristics of the disease. For AML, despite a generally similar approach, treatment protocols may differ considerably from one country to another and may also change depending on clinical or scientific advances.

Generally, after a diagnosis and preparation stage, chemotherapy protocols include several phases: induction of complete remission, remission consolidation, delayed intensification to prevent recurrence of leukemia and maintenance treatment:

**Induction:** This step requires one or more months of treatment and is based on the administration of chemotherapy including several drugs whose goal is to achieve remission, i.e. the disappearance of signs of the disease.

**Consolidation:** This phase comprises chemotherapies administered repeatedly over several days to one month, in order to prevent a relapse. Depending on the treatment's efficacy, the characteristics of the disease and age of the patient, hematopoietic stem cells may be required.

**Delayed intensification:** Intensive chemotherapy may be necessary for one to two additional months. This phase is also called re-induction and is a repeat of the initial induction treatment about 3 to 4 months after the induction of remission. Delayed intensification helps prevent the recurrence of leukemia.

**Maintenance:** This treatment is for patients for whom transplantation is not being considered. It is chemotherapy, taken primarily by mouth for about two to three years.

### 6.6.2 The crucial role of L-asparaginase in patient remission

Asparagine is an amino acid naturally produced by cells for their own use in protein synthesis. This amino acid produced in excess by healthy cells is found in the bloodstream. Cancer cells also need it to grow and survive, but they do not produce it. Therefore, they use circulating asparagine.

The principle of the treatment is to remove circulating asparagine using a specific enzyme: L-asparaginase. This enzyme is able to destroy the asparagine and deprive the cancer cells of an important nutrient, resulting in death of the cells.

The history of L-asparaginase as an antitumor agent began with the initial observations of a cytotoxic effect in 1953 and the confirmation of these results in the early 1960s. Sometime later, L-asparaginase was purified from bacteria (*E. coli*), and it was demonstrated to have an effect on acute leukemia.

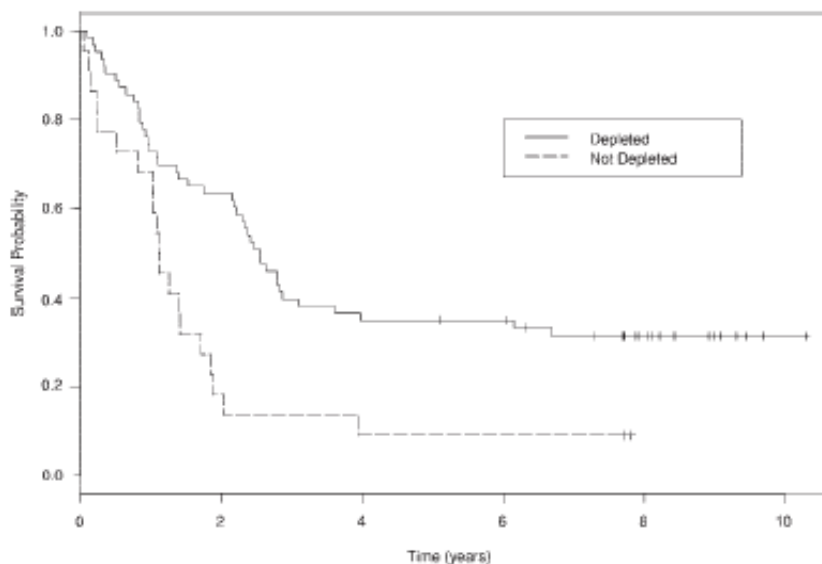
L-asparaginase was introduced into standard ALL treatment in the 1970s. Its use has revolutionized pediatric protocols by improving complete remission rates and duration of remission. It benefits from a significant therapeutic hindsight both with regard to its efficacy and its tolerance.<sup>14</sup>

Asparaginase gradually established itself as a pillar of anti-leukemia chemotherapy. Clinicians place it at the center of the therapy, along with other cytotoxic molecules, and have extended its use to young adults and adults when they can tolerate this therapy.

The objective of clinicians is for the patient to go into complete remission of the disease (i.e. disappearance of the tumor cells) for as long as possible. Current clinical practices are based on systems of intensive use of L-asparaginase (as many doses as early as possible and for as long as possible). Indeed, it has been shown that the **longer the tumor** cells are deprived of asparagine, the higher the chances of complete and maintained remission are, and the longer the remission is sustained<sup>15</sup>.

As the study presented below shows, the patients in whom the level of asparagine was reduced have considerably higher chances of remission and survival than those in whom it was not possible. The graph shows the survival of 63 adult patients with ALL who obtained a good level of asparaginase activity following treatment with asparaginase, as compared to a group of 22 patients for whom asparaginase activity was not sufficiently suppressed (depleted) during treatment.

Survival rates for ALL by asparagine depletion level



Source: Wetzler M et al. CALGB. Blood 2007;109: 4164

In AML, L-asparaginase has been only very partially used to date. It has a Marketing Approval for AML in certain countries only (e.g. Canada), and is used in certain treatment protocols.

As illustrated in the diagram below, the relevance of L-asparaginase treatment and its efficacy for AML have been demonstrated. In 1988, a study conducted on 195 AML patients demonstrated the efficacy of L-asparaginase<sup>16</sup> in addition to the cytarabine-based reference treatment.

The significant risks of side effects for this patient population with often elderly patients and in fragile health are a major obstacle to the use of L-asparaginase.

<sup>14</sup> Stock et al., Leukemia & Lymphoma, (2011)

<sup>15</sup> Silverman et al. Blood 2001

<sup>16</sup> Capizzi & White, The Yale Journal of Biology and Medicine, 1988.



In addition, in vitro experiments have demonstrated the efficacy of L-asparaginase on over 60% of several biological samples from different AML subtypes (M0, M1, M4 and M5), comparable to the results obtained on biological samples of ALL. It is estimated that approximately 50%-70% of patients could respond to an L-asparaginase treatment<sup>17</sup>.

In addition, the Company has a license with the U.S. National Institutes of Health (NIH) on the rights to a diagnostic test to measure the presence of asparagine synthetase (ASNS), an enzyme that produces asparagine, in order to determine tumor sensitivity to asparaginase in relation to treatment with ERY-ASP. We are currently using this diagnostic test on biopsy samples collected in Phase IIb of the clinical trial on AML patients.

**- ALL treatment**

In the case of ALL, the choice of drugs involved in the successive phases of chemotherapy depends on a genetic specificity, the presence or absence of the Philadelphia chromosome. This anomaly is present in around 5% of ALL in children and around 20% to 25% of ALL in adults. Its frequency increases with age.

ALL patients with the Philadelphia chromosome (known as Ph+, “Phi positive”) are treated primarily with monoclonal antibodies, particularly tyrosine kinase (BCR-ABL) inhibitors like imatinib, which is sold by Novartis under the Gleevec®/Glivec® name, and dasitinib, sold by BMS under the name Sprycel®. However, clinical trials have demonstrated the lack of efficacy of imatinib and dasitinib in ALL patients without the Philadelphia chromosome.

The remaining ALL patients, i.e. the majority of patients (~80%) do not have the Philadelphia chromosome (called Ph-, “Phi-negative”). The lymphoblasts of these patients respond to L-asparaginase. Therefore, L-asparaginase treatment has been included in almost all European and American chemotherapy protocols since the 1970s for this type of patient.

The following diagram provides an overview of the key molecules that can be used in chemotherapy cocktails depending on the different phases of treatment.

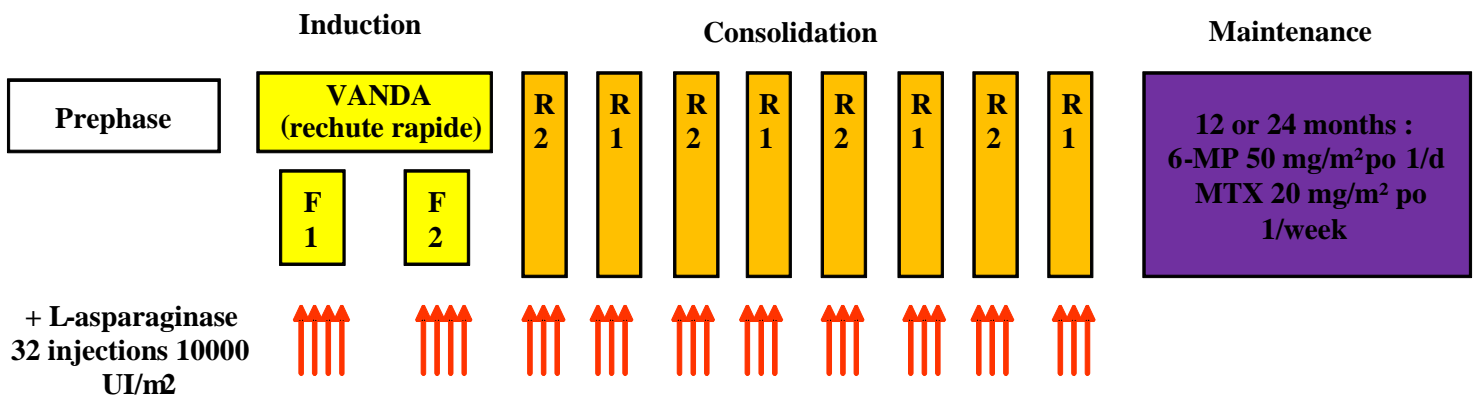
Overview of the substances used in chemotherapy for ALL patients without the Philadelphia chromosome in the COPRALL protocol

	Induction	Consolidation	Intensification	Maintenance
Possible treatments	Cytarabine Methotrexate (MTX) Prednisolone Vincristine (VCR) Doxorubicin Dexamethasone Asparaginase	Cytarabine VCR Cyclophosphamide 6-Mercaptopurine(6-MP) Asparaginase	Cytarabine MTX VCR Dexamethasone Doxorubicin Cyclophosphamide Thioguanine Asparaginase	MTX VCR Dexamethasone Cyclophosphamide 6-MP Thioguanine
Duration of treatment	~1 to 2 months	3 to 9 months	~1 to 2 months	2 - 3 years

<sup>17</sup> Okada et al., Br J Haematology, 2003, L-Asparaginase Sensitivity and Asparagine Synthetase Expression In Primary Tumor Cells From AML Patients Willy Berlier.

The following figure shows an example of a treatment protocol for relapsed patients (COPRALL protocol - France). After a preparation phase, the patient receives intensive treatment with up to 32 injections of L-asparaginase in the induction and consolidation phases.

Example of a protocol for the treatment of ALL (COPRALL protocol)



#### - AML treatment

Acute myeloid leukemia (AML) is a form of cancer that affects bone marrow cells that produce the blood components (red cells, white cells and platelets). Left untreated, it is rapidly fatal because of the risk of infection and bleeding. It is potentially curable with intensive chemotherapy regimens, and the risks of relapse are lower if a bone marrow transplant can be performed, but at the expense of mortality risks related to the transplant, which increase with age. The chances of remission and the risks of relapse vary by age and abnormalities of the karyotypes of leukemic cells.

There are several categories of AML based on the appearance of leukemic cells viewed by microscope (cytology) and the analysis of leukemic cell chromosomes. Numerous treatment protocols have been developed taking this variety of subtypes into account.

Left untreated, AML causes rapid death by infection, bleeding or respiratory and brain disorders by significant increase in white blood cells. The goal of treatment is for abnormal blasts to disappear from bone marrow and increase neutrophils, platelets and hemoglobin in the blood. This state is referred to as “complete remission.” Without further treatment, relapse (recurrence of blasts in bone marrow) is most often observed.

Apart from a minority subtype (AML3) requiring a more specific drug, the all-trans retinoic acid molecule or ATRA which is proven to be effective for this subtype, the treatment is essentially the same for all types of AML.

The choice of treatment depends on the patient’s pre-treatment assessment (cardiac, kidney, liver function) and the physiological age of the patient. AML in children is differentiated from that in subjects under 60 years old and that in subjects > 60 years old.

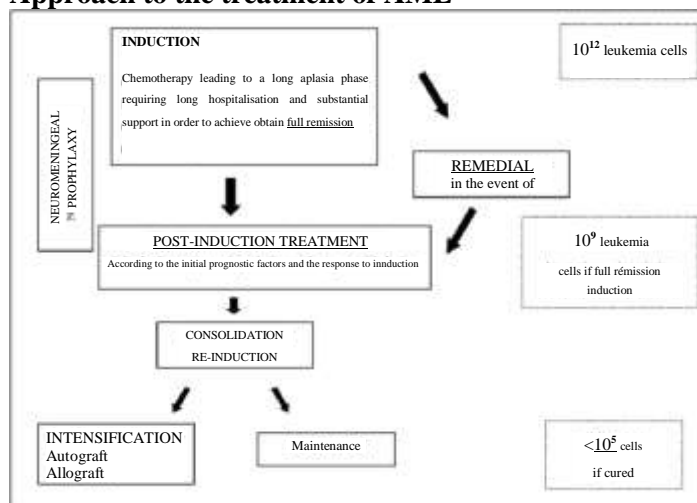
For AML in children, the therapeutic strategy after obtaining complete remission is a bone marrow allograft from an intra-family donor (75% disease-free 5-year survival rate) or treatment intensification with high-dose cytarabine and maintenance treatment with subcutaneous cytarabine and 6-thioguanine (55% disease-free survival).

In AML patients aged 18-65, intensive chemotherapy can be proposed with several phases: an induction phase, a consolidation phase and finally maintenance treatment including either an autograft, a bone marrow allograft or further courses of chemotherapy.

- Induction. Its objective is to achieve remission. The standard used is based on an infusion of cytarabine for 7 days associated with an anthracycline (daunorubicin or idarubicin) for 3 doses (“7+3”).
- Consolidation. This treatment aims to maintain remission. It consists of administering high doses of chemotherapy. Several consolidation rounds are usually needed, requiring additional hospitalizations for varying lengths of time. The treatment consists of high-dose cytarabine (HiDAC) in repeated courses (1 to 4 courses) or hematopoietic stem cell transplantation. In the latter case, it may involve a graft made from a donor (allograft) or stem cells from the patient collected at the end of consolidation treatment (autograft). Stem cells are cells from bone marrow (which are also present in cord blood) from which all blood cells are produced.
- Intensification. This type of treatment is available and tailored to the risk of leukemia relapse and varies from one subject to another in order to obtain long-term remission and recovery. It is based on several courses of chemotherapy similar or identical to that administered during consolidation, i.e. based on a hematopoietic stem cell transplantation. Intensification can only be considered for patients under 60-70 years old because, beyond this age, the body is no longer able to tolerate the adverse effects of this type of treatment.

Remission maintenance treatment (4-12 months) can then be given as appropriate.

### Approach to the treatment of AML



In patients over the age of 65, there is no standard treatment. Intensive chemotherapy treatments cannot be given and conventional bone marrow allografts are not possible. Induction treatment will consist of a treatment similar to that for young subjects but with a lower dose of cytarabine. Post-induction treatment may involve a sequence of high-dose cytarabine if the patient’s physiological condition permits it. Similar to the case for young subjects, it is associated with anthracycline that is different from that used in induction, novantrone or the use of another interposing treatment such as amsacrine. Hematopoietic growth factors could reduce the toxicity of the treatment. Maintenance treatment follows completion of consolidation treatment. Patients not eligible for intensive chemotherapy may also be offered supportive care by transfusions, anti-infectious agents and palliative chemotherapy, with the goal being quality of life, and/or participation in a clinical trial.

## Principles of treatment protocols for AML

	INDUCTION	CONSOLIDATION	INTENSIFICATION	MAINTENANCE (RESERVED FOR AML 3)
SUBJECT < 18 YEARS OLD	ARACYTINE MITOXANTRONE	ARACYTINE HIGH DOSE AMSACRINE VP16 DAUNORUBICINE ASPARAGINASE ALLOGRAFT	OR CYTARABINE HIGH DOSE (HIDAC)	
SUBJECT 18-60 YEARS OLD	STANDARD 7+3 CYTARABINE + IDARBUCINE OR DAUNORUBICINE	HIGH DOSE CYTARABINE (HIDAC) STEM CELL GRAFT		
SUBJECT >60 YEARS OLD	LOW DOSE 7+3	HIGH DOSE CYTARABINE (HIDAC) NOVANTRONE AMSACRINE		
DURATION OF TREATMENT	~ 1 MONTH	6-9 MONTHS	~1-2 MONTHS	4-12 MONTHS

Like the lymphoblasts in the case of ALL, most of the myeloblasts need circulating asparagine to grow and proliferate, even though it is believed that the myeloblasts in AML do not respond as well to L-asparaginase as the lymphoblasts in ALL. The medical rationale for the use of L-asparaginase for the AML is therefore identical.

L-asparaginase is used in some pediatric treatment protocols: for example, in France in the ELAM 02 protocol, in the USA in the COG or St. Jude protocols), or in Canada, where it has marketing approval. However, its toxicity profile prevents its widespread use in fragile children and especially in adult patients, where it is rarely used.

### 6.6.3 Limitations of direct administration of L-asparaginase

In clinical practice, ERYTECH estimates that one third of ALL patients – mostly older adults and relapsed patients – and the majority of adult AML patients are intolerant to L-asparaginase treatment. These patients are considered fragile.

Other patients, mostly children and young adults with ALL, receive L-asparaginase treatment which enables them to achieve remission of the disease and improves survival. Nevertheless, the use of L-asparaginase in these patients may also cause severe side effects including hypersensitivity reactions (anaphylactic shock), pancreatitis and bleeding disorders.

Severe toxic effects of L-asparaginase include:

- Allergic reactions, including anaphylactic shock and hypersensitivity.
- A decrease in coagulation factors. Coagulation problems may be responsible for severe thrombosis or bleeding. L-asparaginase interferes with the liver's production of both procoagulant and anticoagulant proteins.
- Pancreatic toxicity with acute pancreatitis and diabetes. Acute pancreatitis is seen in less than 15% of cases, but can sometimes progress to hemorrhagic or necrotizing pancreatitis, which is usually fatal.
- Liver damage from elevated liver enzymes that requires regular monitoring.
- Brain damage resulting in a state of confusion or clear coma.

Clinicians consider that the risk of serious intolerance has been identified in adult and senior patients with ALL and in patients in relapse. There is indeed an increased risk of liver, pancreatic, and nervous system toxicity, as well as hypersensitivity and bleeding disorders in these fragile patients.

#### 6.6.4 The current market for L-asparaginase

ERYTECH believes that the current market for the different forms of asparaginase is around \$300 million worldwide<sup>18</sup> even though these different forms of treatment actually target only a small number of patients with acute leukemia. ERYTECH believes that a large number of other patients could benefit from an improved treatment based on L-asparaginase. The potential market for other patients, including adult and elderly patients with ALL and all AML patients is not being exploited and could represent more than one billion euros.

The current market for L-asparaginase consists mainly of 3 products: native L-asparaginase (Kidrolase<sup>®</sup>, Leunase<sup>®</sup>, asparaginase medac<sup>®</sup>), Oncaspar<sup>®</sup>, and Erwinase<sup>®</sup>, which represent different formulations and/or different production processes. As a result, these products have distinct profiles, particularly in terms of duration of activity, frequency of injections, and side effects.

The native form (Kidrolase<sup>®</sup>, Leunase<sup>®</sup> or asparaginase medac<sup>®</sup>) is the first L-asparaginase. It was first brought to market in France in 1971. Erwinase<sup>®</sup> and Oncaspar<sup>®</sup> were brought to market for the first time in 1985 and 1994 respectively. These products are indicated for the treatment of ALL, but are not or are very rarely used in patients with AML.

The main L-asparaginase-based drugs are described briefly below:

##### – Native L-asparaginase

The introduction of native L-asparaginase to the standard treatment of ALL in children and later in adults, dates back to the 1970s. This L-asparaginase is purified from *E. coli* bacteria.

Native L-asparaginase remains the first-line treatment for ALL in children in many European countries. Because of its general toxicity, this native form is rarely or not used in fragile patients. Its market is in steady decline, faced with competition from other more recent formulations.

The native L-asparaginase is mainly produced by the Japanese company Kyowa and distributed in Europe by Jazz Pharmaceuticals (following the acquisition of Eusa Pharma, formerly OPI, in June 2012,) under the brand name Kidrolase<sup>®</sup>, and by the German company Medac under the L-asparaginase medac name.

In the United States, the native form (Elspar<sup>®</sup>) was recently withdrawn from the market because of production problems and because of competition with the pegylated form (Oncaspar<sup>®</sup>).

##### – PEG-asparaginase

PEG-asparaginase is an L-asparaginase from *E. coli*, pegylated (attachment of a polyethylene glycol group to the enzyme) so as to reduce its toxicity, including immune and allergic reactions, and to extend its duration of action (half-life).

PEG-asparaginase is typically administered in patients with an allergic reaction to native L-asparaginase. In some countries (United States, United Kingdom), it has almost completely replaced native L-asparaginase in children. PEG-asparaginase has been the subject of numerous publications in pediatrics but comparatively few studies in relapsed patients or adults. In practice, the incorporation of PEG-asparaginase in chemotherapy for adults is still uncommon because of the side effects feared by clinicians.

The only form of PEG-asparaginase authorized on the market is Oncaspar<sup>®</sup>. This injectable drug is registered in the United States, Germany, and Poland, and is available in other countries through special approvals. It was developed by Enzon, a company acquired by Sigma Tau in November 2009. Oncaspar<sup>®</sup>

<sup>18</sup> Source: Jazz Pharmaceuticals and Erytech

was previously distributed in Europe by Medac; Sigma Tau assumed direct marketing in August 2012. Baxalta purchased the Oncaspar® product from Sigma-Tau in 2015.

ERYTECH estimates that approximately one third of current sales of L-asparaginase are related to the use of PEG-asparaginase. Worldwide sales of Oncaspar® totaled approximately \$100 million<sup>19</sup> in 2014.

– **L-asparaginase derived from *Erwinia chrysanthemi***

L-asparaginase produced by *E. chrysanthemi* bacteria is marketed by Jazz Pharmaceuticals (previously by EUSA Pharma) in Europe and in the United States under the brands Erwinase® and Erwinaze® respectively. The product has been available in some European countries since 1985 and in the United States where it was approved again in November 2011.

Worldwide sales revenue of Erwinase® published by Jazz Pharmaceuticals for 2014 was \$199.7 million.

The product is positioned as second-line treatment in cases of hypersensitivity reactions to L-asparaginase derived from *E. coli* (the native form or the pegylated form). Immune reactions (allergies and antibodies) experienced by patients to the form produced with *E. coli* are specific to that form in particular, and do not target L-asparaginase derived from *Erwinia chrysanthemi*. However, the treatment based on Erwinase® can generate an immune response with development of anti-Erwinase antibodies itself.

The differences in half-life among the different preparations have the effect of a more frequent administration of Erwinase® over the form derived from *E. coli*.

In the United States, for ALL patients who have just been diagnosed and for ALL patients in relapse or resistant, physicians generally prescribe Oncaspar as first-line treatment, or Erwinaze if Oncaspar cannot be tolerated by the patient. In Europe, depending on the country, either the native L-asparaginase or Oncaspar are generally used for the initial treatment of ALL patients who have just been diagnosed, or for patients in relapse or resistant, with Erwinaze also used when one of these forms of L-asparaginase cannot be tolerated by the patient.

To the Company's knowledge, the following new forms of asparaginase are under development:

- Medac, a German company based in Hamburg, is developing a recombinant L-asparaginase under the name Spectrila and received a favorable recommendation from the EMA in November 2015. This favorable recommendation was followed by the granting of a centralized MA in January 2016. Phases II and III results have shown efficacy, a life span, and a side-effect profile quite similar to native L-asparaginase.<sup>20</sup>
- Medac is also developing a pegylated form currently in Phase I/II; and
- Jazz Pharmaceuticals is developing a pegylated recombinant form of its *Erwinia* L-asparaginase currently in Phase I.

The L-asparaginase market has seen four major transactions finalized or in progress which are part of a more general trend in interest from pharmaceutical groups in rare and orphan diseases. ERYTECH believes that these transactions were performed based on particularly attractive valuations:

- In August 2015, the pharmaceutical company Shire, listed on the London Stock Exchange, launched a hostile takeover for \$30 million (£19 million) on Baxalta, a company that specializes in the treatment of rare diseases.
- In June 2012, Jazz Pharmaceuticals acquired EUSA for \$650 million in cash plus a \$50 million earn-out based on certain deferred sales objectives. The transaction values EUSA at about 3x sales expected by the company for 2013 (\$210 million to \$230 million). Erwinaze® is the principal product of EUSA and represents approximately two thirds of sales (revenues of \$125 million expected at the time of the acquisition;

<sup>19</sup> Baxalta Corp Pres. Corporate Presentation

<sup>20</sup> Borghorst et al., Pediatric Hematology and Oncology, 2012



\$131.9 million realized in 2012, the year after the marketing approval in the United States; \$200 million realized in 2014).

- In November 2009, Sigma Tau acquired Enzon's specialty drug business activities for \$300 million, plus an earn-out of up to \$27 million contingent upon reaching certain goals. This transaction involved four marketed drugs, Oncaspar<sup>®</sup>, Adagen<sup>®</sup>, DepoCyt<sup>®</sup>, and Abelcet<sup>®</sup>, as well as a site in the United States. These four products recorded total sales of \$116.5 million in 2009, including \$52.4 million for Oncaspar<sup>®</sup>.
- In March 2007, EUSA acquired the French company OPi specializing in rare and orphan diseases for €110 million. OPi held a portfolio of specialty products including Kidrolase<sup>®</sup> (L-asparaginase derived from Escherichia coli) and Erwinase<sup>®</sup> (crisantaspase, L-asparaginase derived from Erwinia chrysanthemi) as well as monoclonal antibodies at various stages of preclinical and clinical development. OPi posted sales revenue of €18 million in 2006 and was profitable for the second consecutive year.

To the Company's knowledge, the more advanced products under development that may be able to treat ALL without the Philadelphia chromosome or AML are:

- Amgen, which is developing blinatumomab, product in development purchased with Micromet in January 2012. Blinatumomab is currently marketed in the United States and Europe for patients ALL line-B in relapse or resistant to existing treatments. This product is also in Phase 3 for other patients (first-line and second-line, pediatric and young adults). Blinatumomab is in Phase II for the treatment of patients with Diffuse Large B-Cell Lymphoma.
- Pfizer is developing inotuzumab ozogamicin, which received orphan drug designation in 2013, in the United States and Europe, as well as disruption treatment designation in 2015 in the United States, in the treatment of patients with ALL. The drug candidate is currently in Phase 3 with line-B ALL patients in relapse or resistant to existing treatments (in first-line treatment and in second-line treatment). In addition, this drug candidate in Phase 2 in the treatment of patients with Diffuse Large B-Cell Lymphoma (in first line) and in the treatment of patients with chronic myelocytic leukemia (in second line).
- Marquibo<sup>®</sup>, a new formulation of Vincristine, developed by the American company Talon Therapeutics was approved in the US in 2012. Talon was acquired by Spectrum Pharmaceuticals in 2013.
- New approaches based on modified T-cells under development by companies such as Juno Therapeutics and Novartis have shown promising Phase 1 results.

ERYTECH believes that these products can be complementary with GRASPA<sup>®</sup>.

## **6.7 ERY-ASP/GRASPA<sup>®</sup>: An innovative treatment entering the market in ALL**

Noting a real need for an L-asparaginase-based drug, ERYTECH developed the product ERY-ASP/GRASPA<sup>®</sup>. ERY-ASP/GRASPA<sup>®</sup> consists of a red blood cell encapsulated L-asparaginase. Encapsulation allows L-asparaginase to destroy asparagine within the red blood cell, without causing allergic reactions and reducing other side effects. ERY-ASP/GRASPA<sup>®</sup> offers prolonged therapeutic efficacy in comparison with other forms and a considerably improved tolerance profile allowing the treatment of fragile patients.

ERYTECH has conducted five clinical trials since 2006, four of which in ALL, in order to establish the efficacy and safety of use of ERY-ASP/GRASPA<sup>®</sup>.

Based on completed clinical studies, ERYTECH filed application for marketing approval through the centralized procedure for Europe in 2015 for ALL, and hopes to obtain a marketing approval by late 2016 / early 2017 in order to launch product marketing in 2017.

In the meantime, ERYTECH in 2014 launched an open trial in order to obtain expanded access (Expanded Access Program or EAP) to give access to GRASPA<sup>®</sup> to patients who are allergic to all current forms of asparaginase. In the context of this EAP, on the date of this Reference Document, 13



patients have been treated with several doses of GRASPA<sup>®</sup> and the Company has received a positive opinion from the DSMB at the end of the tolerance analysis on the first seven patients treated. Recruitment will continue in the context of the EAP while waiting for the Company to launch a global pivotal clinical trial on these doubly allergic patients.

The European Drug Agency (EMA) and the American Food and Drug Administration (FDA) have granted the status of orphan drug to ERY-ASP/GRASPA<sup>®</sup> in ALL, which gives it marketing exclusivity after it obtains marketing approval on the product for 7 and 10 years in the United States and Europe respectively.

#### 6.7.1 L-asparaginase encapsulated for greater efficacy and improved safety

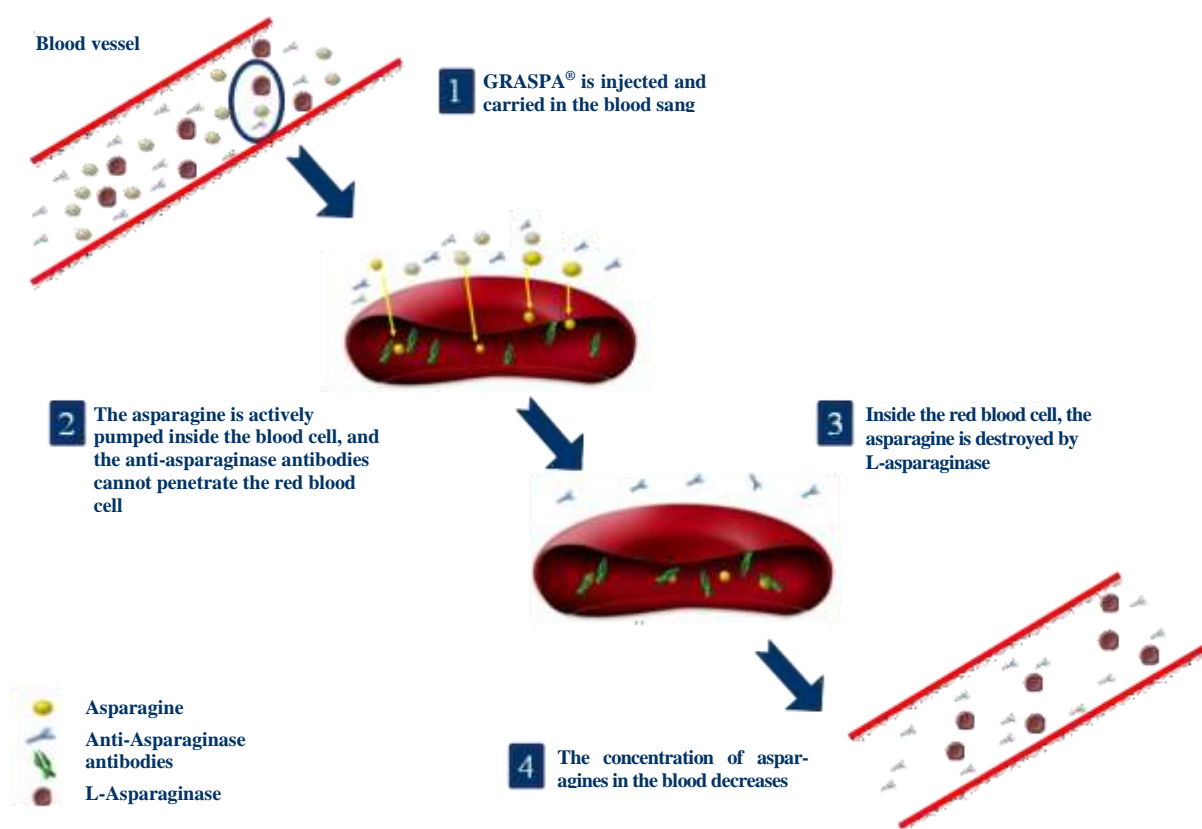
ERY-ASP/GRASPA<sup>®</sup> consists of the encapsulation of the enzyme L-asparaginase. The red cell membrane protects the L-asparaginase from the antibodies that are present in the patient's blood and would likely substantially lessen or completely neutralize the enzyme activity or cause a hypersensitivity reaction. Thus, L-asparaginase remains active within the red blood cell without causing immune or allergic reactions in the patient. The red blood cells are biocompatible vehicles with a half-life of around one month in the body. This half-life, coupled with the protection of the cellular membrane, allows the therapeutic active substances that have been encapsulated in the cell to remain longer in the body, thus increasing the duration of their therapeutic effect and their potential efficacy with lower doses and fewer injections.

The encapsulation of L-asparaginase therefore not only significantly improves the drug's safety profile but also maintains the therapeutic efficacy of the enzyme over a long period compared to directly administering it to the patient. For this reason, ERY-ASP/GRASPA<sup>®</sup> will be able to be administered to fragile patients who cannot receive the current forms of L-asparaginase and offer all patients an effective treatment with fewer injections and fewer side effects.

As illustrated in the following diagram, asparagine is an amino acid that naturally enters the red blood cell and ERYTECH's technology does not interfere with this natural mechanism<sup>21</sup>. The enzyme encapsulated in the cell, L-asparaginase, can then degrade asparagine into L-aspartic acid and ammonia. The concentration of asparagine in the patient's blood decreases and leukemic and cancer cells are deprived of the asparagine they need to live, grow and develop.

Mode of action

<sup>21</sup> Ataulakhanov 1985



## 6.7.2 Clinical results and ongoing clinical programs for acute leukemia

Clinical development program for acute leukemia

At December 31, 2015:

Clinical trial	Status	Number of patients included in the study
Phase I/II study in adults and children with relapsed ALL (Europe)	Completed	24
Phase II study in patients over the age of 55 for first-line treatment (Europe)	Completed	30
Phase II/III study in adults and children with relapsed ALL (Europe)	Completed	80
Phase I/II study in adults over the age of 40 with ALL (in the United States)	Ongoing	12-18
Phase IIb study in patients over the age of 65 with AML (Europe)	Ongoing	123
Expanded Access Program for ALL in children and adults not eligible for other forms of asparaginase (France)	Ongoing	N/A
<b>Total</b>		<b>269 – 275</b>

This section presents the protocols for these completed and ongoing clinical studies, and provides a breakdown of the results:

Phase I/II clinical trial in adults and children with relapsed ALL

Between 2006 and 2009, ERYTECH conducted a Phase I/II randomized, multi-center (France and Belgium) clinical trial of GRASPA® in comparison with the reference treatment (free L-asparaginase – Kidrolase®) on 24 patients - children and adults with ALL in relapse. The study has demonstrated the safety use of GRASPA®, its efficacy over time in reducing the level of plasma asparagine in a single injection by an amount equivalent to that observed after up to 8 injections of free L-asparaginase (standard treatment), as well as fewer side effects associated with L-asparaginase (high-grade allergic reaction and cases of reduced coagulation disorders).

#### Study protocol:

The main objective of this comparative study was to determine the relationship between the dose of GRASPA® (three doses tested: 50, 100 and 150 IU/kg) administered and the period during which plasma asparagine was reduced (depletion) in the sick patient. The trial was also designed to assess the efficacy profile of GRASPA® in comparison with the standard treatment through the duration of activity of the asparaginase, as well as the tolerance of the product through the study of side effects related to the encapsulated L-asparaginase GRASPA®.

The protocol for the clinical trial consists of treating a portion of the adult patients or children in ALL relapse, using the standard treatment, i.e. chemotherapy combined with free asparaginase Kidrolase®, then the rest of the patients with chemotherapy associated with GRASPA®. Patients were randomly distributed into 4 groups of 6 people: three groups received three gradual doses of GRASPA® (50, 100 and 150 IU/kg) in parallel and on a double-blind basis in addition to chemotherapy; the 4th control group received only the free asparaginase standard treatment (Kidrolase®) in combination with chemotherapy.

#### Results:

This Phase I/II study showed that GRASPA® produced an average asparagine plasma depletion duration of 18.6 days after the first injection dosed at 150 IU/kg, a period equivalent to the average depletion observed in the control group treated with Kidrolase® (which has an average depletion duration of 20.6 days after 8 injections of a 10,000 IU/m<sup>2</sup> dose administered every three days).

A reduction in side effects was also observed for GRASPA®, particularly with regard to the occurrence of allergies, pancreatitis or coagulation disorders regardless of the product dosage administered. The table below presents the main clinical results of the Phase I/II study in adults and children with relapsed ALL during the first treatment cycle.

#### Clinical results of the Phase I/II study in adults and children with relapsed ALL

	Kidrolase® (standard L-asparaginase) (n=6)	GRASPA® (n=18)
	N (%)	N (%)
Allergic reaction	3 (50%)	0 (0%)
including high grade (3 or 4)	2 (33%)	0 (0%)
Clinical pancreatitis	0 (0%)	0 (0%)
Pancreatic enzyme elevation	1 (17%)	3 (16%)
Liver problems	3 (50%)	7 (38%)
Hypoalbuminemia	2 (33%)	0 (0%)
Coagulation disorder	4 (67%)	3 (17%)
including clinical thrombosis	1 (17%)	0 (0%)

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Source: Domenech e.a, BJH 2010

The injections of GRASPA® in dosages of 50 IU/kg were too weak to result in depletion of the L-asparaginase, even though injections with higher dosages resulted in sufficient depletion in 85% and 71% of the patients who received dosages of 100 and 150 UI/kg respectively. The patients in the groups that received the two highest doses presented rates of complete remission of 77% and 64% respectively.

***Phase II clinical trial in patients over the age of 55 with ALL as first-line treatment***

In 2008, ERYTECH conducted a Phase II, dose-escalation clinical trial on GRASPA® as first-line treatment in 30 patients over the age of 55 with ALL and without the Philadelphia chromosome (Ph-ALL). These clinical trials confirmed a favorable tolerance profile for GRASPA® in a particularly fragile population of older adult patients, and an absence of clinical allergies and absence of pancreatitis. Moreover, this trial showed that GRASPA® (100 IU/kg) resulted in complete remission for 77% of patients with a median survival improved by six months compared to historical data.

*Study protocol:*

The study's main objective was to determine the maximum tolerated and effective dose of GRASPA® (among the three doses of 50, 100 and 150 IU/kg) in combination with chemotherapy in the population studied. This clinical trial also aimed to evaluate the side effects related to the investigational drug in combination with chemotherapy, its pharmacokinetic and pharmacodynamic parameters and the rate of complete remission after treatment.

The study was open-label with a three-patient cohort and included escalating doses of GRASPA® (50 IU/kg, 100 IU/kg and 150 IU/kg). After administration and review of the clinical response of the first cohort to the lower dose of GRASPA®, an independent monitoring board approved the transition to the higher dose. Patients were monitored every three to four weeks and then every two to three months to collect data pertaining to patient survival.

*Study results:*

The following table shows the main results of the Phase II clinical trial by dose of GRASPA® administered:

***Clinical results of the Phase II study in patients over the age of 55 with ALL as first-line treatment***

	GRASPA® (n=3)	50	GRASPA® 100 (n=13)	GRASPA® 150 (n=14)
	N (%)	N (%)	N (%)	N (%)
Clinical allergies	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Clinical pancreatitis	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Pancreatic enzyme elevations	1(33%)	2 (15%)	3 (21%)	3 (21%)
Thrombosis/attack	1(33%)	1 (8%)	2 (14%)	2 (14%)
Reduction of ATIII	2 (67%)	3 (23%)	7 (50%)	7 (50%)
Complete remission	2/3 (67%)	10/13 (77%)	9/14 (64%)	9/14 (64%)

Median survival	-	15.6 months	9.5 months
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Source: Hunault – Berger e.a., ASH abstract #1473, 2012

***Phase II/III clinical trial in adult and pediatric patients in relapse in ALL***

The GRASPIVOTALL study (GRASPALL 2009-06) is a controlled, multi-center Phase II/III clinical trial performed on 80 children and adults with relapsed or resistant acute lymphoblastic leukemia (ALL). The study is a three-arm trial. The first two compare GRASPA® with native E. Coli L-asparaginase, both in association with standard chemotherapy (COOPRALL), in a randomized study with a proportion of one to one in patients without a history of allergy to L-asparaginase. The third arm is an open study evaluating GRASPA® in patients who have had allergic reactions to L-asparaginase during first-line treatments (GRASPA-s).

Analysis of the data from the GRASPIVOTALL clinical trial, after one year of monitoring, demonstrates that the study convincingly achieved its primary objectives, and its secondary objectives confirm a favorable profile for the clinical efficacy of GRASPA®. The study also shows favorable results in patients with histories of allergies to L-asparaginase.

The primary evaluation criterion of this study consisted of two objectives, in line with the opinion of the CHMP:<sup>22</sup> a) a higher tolerance, resulting in a significant reduction in the incidence of allergic reactions to GRASPA® compared with the control group, and b) a duration that was not lower of the asparaginase activity, above the threshold of 100 UI/l, during the induction phase in non-allergic patients. The two criteria needed to be satisfied for the study to be considered positive. The main secondary objectives of efficacy involved complete remission (CR), minimal residual disease (MRD), progression-free survival (PFS), and overall survival (OS).

The primary objectives achieved were as follows:

- Statistically significant reduction in allergic reactions: none of the 26 (0%) patients treated with GRASPA® had an allergic reaction, as compared to 13 patients out of 28 (46%) treated with native L-asparaginase in the control group (p<0.001).
- Statistically significant increase in the duration of activity of the circulating asparaginase: in the GRASPA® group, the asparaginase levels were maintained below 100 IU/l for 20.5 days on average, with at most 2 injections during the first month of treatment (induction phase), as compared to 9.6 days in the control group (p<0.001).

The secondary objectives confirm a favorable profile for the clinical efficacy of GRASPA®. At the end of the induction phase, 15 patients (65%) in the GRASPA® group showed complete remission, as compared to 11 patients (39%) in the control group.

Equally promising results were seen in patients with histories of allergies to L-asparaginase. A favorable clinical profile was found in patients with histories of allergies to L-asparaginase. Only three patients had slight allergic reactions.

These results confirm the prior observations made with GRASPA® in the randomized, progressive dosage Phase I/II in 24 patients with a relapse of their ALL, and the Phase II study in ALL patients over the age of 55 who received first-line treatment.

**Summary table of the results of Phase III of the GRASPIVOTALL clinical trial with ERY-ASP/GRASPA®:**

	Randomized groups GRASPA®    L-ASP	HypSen group GRASPA®
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<sup>22</sup> Based on the scientific opinion obtained by the Scientific Advice Working Party (SAWP)/Commission for Human Medicinal Products (CHMP) in the European Drug Agency (EMA).

	N=26	N=28		N=26
Primary objectives				
Duration with asparaginase activity >100 UI/l (days)*	20.5±5.2	9.4±7.4	p<0.001	18.6±6.3
Hypersensitivity to asparaginase				
All grades	0 (0%)	13 (46%)	p<0.001	3 (12%)
Grade ≥ 3	0 (0%)	7 (25%)		0 (0%)
Main secondary objectives				
Complete remission**	17 (65%)	11 (39%)	p < 0.05	14 (54%)
Overall Survival at 6 months	92.3%	78.6%		73.1%
Overall Survival at 12 months	76.9%	67.9%		50.0%
Event Free Survival at 6 months	75.7%	60.7%		60.4%
Event Free Survival at 12 months	64.9%	48.6%		50.3%

\*measured in total blood\*\* at the end of induction

On May 30, 2015, the Company presented the complete results of its Phase III pivotal study on GRASPA® in acute lymphoblastic leukemia (ALL) at the 51st Annual Congress of the American Society of Clinical Oncology (ASCO).

The presentation was titled:

“Clinical activity of ERY001 (erythrocyte encapsulated l-asparaginase) and native l-asparaginase (L-ASP) in combination with COOPRALL regimen in Phase III randomized trial in patients with relapsed acute lymphoblastic leukemia (ALL)”

The main conclusions of the study presented were as follows:

- GRASPA®, combined with chemotherapy, demonstrated the maintenance of activity for the asparaginase longer than with L-ASP for the treatment of patients with ALL. The duration of activity of asparaginase greater than 100 IU/l was 20.5 days in the GRASPA® group versus 9.4 days in the control group L-ASP (p < 0.001).
- GRASPA® demonstrated a significant reduction in the risk of hypersensitivity reactions when compared with the L-ASP. No hypersensitivity reactions of any kind were observed in the GRASPA® treatment group, compared with 46% in the L-ASP control arm (p < 0.001).
- The prolonged activity of the asparaginase resulted in an improvement in the full remission rate. 65% of the patients in the GRASPA® group were thus in full remission after the induction phase, compared with 39% of the patients in the control group (p=0.026).
- The treatment was generally well tolerated, with a low risk of major incidents such as coagulation disorders (35% of the patients in the GRASPA® group compared with 82% of the patients in the control group, and 35% of the patients in the hypersensitive group<sup>23</sup>), pancreatic toxicities (27% of the patients in the GRASPA® group compared with 50% of the patients in the control group, and 27% of the patients of the hypersensitive group) and hepatic toxicities (19% of the patients in the GRASPA® group versus 43% of the patients in the control group and 27% of the patients in the hypersensitive group).

<sup>23</sup> Percentage of patients with at least one adverse effect related to the medication during the induction phase.



- The favorable profile of harmless effects and efficacy of GRASPA® offers effective alternative options for patients previously treated with asparaginase, particularly those who have already developed a hypersensitivity to asparaginase derived from E.coli.
- The plenary session was pleasantly closed by the commentator, who concluded by considering GRASPA® as an “advance.” The main role of the commentator is to give to the oncology medical community a constructive criticism on the research, the questions discussed, the results presented, and the ability of the publications to open new perspectives in this medical area.

On December 8, 2015, at the 57<sup>th</sup> annual conference of the American Hematology Society, the Company announced the presentation of additional data from the pivotal Phase II/III study with GRASPA®, in addition to the data that already supported the potential benefit of GRASPA® in combination with chemotherapy in the treatment of ALL.

The presentation included, in addition to the tolerance and efficacy data already reported:

- Two-year monitoring of event-free survival (EFS) and overall survival (OS). Two-year survival data confirm the positive trend that was already observed after one year of monitoring. Median event-free survival was 11.8 months in the group treated with the native L-asparaginase, whereas that median was not yet reached in the arm treated with GRASPA® after 24 months of monitoring. Median overall survival was not reached in either group. The main conclusion of this presentation is that the safety profile and favorable efficiency of GRASPA® offer an effective alternative for patients who have previously been treated with therapy that includes asparaginase.
- An average period of asparaginase activity above the threshold of 100 IU/L during the 20-day induction phase ( $\pm 5.2$  days) in the GRASPA® arm versus 9.4 days ( $\pm 7.4$  days) in patients who received the native L-asparaginase ( $p < 0.001$ ). In addition, L-asparaginase activity was maintained for 18.6 days ( $\pm 6.3$  days) in patients who had a history of allergic reactions. This prolonged activity of the enzyme with GRASPA® was observed across various population subgroups (according to age, risk, and presence or absence of a history of allergic reactions). The difference between GRASPA® and the native L-asparaginase was more significant in adult or high-risk patients, since the average length of activity was 3.2 days and 6.3 days respectively with the native L-asparaginase versus 19.3 days and 20.9 days with GRASPA®.
- The 80 patients who were treated in the Phase II/III study had received an initial line of treatment based on L-asparaginase. One-third of these patients had developed an allergic reaction to L-asparaginase; 58% of these patients had a positive basic antibody level. In the other two-thirds, approximately 25% also had a positive basic antibody level. GRASPA® has consistently demonstrated a period of greater activity and a lower frequency of allergic reactions regardless of the basic antibody level. Five out of seven patients (71%) of those treated with native L-asparaginase who had a positive antibody level have developed allergic reactions, versus one in 21 (5%) in the GRASPA® group. A positive antibody level appeared to be associated with a drop in clinical activity in all treatment arms. These data provide a further rationale to investigate GRASPA® among patients with ALL in the first line of treatment.



### ***Phase IIb clinical trial in patients over the age of 65 with AML***

The ENFORCE 1 study is a multicenter international randomized Phase 2b study that evaluates the efficacy and safety of GRASPA® in the treatment of patients over 65 who are newly diagnosed with AML and are unable to receive intensive chemotherapy. Generally, L-asparaginase is very rarely used for this indication. Although the efficacy of this treatment has been demonstrated for AML, the risk of side effects for this fragile population of often elderly patients is too great to justify the administration. The main goal of this study is to assess the efficacy of GRASPA® when it is added to the standard product (cytarabine in low doses). To do this, overall survival (OS) (based on a recently approved protocol amendment that replaces progression-free survival (PFS) with OS, which is considered to be a better evaluation criterion for this indication) will be analyzed between patients who have received GRASPA® in combination with low doses of cytarabine, and patients who have received only low doses of cytarabine. This study plans to recruit 123 patients, 2/3 of whom will be treated with GRASPA®. The study protocol includes monitoring patients for 24 months, an analysis of the first 30 and 60 patients to analyze tolerance by a Data Safety Monitoring Board (DSMB), and a third interim analysis when sixty patients have experienced a progression of their disease.

The first two reviews have been conducted by the DSMB (a committee of independent experts) on 30 and 60 patients respectively. The first analysis by the DSMB was performed in November 2013, and the second in August 2014. The committee of independent experts has issued two favorable opinions with regard to the continuation of this clinical trial after evaluation of the product's safety in the first 30 and 60 patients treated.

In addition, on January 6, 2016, the Company announced that the DSMB had conducted its third safety review of the Phase IIb ENFORCE 1 study in acute myeloid leukemia (AML). This third assessment by the DSMB involved 105 patients and, as for the first two assessments, did not identify any tolerance or safety concerns. The DSMB also noted that the inclusion of the remaining patients was not likely to change their observations regarding the main endpoints, but that it could improve the study's statistical power. Based on the DSMB's comments, ERYTECH decided to continue enrolment in the trial until completion, which is expected during the first half of 2016. To date, more than 90% of the 123 patients have been included in the study through more than 20 clinical centers active in France, Spain, Finland, Norway and Italy. The first results of the study are expected in 2017.

Depending on the results of this study, ERYTECH will determine the next steps in the development of this research program.

On May 31, 2015, the Company presented a poster on the design of the current Phase IIb trial, titled: "GRASPA-AML 2012-01 study: A multi-center, open, randomized Phase 2b trial evaluating ERY001 (L-asparaginase encapsulated in red blood cells) plus low-dose cytarabine vs low-dose cytarabine alone, in treatment with newly diagnosed acute myeloid leukemia (AML) elderly patients, unfit for intensive chemotherapy"

#### **6.7.3 Obtaining orphan drug designation and its benefits**

The regulatory authorities in Europe (EMA) and in the United States (FDA) have established specific procedures for marketing approval and reimbursement for drugs that treat orphan diseases in order to encourage the development and innovation efforts for these diseases with a very small number of patients. In particular, requirements for the necessary clinical studies are adjusted to take into account the small patient population and procedures for obtaining Marketing Approval (MA) are often facilitated and accelerated to meet public health needs.

The major advantage of this legislation is to allow manufacturing pharmaceutical companies selling products with orphan drug designation to take advantage of exclusive marketing after obtaining an MA for the product for 7 and 10 years, in the United States and Europe respectively.

The EMA and FDA have granted “Orphan Drug Designation” to ERY-ASP/GRASPA® in ALL, AML and pancreatic cancer.

#### 6.7.4 Marketing GRASPA®

On the basis of the results from the Phase II/III clinical trial in adults and children with ALL in relapse, and based on previous studies, ERYTECH filed a request for MA through the European centralized procedure in September 2015, and hopes to obtain marketing approval by late 2016 / early 2017 in order to begin marketing the product in 2017.

The Company will seek the broadest indication possible for its MA from the health authorities. It will then be up to the health authorities to accept it or not, and to specify whether additional trials are necessary to obtain the MA (cf. Section 4.4.1 and Chapter 6.1).

#### 6.7.5 Positioning of GRASPA® on the market

GRASPA® will be marketed by Orphan Europe (Recordati Group) in 38 European countries and by Teva Group in Israel. The product’s positioning in terms of marketing strategy will be developed in consultation with ERYTECH.

For ALL, ERYTECH anticipates that the dynamics of adopting the product will begin with the fragile populations first, such as older adult and elderly patients who cannot receive the current forms of L-asparaginase, and with relapsed or resistant adult and pediatric patients who also cannot be treated with L-asparaginase. The use of GRASPA® can be naturally extended to other patients with the clinical experience acquired by the onco-hematologists and by capitalizing on the proven safety of use of GRASPA®.

Worldwide sales for the three existing forms of treatments based on L-asparaginase are estimated at \$300 million<sup>24</sup>. However, these forms of treatment actually target only a limited number of patients with acute leukemia, and the Company believes that a large number of other patients could benefit from a perfected L-asparaginase treatment.

The lack of an L-asparaginase-based treatment that is approved and/or used in AML will allow GRASPA® to be positioned for first-line treatment for these patients. Clinicians have expressed strong interest in being able to use L-asparaginase in the treatment of AML and ERYTECH intends to meet this demand with GRASPA®.

### 6.8 Commercialization of GRASPA® in Europe and Israel

ERYTECH has signed two major partnership agreements to commercialize GRASPA® in 38 European countries with Orphan Europe (Recordati Group) and in Israel with Teva Group. Thanks to the innovative nature of GRASPA®, its ability to satisfy unmet medical needs and its advance in clinical development, ERYTECH was able to obtain favorable terms, particularly with regard to the sharing of future profits. Both partners have recognized trade capacities and can effectively promote GRASPA® in their respective territories.

Furthermore, it should be noted that there are relatively few potential prescribers of GRASPA® in each country, mainly hemato-oncologists, who are clearly identified. Therefore, awareness of specialized products such as GRASPA® and adoption of the drug can occur very quickly. In addition, GRASPA® does not require the modification of existing ALL treatment protocols since L-asparaginase is already included in them. For specialty products like GRASPA®, the commercial and promotional resources

<sup>24</sup> Source: Jazz Pharmaceuticals and ERYTECH

required are modest compared to other drugs, in general practice for example, thereby making high margins possible.

European partnership with Orphan Europe (Recordati Group) for commercialization in Europe:

On November 23, 2012, ERYTECH signed an exclusive licensing and marketing agreement with Orphan Europe (Recordati Group), a company specialized in the development, production, and marketing of drugs for orphan diseases. Orphan Europe is a subsidiary of Recordati, a major pharmaceutical group in Europe.

Orphan Europe (Recordati Group) holds a portfolio of orphan drugs already commercialized in different fields, including neonatal, pediatrics and metabolic disorders.

Orphan Europe (Recordati Group) is a leading player in the field of orphan diseases and has the medical, clinical, regulatory and commercial expertise to market and effectively commercialize GRASPA® in Europe. Orphan Europe is a strategic business for Recordati, which acquired the company in 2007 for €135 million and built it up further with the acquisition of a portfolio of rare and orphan disease drugs in the United States for \$100 million.

Orphan Europe (Recordati Group) will market GRASPA® for the treatment of ALL and AML in 38 European countries, including all the countries in the European Union. The parties have the opportunity to discuss the extension of this agreement to other areas around Europe and other indications.

ERYTECH is retaining production of GRASPA® at its Lyon site and will supply Orphan Europe in the various European countries where the drug will be sold. Orphan Europe (Recordati Group) has agreed not to participate in the development or marketing of competing products containing L-asparaginase for the treatment of ALL or AML.

Pursuant to this agreement, Orphan Europe (Recordati Group) paid €5 million on signing. Orphan Europe (Recordati Group) will have to pay ERYTECH up to €37.5 million in future payments based on various clinical, regulatory and commercial events, and Orphan Europe (Recordati Group) will share the clinical development costs of GRASPA® in AML. ERYTECH will receive a price for product delivered and royalties on the sales made by Orphan Europe (Recordati Group) with GRASPA®, for a total of up to 45% of the net sale price.

Separately, another Recordati Group company subscribed convertible bonds that were converted into an equity stake in ERYTECH's share capital worth €5 million in the initial public offering on Euronext Paris in April 2013.

#### **Partnership with Teva Group for marketing in Israel:**

On March 28, 2011, ERYTECH signed a licensing and exclusive distribution agreement with Teva Group, a global player in the pharmaceutical industry based in Israel, to distribute GRASPA® in that country in the treatment of ALL. Additionally, if other marketing authorizations are issued in Europe for GRASPA® in indications other than ALL, Teva may choose to extend its marketing exclusivity to such other indications in Israel. Teva Group is a diversified pharmaceutical group with a strong strategy in innovative specialized products and particularly in therapeutic fields such as the central nervous and respiratory systems, women's health, oncology, and pain.

In accordance with the terms of the agreement, Teva Group will submit the application for approval of the drug for ALL in Israel and ensure marketing and distribution in the long term in that country. Teva Group will make milestone payments and share net earnings of product sales in Israel.

### **Marketing strategy for other countries:**

ERYTECH retains all rights to ERY-ASP outside the 38 European countries covered by the partnership with Orphan Europe (Recordati Group) for ALL and AML, and in Israel with Teva Group for ALL. In particular, ERYTECH retains all rights to commercialize ERY-ASP outside Europe and Israel, particularly in the United States, for the treatment of ALL and AML, and in all other indications, such as solid tumors for example, outside Israel. ERYTECH also retains all rights to develop and market its other candidate products.

Subject to obtaining the MAs, ERYTECH hopes to begin marketing activities through the creation of a targeted sale and marketing unit to commercialize its products in the United States and abroad. ERYTECH believes that this unit will allow it to target the community of physicians specializing in the treatment of patients for whom its candidate products have been developed. ERYTECH will be able to sign other marketing and distribution agreements with third parties in specific geographic areas, such as Russia, Turkey, other countries in the Middle East, and all African countries, for all its candidate products that have received a marketing approval. In some of these countries, Orphan Europe (Recordati Group) has a right of first negotiation.

ERYTECH is also planning to develop a sales and marketing management unit in order to create and implement its marketing strategies for any products it will market directly and to oversee and support its sales teams force. The responsibilities of this unit will include developing educational initiatives on the Company's products on the market, and the establishment of a network with opinion leaders in the relevant fields of medicine.

### **Commercial scale industrial process and secure supply**

The Company has a production unit with enough capacity to cover the needs of the European market for approximately the first two years after initial marketing. This unit meets the highest requirements of ANSM and has "Établissement Pharmaceutique Exploitant" regulated status.

The Company has secured its supply for the main raw materials needed to manufacture ERY-ASP/GRASPA®:

L-asparaginase: ERYTECH Pharma and Medac have signed two worldwide exclusive long-term agreements according to which Medac supplies ERYTECH with two forms of asparaginase that ERYTECH uses for the production of ERY-ASP/GRASPA®, for clinical trials and for the sale of ERY-ASP/GRASPA®, for the therapeutic indications defined by ERYTECH. Medac is a German pharmaceutical company based near Hamburg that commercializes L-asparaginase (see also Chapter 22 of this Reference Document).

Red blood cells: ERYTECH signed two supply contracts with the Établissement Français du Sang [French Blood Facility] and the American Red Cross, two well-known blood banks, for transfusion quality human red blood cells.

## **6.9 Development of ERY-ASP for leukemia in the United States**

ERYTECH's objective is to develop ERY-ASP in the United States, which represents a significant potential market for ALL and AML.

ERYTECH plans to capitalize on the clinical studies already completed or underway in Europe and replicate the clinical development of ERY-ASP in the United States. On March 21, 2013 ERYTECH obtained Investigational New Drug (IND) approval from the FDA to begin a Phase Ib clinical trial in ALL, and began recruiting its first patients in the third quarter of 2014. ERYTECH believes that this clinical trial will be finalized in 2016. This study will also make it possible to pursue clinical development for ALL and AML alone or in a partnership. Further clinical development may include

Phase II/III clinical trials for ALL and AML and could make it possible to submit an initial application for a market authorization by 2018/2019 for the indication of “double allergic” patients.

ERYTECH has established a close partnership with the American Red Cross in Philadelphia. Under this agreement, the American Red Cross will provide red blood cells, a classified production area and staff trained by ERYTECH, under the supervision of an ERYTECH representative seconded to Philadelphia.

In April 2014, ERYTECH created a subsidiary in the United States (Cambridge), ERYTECH Pharma Inc., 100% held by the parent company, ERYTECH Pharma.

### **Phase I clinical trial in adult patients as first-line treatment for ALL**

In 2013, ERYTECH launched a Phase Ib clinical trial in the United States for patients over 40 years of age without the Philadelphia chromosome as first-line treatment in ALL, in combination with the standard chemotherapy (CALGB chemotherapy in the United States), in a sample of 12 to 18 patients with escalating doses (50 to 150 IU/kg).

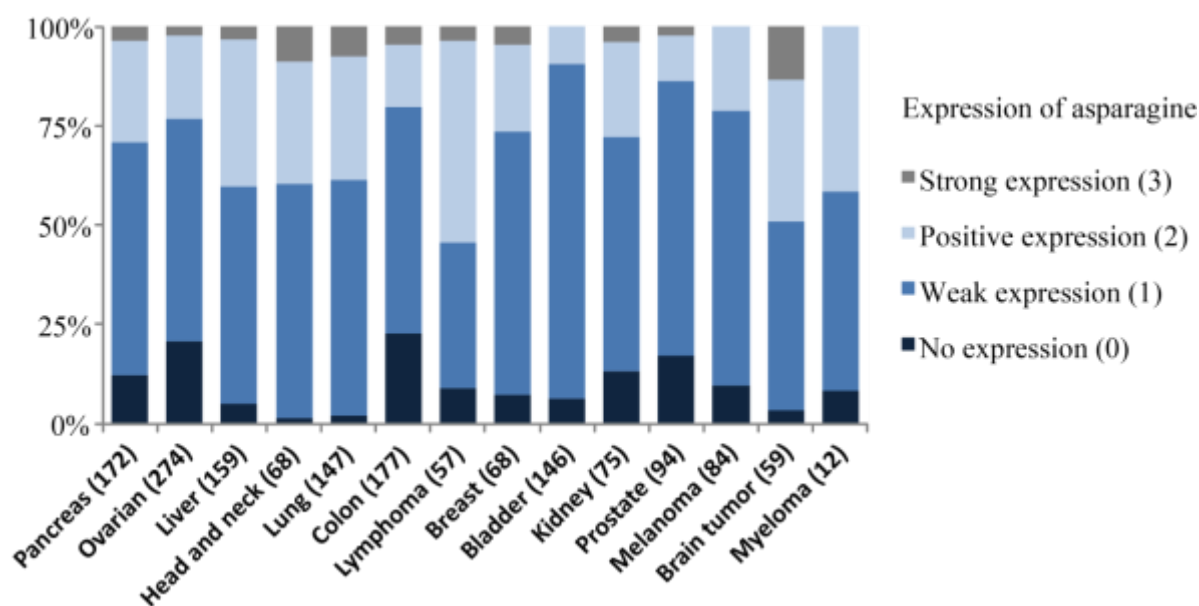
This multi-center, non-randomized clinical trial strictly in the United States aims mainly to validate the toxicity, safety and efficacy profile of ERY-ASP, in combination with standard chemotherapy. This Phase Ib trial is the first clinical trial conducted by ERYTECH in the United States. As a toxicity study, the results will also be used in the Phase I AML trial.

The safety data for the first cohort of three patients dosed at 50 UI/Kg were reviewed in June 2015 by a steering committee consisting of members of the DSMB and investigators in the study. No safety concerns were identified and this steering committee recommended escalating the dose to 100 UI/Kg. In addition, the study was amended to lower the age for patients' inclusion from 40 to 18, and remove the waiting periods between each patient. The request to modify the protocol has been submitted to the relevant Institutional Review Committees (IRC) for approval. The Company expects this study to be completed in 2016.

### **6.10 Potential new indications for ERY-ASP: Solid tumors**

As with leukemia, the rationale of treating tumor cells deprived of asparagine synthetase is also applicable to solid tumors, as long as they do not express asparagine synthetase and need to consume the asparagine contained in the plasma. Thus, ERYTECH conducted a study in collaboration with the MD Anderson Cancer Centre to assess the proportion of tumors potentially sensitive to asparaginase, i.e. tumors that produce little or no asparagine synthetase.

Sensitivity of some solid tumors to asparagine deprivation



Source: Dufour et al., “Pancreatic Tumor Sensitivity to Plasma L-Asparagine Starvation,” *Pancreas*, 2012

ERYTECH also validated an immunohistochemistry test using tumor tissue to detect whether the tumor produces asparagine synthetase and therefore whether it is resistant or sensitive to asparaginase.

Moreover, the Company entered into an exclusive license agreement with the NIH to develop a companion test to determine tumor sensitivity to asparaginase. The test is currently used in clinical trials and could be developed commercially with an industrial partner.

ERYTECH has conducted a Phase I study on pancreatic cancer to demonstrate the safety of ERY-ASP. The clinical trial demonstrated that ERY-ASP was well-tolerated even at high doses. With these initial clinical results for solid tumors, ERYTECH has launched a Phase II study for pancreatic cancer and plans to expand this development to other solid tumors of interest.

ERYTECH is preparing for the launch of a Phase II study on non-Hodgkin lymphoma. The Company believes that it will be able to use the safety data collected during its other clinical trials conducted to date as a basis for beginning this clinical trial directly in Phase II.

#### Phase I and Phase II clinical trials on pancreatic cancer

In 2011, ERYTECH finalized a Phase I open clinical trial on 12 patients with pancreatic cancer at four sites in France. The patients participating in the study were divided into four groups of three patients. ERY-ASP was administered by injection of four different doses: 25 IU/kg, 50 IU/kg, 100 IU/kg or 150 IU/kg. The main objective of this study was to determine the maximum tolerance dosage of the product. The second objective of the study was to assess the safety and preliminary efficacy indicators of the product. No toxicity limiting the dose was reported, even for the strongest dose administered in the study. The treatment led to a depletion of the asparagine with a trend toward extension of the duration of depletion with a higher dose. The results of this study were used as a basis for more advanced clinical research with a dose of 150 IU/kg.

In 2014, based on the initial clinical results in solid tumors, ERYTECH continued the development of ERY-ASP in pancreatic cancer in a Phase II study with patients as the second line of treatment.

The Phase II study initially involved a total of 90 patients randomized at a 2:1 ratio between the standard treatment (Gemcitabine or Folfox) with or without ERY-ASP.



Clinical trial	Status	Number of patients included in the study
Phase I study on pancreatic cancer (France)	Completed	12
Phase II study on pancreatic cancer (France)	Ongoing	100
<b>TOTAL</b>		<b>102</b>

In the context of this clinical trial, ERYTECH is using a diagnostic test developed by the NIH which the Company holds under a license to assist it in the identification of cancer cells that might respond to the GRASPA® L-asparaginase treatment and, based on the results of these tests, ERYTECH stratifies the patient population. The main evaluation criterion for this clinical trial is progression-free survival at 4 months after the start of treatment in patients whose tumors are deficient in ASNS.

The DSMB conducted safety analyses of the product in the first three patients treated with the two combinations (Gemcitabine or FOLFOX), and a third broader analysis of the product in the first 24 patients was performed by this DSMB. In each of these analyses, no safety problem was identified by the DSMB. The initial goal to recruit approximately 90 patients was met recently and ERYTECH has chosen, and announced in its February 23, 2016 press release, to continue recruitment in order to increase the statistical power of the study and to better assess the treatment in sub-groups. The first results of the trial are expected by the end of 2016.



## 6.11 Other ERYCAPS development projects

ERYTECH's platform technology is versatile and opens up many possibilities for developing new drugs. The demonstration of the efficacy of the technology was mainly achieved with asparaginase, but it is possible to encapsulate into red blood cells other enzymes, molecules or proteins for which long-duration therapeutic activity or rapid or precise targeting is desired.

### TEDAC/ERY-MET/ERY-ADI

In addition to its pipeline of products centered on the treatment based on L-asparaginase, ERYTECH is using its ERYCAPS technology to identify other enzymes able to induce tumor starvation. ERYTECH has received grants from BPI France to finance its research program TEDAC, which is intended to identify other agents able to induce tumor starvation as well as the companion diagnostic tests. In pre-clinical studies conducted within the TEDAC program, ERYTECH has identified two other amino acids and their respective enzymes, methionine- $\gamma$ -lyase (MGL) and arginine deiminase (ADI) which, according to the Company could be promising treatments once encapsulated into red blood cells. ERYTECH is planning to launch a Phase I clinical trial in the second half of 2016 for its ERY-MET candidate product, which is composed of MGL encapsulated in red blood cells, and a subsequent clinical trial in 2017 for its ERY-ADI candidate product, which is composed of ADI encapsulated in red blood cells.

### Enzyme Replacement Therapies or ERT

ERYTECH believes that its platform also offers other attractive development opportunities, beyond oncology, in enzyme replacement therapies.

Enzyme replacement therapy is a treatment that aims to replace a defective or missing enzyme in a patient. An important class of genetic diseases also called hereditary metabolic diseases is caused by the lack of encoding genes for enzymes involved in the conversion of substances (substrates) into other substances (products). In most of these pathologies, the symptoms associated with the enzyme deficiency will be caused either by a toxic accumulation of the substrates, or by a decrease in the ability to synthesize essential products. The potential of new medications in this area is important because a limited number of lysosomal storage diseases and, more broadly, inherited metabolic diseases have treatments, and existing therapies face significant challenges.

Erytech is investigating the use of its ERYCAPS technology to enable long circulating enzymatic activity or specific targeting of certain cells, as these applications may result in new enzyme replacement therapy product development opportunities.

ERY-ERT is the latest preclinical development that the Company dedicated to enzyme replacement therapies (ERT), a medical strategy that consists of administering the enzymes to patients in whom they are absent or inadequate.

Most diseases due to insufficient enzymes are linked to genetic diseases; ERTs are administered throughout the life of the patient, and this can potentially cause immune reactions that reduce the efficacy of the treatment.

Based on the results that the Company has obtained with ERY-ASP, the encapsulation of ERT enzymes in red blood cells should extend their lifespan in the bloodstream, thus reducing both the frequency of administration and the possibility of immune reactions.

ERYTECH has also conducted pre-clinical research on enzymes like phenylalanine hydroxylase (PAH) for the treatment of phenylketonuria (PKU) in collaboration with the company Genzyme, and is studying other opportunities for collaboration for other potential applications of ERT.

## **Immunotherapy**

In addition to the use of the ERYCAPS platform for enzyme encapsulation in order to increase their effect and reduce their toxicity, ERYTECH believes that it is able to expand the use of its ERYCAPS platform to develop cancer vaccines. This consists in the development of a new anti-tumor vaccine using the immunotherapy technology or ERY-VAX by intra-erythrocyte encapsulation of tumor antigens and adjuvant(s) to activate immune cells in situ and generate an immune response.

By loading red blood cells with specific antigens, then modifying the membrane of the cells subsequently to make them target specific antigen-presenting cells in the liver or spleen, ERYTECH believes it holds promising clinical research into cancer vaccination applications. The use of red blood cells as tumor-specific antigen carriers makes it possible for them to be delivered specifically and simultaneously to dendritic cells, immune cells. Red blood cells are processed to direct themselves toward dendritic cells which will capture them, absorb them, and thus incorporate the antigens associated with the tumor cells. This results in a classic immune response, i.e. the immune cells introduce these antigens to lymphocytes which are stimulated to specifically become cells responsible for destroying the tumor.

Furthermore, this technology also makes it possible to consider the encapsulation of adjuvants in order to optimize the efficacy of the vaccination.

In pre-clinical studies on three different antigens loaded into red blood cells, ERYTECH has observed promising proof-of concept in three different tumor models. In these studies, ERYTECH has observed a significant increase in the responses of the T Lymphocytes specific to the antigens and delays in tumor growth when the encapsulated antigens, modified to target the liver or spleen, were injected into mouse tumors, as compared to the injections of free form antigens.

The Company is planning to continue to develop this platform in order to validate the initial preclinical data and to define a development strategy for its programs in the preliminary phase. Among the possibilities, the Company may consider the creation of a spin-off company for this technology if it believes it can optimize shareholder value.

## **6.12 Regulations applicable to the Group**

### **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, labelling, 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 a vast program of non-clinical evaluations, also referred to as pre-clinical, laboratory evaluations, preclinical studies in animals and formulation studies performed in accordance with the regulations in force, particularly the FDA's Good Laboratory Practices (GLP);
- submission to the FDA of an Investigational New Drug application (IND) that must enter into effect before the start of clinical trials in humans;
- completion of adequate, correctly controlled trials in humans, in accordance with the regulations in force for INDs and other regulations relating to clinical trials, which are sometimes called Good Clinical Practices (GCP), in order to establish the safety and efficacy of the candidate product in the indication proposed;
- submission of a BLA to the FDA;
- satisfactory completion of an FDA pre-authorization inspection of the manufacturing units in which the product is produced in order to inspect the application of the FDA's current Good Manufacturing Practice (cGMP), and to ensure that the premises, methods and control procedures are appropriate to preserve the nature, dosage, quality, purity and strength of the product;
- possible FDA audit of the preclinical and/or clinical study centers that generated the data provided in support of the BLA; and
- review and validation of the BLA by the FDA before any marketing or sale of the product in the United States.

The data to be provided in support of a BLA are generated within two distinct development phases: the preclinical phase and the clinical phase. The pre-clinical 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 pre-clinical 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](http://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 conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

### **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 labelling 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 pre-clinical 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, sixty 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, pre-clinical 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 interpret 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 labelling or may condition the approval of the BLA on other changes to the proposed labelling, 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 payer 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.

Regulatory, legislative changes or the interpretation of the existing regulations could have repercussions for the Company's activities in the future, requiring for example: (i) changes in its production agreements and/or its commercial operation; (ii) additions to or changes in the labelling of its products; (iii) the recall or shutdown of its products; (iv) requirements to log data and/or provide additional documentation. 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 a patent applicable to an approved drug is eligible for the extension. In addition, the request for extension must be submitted before 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 pre-clinical and clinical research in the European Union are subject to significant regulatory controls. 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. In order to improve the current system, a new regulation, Regulation 536/2014/EU governing clinical trials for drugs for human use, which repeals Directive 2001/20/EC, was adopted on April 16, 2014 and published in the Official Journal of the European Union on May 27, 2014. This regulation on clinical trials is intended to harmonize and streamline the process for authorizing clinical trials, by simplifying the procedures for reporting adverse events, improving supervision of clinical trials and by strengthening the transparency of these trials. It entered into effect on June 16, 2014, but will not apply before May 28, 2016. Until that date, Directive 2001/20/EC governing the conduct of clinical trials remains in force. In addition, the transitional provisions of the new Clinical Trials Regulation offer 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 or nationally:

- the community MA, issued by the European Commission through the centralized procedure, on the basis of the opinion issued by the Committee on Medicinal Products for Human Use (CHMP), the European Medicines Agency (EMA), which is valid through the 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.
- the national MAs, issued at the national level by the authorities of the Member States of the EEA, which cover only their respective territories, are available for products not within the scope of mandatory application of the centralized procedure. Where a product has already been authorized for marketing in a Member State of the EEA, this National MA can be recognized in other Member States through the Mutual Recognition Procedure. If the product has not received a National MA in any Member State at

the time of application, it can be approved simultaneously in various Member States through the Decentralized Procedure. Under the Decentralized Procedure an identical dossier is submitted to the competent authorities of each of the Member States in which the MA is sought, one of which is selected by the applicant as the Reference Member State, or RMS. The competent authority of the RMS prepares a draft assessment report, a draft summary of the product characteristics, or SmPC, and a draft of the labelling and package leaflet, which are sent to the other Member States, referred to as the Concerned Member States, or CMSs, for their approval. If the CMSs raise no objections, based on a potential serious risk to public health, to the assessment, SmPC, labelling, or packaging proposed by the RMS, the product is subsequently granted a national MA in all the Member States (i.e. in the RMS and the CMSs).

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.

### **Orphan Drugs**

In the European Union, Regulation (EC) No 141/2000, as amended, states that a drug will 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.

Regulation (EC) No 847/2000 sets out further provisions for implementation of the criteria for designation of a drug as an orphan drug. 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.

If a Community MA in respect of an orphan drug is granted pursuant to Regulation (EC) No 726/2004, regulatory authorities will not, for a period of 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. However, this period may be reduced to six years if, at the end of the fifth year, it is established for the drug in question that the orphan drug designation criteria are no longer being met; in other words, when it is demonstrated on the basis of available proof that the product is profitable enough that it no longer justifies marketing exclusivity.

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.

Regulation (EC) No 847/2000 lays down definitions of the concepts ‘similar drug’ and ‘clinical superiority’. Other incentives available to orphan drugs in the European Union include financial incentives such as a reduction of fees or fee waivers and protocol assistance. Orphan drug designation does not shorten the duration of the regulatory review and approval process.

## Other European Regulatory Matters

### French Regulatory Framework

In the European Union, the regulation governing clinical trials is currently based on Directive 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 Act 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. Law 2004-806 abolishes the prior notification procedure introduced by the Law Huriet-Sérusclat of December 20, 1988. Indeed, Article L. 1121-4 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. Under Article L. 1123-7 PHC, the Ethics Committee shall 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 pre-clinical 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; this procedure may not, however, be applied more than once. If the sponsor does not alter the content of its request, the request is considered rejected. Under R. 1123-32 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 for clinical trials on medicines for human use as referred to in Article L. 1121-3 of the Public Health Code. Good Clinical Practice rules, or 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 shall apply to all clinical trials, including pharmacokinetics, bioavailability and bioequivalence studies in healthy volunteers as well as Phase 2 to Phase 4 clinical trials.

Personal data collected during clinical trials should be declared in simplified form to the French Data Protection Agency (Commission Nationale de l'Informatique et des Libertés, or CNIL). Patients then have a right to access and rectify this data pursuant to Law 78-17 of January 6, 1978, as amended, on data protection.

The main French regulatory texts concerning the conduct of clinical trials are as follows:

- Law 2004-806 of August 9, 2004 concerning public health policy;
- Decision of November 24, 2006 defining the rules for good clinical practices;
- Decision of January 13, 2011 concerning good manufacturing practices;
- Law 78-17 of January 6, 1978 as amended and its implemented decrees governing the protection of data;

- Law 2002-3003 of March 4, 2002 and its implementing decrees governing patient rights and the quality of the health care system;
- Decision of January 5, 2006 approving a standardized methodology for the processing of personal data performed in the context of clinical trials (standardized methodology MR-001);
- Law 2011-2012 of December 29, 2011 concerning the strengthening of drug health safety and health products; and
- Law 3000-230 of March 13, 2000 concerning electronic signatures, as amended, Decree 2001-272 of March 30, 2001 and Decree 2002-535 of April 18, 2002 concerning electronic signatures. Status of French pharmaceutical laboratories

### **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. For GRASPA<sup>®</sup>, distribution agreements have been signed with Orphan Europe and Teva to market it in Europe and Israel, respectively. These distributors will be responsible for obtaining coverage and reimbursement for GRASPA<sup>®</sup> in these respective territories if the marketing authorization is issued. 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 payers, such as government health programs, commercial insurance and managed healthcare organizations. These third-party payers are increasingly reducing reimbursement levels for medical products and services. The process for determining whether a third-party payer 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 payer will pay for the drug product once coverage is approved. Third-party payers 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 payer's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Further, one payer's determination to provide coverage for a product does not assure that other payers 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 payer 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. We cannot predict the full impact of the ACA on pharmaceutical companies, as most 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, which, due to subsequent legislative amendments, will stay in effect through 2025 unless additional congressional action is taken. In addition, on January 2, 2013, Barack Obama signed the American Taxpayer Relief Act (ATRA) of 2012, which delayed for an additional two months the budget cuts mandated by the "sequestration" measures of the Budget Control Act of 2011. The ATRA, among other results, also reduced the Medicare payments paid to different service providers, including hospitals, imaging centers and cancer centers, and extended the time limit from three to five years for government collection of surplus payments paid to service providers. The way in which drug manufacturers set the prices of their products has recently been under close scrutiny by the US government. For example, there have recently been US congressional investigations and bills drafted aimed at, among other things, increasing transparency in drug pricing, reviewing the links between manufacturers' pricing and their patient-oriented programs, and reforming the methodology used in the government's drug reimbursement program. 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 payers 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 Anti-Kickback Statute (federal anti-corruption law) in the United States, which prohibits persons from soliciting, receiving, offering or paying a remuneration (including any bribe, any under-the-table payment or any reduction), with full knowledge and willingly, directly or indirectly, in cash or in-kind to induce, reward or in return for the recommendation of a person, or the purchase, rental, order or recommendation of an article, an asset, a facility or a service reimbursable under a federal healthcare program, such as Medicare and Medicaid;
- the federal civil and criminal laws concerning false assertions, and the civil laws on financial sanctions, which impose penalties and trigger civil reporting measures against persons and organizations who present, with full knowledge, or cause the presentation of claims of payment from Medicare, Medicaid or other third-party payers that are false or fraudulent, or make a false declaration or false registration for the payment of a false claim, or avoid, decrease or hide an obligation to pay money to the federal government, including providing inaccurate invoices or coding information to clients, or promote a drug without an MA;
- the Health Insurance Portability and Accountability Act (HIPAA) of 1996, which created new federal criminal laws prohibiting the execution of a plan intended to defraud any health insurance plan or to misappropriate, with full knowledge and deliberately, funds from healthcare programs, the prevention, with full knowledge and deliberately, of a criminal investigation of a healthcare violation, the falsification, hiding or covering-up, with full knowledge and deliberately, an important fact, or the production of false declarations of fraudulent declarations concerning the delivery of or payment for health services;
- the Physician Payments Sunshine Act (a federal law ensuring transparency in the compensation received by physicians), signed in the context of the ACA, which requires that the manufacturers of drugs, devices, biologics and medical supplies monitor and declare, every year, the remuneration paid to the CMS and other transfers of value to physicians or hospitals, and certain interests in property or investments held by physicians or the members of their immediately family;
- HIPAA, as amended by the Health Information Technology and Clinical Health Act (HITECH) and its implementing regulations, which impose certain obligations on covered organizations and their partners in terms of confidentiality, security, and transmission of personally identifiable health information; and
- state or foreign laws equivalent to each of the laws and federal regulations listed above, including state anti-corruption laws concerning false claims, which may apply to articles or services reimbursed by any third-party payer, including commercial insurers; the state laws governing transparency or marketing applicable to manufacturers, the scope of application of which can be broader than the federal requirements; the state or foreign laws that require that biopharmaceutical companies comply with the optional compliance recommendations of the biopharmaceutical sector and the relevant compliance recommendations promulgated by the federal government, as well as the state laws governing the confidentiality and security of health information under certain circumstances. Most of these laws differ significantly from each other and may not have the same effect as HIPAA, which makes compliance efforts more complex.

The ACA broadened the reach of the federal fraud and abuse laws by, among other things, amending the intent requirement of the 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 this statute or specific intent to violate it 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 federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal 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, 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.



## 7 ORGANIZATION CHART

As of the date of this document, the Company does not have any branches or secondary facilities.

It wholly owns the subsidiary “ERYTECH Pharma, Inc.,” incorporated in Delaware (U.S.) on April 9, 2014, and headquartered at Riverfront Office Park, One Main Street, Cambridge, MA 02142, USA.

The purpose of the subsidiary is:

- the research, manufacture, import, distribution, and commercialization of experimental drugs, medications, devices, and equipment;
- the provision of all advisory services associated therewith;
- and generally, all financial, commercial, industrial, civil, real estate, or security-related transactions, such as may directly or indirectly relate to one of the purposes specified or such as may facilitate their fulfillment.

To date, the subsidiary ERYTECH Pharma Inc. operates only to support the Company in the United States, primarily for the Company’s medical division, to advance the MA application, and to accelerate clinical trials in the United States via its employees and external consultants. The R&D activities and clinical trials themselves are carried out and supported exclusively by the Company, as the sponsor.

Its executive officers are Gil Beyen (Chairman) and Eric Soyer (Treasurer and Secretary).

Its share capital is one dollar.

The key financial aggregates of the Company’s subsidiary as of December 31, 2015, are presented in Note 5 "Financial Assets" in the Notes to the Company’s financial statements in Section 20.2 "Corporate financial statements prepared (French standards) for the year ended December 31, 2015” of this Reference Document.

Intra-Group financial flows are presented in Section 19.1 "Intra-Group Transactions” of this Reference Document.

## 8 REAL ESTATE PROPERTY, MANUFACTURING PLANTS AND EQUIPMENT

### 8.1 Real Estate and Movable Property

The Group leases premises in France, located at Bâtiment Adénine – 60 avenue Rockefeller – 69008 Lyon as well as in the United States at Riverfront Office Park, One Main Street Cambridge, MA 02142. The Group does not own any real estate assets.

The items pertaining to these leases are summarized in the table below:

Address	Nature of the premises	Lease date of effect	Term	Rent
Bâtiment Adénine 60 Avenue Rockefeller 69008 Lyon France	Commercial (Laboratories and Offices)	07/01/2015	06/30/2024 with an early termination option for the Company in June 2019 or June 2021	<b>€404,124 (excluding VAT) in annual rent and rental charges</b>  <b>Re-invoicing share of property tax</b>
Riverfront Office Park One Main Street Cambridge, MA 02142 United States of America	Commercial (Offices)	1 <sup>st</sup> half 2016	1 <sup>st</sup> half 2019	<b>\$167,856.00 annual rent</b>

The Group believes it has the premises necessary for its development needs in Europe, and it intends to increase its capacities in the United States, potentially by leasing new premises, to allow it to expand its clinical trials and prepare its business development.

In addition, the Company owns the following significant assets:

Material type	Acquisition date	Gross value (excl VAT)	Net value (excl VAT)
Electronical datas management	2010	50 588	-
	2014	8 000	4 208
	2015	41 000	35 762
Tooling equipment	2006	22 125	-
	2007	39 535	-
	2008	79 993	-
	2009	28 000	-
	2014	374 218	279 891
General equipment, fixtures and fittings	2007	42 600	7 773
	2008	47 098	12 825
	2015	121 834	120 303
Plant equipment	2008	615 413	126 791
	2009	130 330	42 598
Computers equipment	2013	32 627	14 491
	2015	33 684	29 712
	<b>Total</b>	<b>1 667 044</b>	<b>674 354</b>

The Company also uses a significant amount of equipment located at the production or pre-clinical research sites financed through leasing-purchase agreements or “lease-backs”:

Material type	Acquisition date	Value (excl VAT)
Computers equipment	2010	110 104
	2011	40 000
	2013	240 413
	<b>Total</b>	<b>390 517</b>

## 8.2 Environmental constraints that may affect the use of assets

With the exception of the risks described in Section 4.1.14 “*Risks related to health, safety, and the environment,*” the Company has no environmental impact that could affect the use of its tangible assets (see also Appendix 2 of the Reference Document “Policy with regard to environmental, social, and societal responsibility”).

## 9 REVIEW OF EARNINGS AND FINANCIAL POSITION

### 9.1 General overview

The Group's main activity is research and development in the areas of treatment of acute leukemia and other orphan diseases through the use of its technology platform, which encapsulates active ingredients in red blood cells.

Since its creation, the Group has concentrated its efforts on:

- The development of a patented technological platform based on the encapsulation of enzymes in red blood cells, which offers an innovative approach to the treatment of acute leukemia and other solid tumors. The development of the main product, Graspas®, which began when the Group was founded, has led to the issuing of 13 families of patents held in the Group's name. The Group has also implemented a patented industrial process capable of producing clinical batches of Graspas®, and capable of meeting demand upon the commercialization of the product.
- The implementation of clinical study programs in order to validate Graspas® initially in terms of safety of use and toxicology through a Phase I clinical study in acute lymphoblastic leukemia (ALL) in adult and pediatric patients with relapsed ALL. Based on the results obtained, the Group performed a Phase II clinical study that likewise demonstrated the safety of the product's use and its efficacy in patients older than 55 years of age with ALL. The Group completed a Phase III clinical study, at the end of which ERYTECH Pharma submitted an application in September 2015, for approval to market of Graspas® in Europe for the treatment of ALL. The Group expects to obtain marketing authorization by late 2016 / early 2017 and launch the commercialization of the product in 2017. It has also initiated a Phase IIb trial on acute myeloid leukemia (AML) and a Phase II trial on pancreatic cancer.

The Group's business model is to develop its products up to the point of obtaining authorization for their commercialization in Europe and Israel and, as a second step, in the United States. Commercial partnerships established by ERYTECH Pharma will allow for the distribution of Graspas® in Europe and Israel. Various distribution options in the United States and the rest of the world are under review. ERYTECH Pharma has the capacity to ensure the supply of Graspas® for approximately the first two years of its sale in Europe, through its production unit in Lyon.

### 9.2 Comparison of the last two years

Comparison of the last two fiscal years below concerns the financial statements prepared in accordance with IFRS standards. The financial statements prepared in accordance with French standards are commented on in Chapter 20.

#### 9.2.1 Operating profit breakdown

##### 9.2.1.1 Revenue and other income from activities

As of the date of this Reference Document, the products developed by the Company have not generated any revenues.

The other income from activities is composed of the following elements:

(in K€)	31.12.2015	31.12.2014
Research tax credit	2 219	1 524
Subsidies	368	271
Other income	341	231
<b>Operating income</b>	<b>2 929</b>	<b>2 026</b>

The Company's other income from activities amounted to €2,929 k and €2,026 k, respectively, for the fiscal years ended December 31, 2015, and December 31, 2014, i.e. a 44.6% increase.

The Company's other income from activities was generated mainly by research tax credits (see Section 9.4.2.1 of this Reference Document) and subsidies for preclinical research programs in partnership with BPI France (see Note 7.10 "Debt" in the Notes to the IFRS financial statements in Section 20.1 "Financial statements prepared in accordance with IFRS standards for the year ended December 31, 2015").

"Other income" corresponds to the sum of the internal costs sustained by the Group within the scope of the AML study, and re-invoiced to the company Orphan Europe to this end. The other external costs associated with this clinical trial were re-invoiced to Orphan Europe with no margin, and do not appear under income from activities, but rather deducted from the associated expenses.

### 9.2.1.2 Operating expenses

#### Cost of sales

As of December 31, 2015, no cost of sales existed relative to the manufacture of batches of GRASPA®. Costs related to the manufacture of ERY-ASP within the context of pre-clinical studies or clinical trials are included in the fees for R&D and clinical studies.

#### Expenditures for research and development

The Company engaged significant efforts in R&D projects to develop innovative drug candidates. R&D costs cover mainly:

- outsourcing, collaboration and consulting costs that relate mainly to the cost of external consultants such as CRO (Contract Research Organization) that conduct the Company's clinical trials and non-clinical studies.
- personnel costs including salaries, post-employment benefits, and share-based payments for Company employees in R&D roles;
- license and intellectual property costs;
- real estate acquisitions and leases as well as conferences and travel costs;
- depreciation and amortization charges and other provisions.

As of Dec. 31 in thousands of €	2015	2014
ERY-ASP/GRASPA	1,805	1,310
TEDAC/ERY-MET/ERY-ADI	1,523	221
<b>Total direct R&amp;D costs</b>	<b>3,328</b>	<b>1,531</b>
Consumables	805	313
Rent and maintenance	304	492
Services, subcontracting and fees	1,896	1,531

Personnel expenses	3,977	2,443
Depreciation and amortization charges and provisions	250	222
Other	216	81
<b>Total indirect R&amp;D costs</b>	<b>7,448</b>	<b>5,082</b>
<b>Total R&amp;D costs</b>	<b>10,776</b>	<b>6,613</b>

Over the periods presented, the total amount of expenditures for research and development increased sharply from €6,613 k in 2014 to €10,776 k in 2015, i.e. an increase of 63%. R&D expenditure mainly related to completed or ongoing clinical trials for ERY-ASP/GRASPA® amounting to €1,805 k and €1,310 k in 2015 and 2014 respectively, the TEDAC program amounting to €1,523 k and €221 k in 2015 and 2014 respectively, and the continuing Phase II trial for pancreatic cancer in France.

R&D costs mainly include costs related to preclinical studies and fees for consultants and scientists. The increase in R&D costs between 2014 and 2015 is mainly due to the €1,302 k increase in external services directly linked to the TEDAC program and to the €1,534 k increase in personnel expenses.

Costs related to clinical studies primarily include costs of raw materials related to the purchase of supplies necessary for the production of clinical batches of GRASPA®, the staff dedicated to ERYTECH's clinical studies, as well as the outsourcing of monitoring and services relating to the marketing authorization application in 2015.

This table shows the significant increase in the clinical trials item from 2014 to 2015, due to the high level of clinical activity as mentioned above.

Costs associated with intellectual property decreased by €37 k between 2014 and 2015.

#### General expenses

General expenses comprise primarily the personnel expenses, including share-based payments for administrative staff. They also include structural costs for the head office, the compensation of directors, external expenses such as accounting, legal, human resources, marketing and communications expenses, as well as travel expenses (excluding scientific conferences).

They totaled €4,361 k and €7,736 k for the financial years ending December 31, 2014, and 2015, i.e. a 77% increase.

<b>as of Dec. 31 in thousands of €</b>	<b>2015</b>	<b>2014</b>
Overheads and general expenses	7,736	4,361
<i>o/w Personnel expenses</i>	<i>1,627</i>	<i>2,368</i>

The Company recorded a significant increase in its overheads and general expenses, mainly due to the increase in external services, outsourcing and fees to develop its strategy in the United States, the NASDAQ initial public offering and the BSA<sub>2014</sub> warrants awarded to directors in 2015 in the amount of €1,593 k (see Note 6.4 "Share-based payments (IFRS)" in the Notes to the IFRS financial statements in Section 20.1 "Financial statements prepared in accordance with IFRS standards for the year ended December 31, 2015").

#### **9.2.1.3 Net income breakdown**

##### Financial Income (Loss)



The net financial results showed a profit of €567 k for 2015, as compared to a profit of €68 k in 2014. This financial result mainly reflects (i) the cash surplus from the capital increase in October 2014 being placed in a term deposit and (ii) currency translation gains connected with the purchase of services expressed in dollars.

The breakdown of the item is shown in the table below:

(in K€)	31.12.2015	31.12.2014
Interests on leases	(5)	(7)
Other finance expenses	.....(59)	.....(67)
<b>Total finance expense</b>	<b>(64)</b>	<b>(73)</b>
Income from disposal of short term investments	524	141
Other finance income	.....107	.....1
<b>Total finance income</b>	<b>631</b>	<b>142</b>
<b>Total finance income</b>	<b>567</b>	<b>68</b>

This table primarily shows that, for the periods presented:

- Interest on leases declined slightly from 2014 to 2015, due the end of some lease financing agreements during financial year 2015.
- This resulted in a downward shift in the net cost of debt, which decreased from €73 k in 2014 to €64 k in 2015.
- Interest income corresponds to the interest on term deposits.
- Other financial income and expenses relate to currency translation gains and losses.

#### Income taxes

Given the deficits over the past 3 financial years, the Company has not recorded income tax expenses, nor taxable income associated with activation of the loss that can be carried forward.

#### 9.2.1.3 Net earnings and net earnings per share

Net loss amounted to €8,860 k for the year ended 2014 and €15,016 k for the year ended 2015.

The loss per issued share (weighted average number of shares outstanding in the financial year) was €1.51 for the year ended in 2014 and €2.16 for the year ended in 2015.

### **9.3 Non-tax deductible expenses**

The Company has made the following tax add-backs to its earnings:

- Tax on company passenger vehicles, in the amount of €5,929
- Excess depreciation on passenger vehicles rented, in the amount of €20,013
- Non-deductible portion of attendance fees paid, in the amount of €90,432

## 9.4 Balance sheet analysis

### 9.4.1 Assets

#### 9.4.1.1 Non-current assets

Net non-current assets amounted to €1,080 k at December 31, 2014, and €1,076 k at December 31, 2015, respectively.

Non-current assets include tangible and intangible assets (concessions, patents, licenses, software), non-current financial assets (deposits and sureties), and deferred taxes.

as of Dec. 31 in thousands of €

	2015	2014
<b>NON-CURRENT ASSETS</b>		
Intangible assets	61	31
Tangible assets (property, plant & equipment)	918	967
Non-current financial assets	97	82
Other non-current assets		
Deferred tax assets		
<b>TOTAL NON-CURRENT ASSETS</b>	<b>1,076</b>	<b>1,080</b>

In 2015, there was a slight decline in tangible assets primarily dedicated to the pre-equipped production site.

Moreover, non-current financial assets primarily consisting of deposits and sureties have remained relatively stable over the last two financial years.

Loss carry forwards were capitalized only up to the amount of deferred tax liabilities; the amounts capitalized were not significant.

#### 9.4.1.2 Current assets

Net current assets amounted to €39,526 k and €51,929 k in 2014 and 2015 respectively.

In 2015, the amount of net current assets increased significantly due to the fact that the capital increase strengthened the Group's cash flow, and due to the increase in the research tax credit as a result of the very significant increase in Research activity. As of December 31, 2015, the Company had not received the research tax credit owed for 2014 amounting to €1,524,000 due to an ongoing tax audit. This tax audit was completed in February 2016 without any major reassessment by the tax authorities. The Company therefore hopes to receive the research tax credit owed for 2014 in the next few months and has already received other tax refunds.

as of Dec. 31 in thousands of €

	2015	2014
<b>CURRENT ASSETS</b>		
Inventories	166	198
Trade accounts receivable	424	105
Other current assets	5,705	2,235
<i>o/w Research Tax Credit (CIR)</i>	<i>3,743</i>	<i>1,524</i>
<i>o/w tax and other receivables</i>	<i>1,190</i>	<i>494</i>

<i>o/w Shareholders - Cash contributions (1)</i>	553	
<i>o/w Prepaid expenses</i>	220	217
<i>o/w Other subsidies receivable</i>		
Cash and cash equivalents	45,634	36,988
<b>TOTAL CURRENT ASSETS</b>	<b>51,929</b>	<b>39,526</b>

(1) Total cash contributions as of December 31, 2015, reflect the exercise of 7,508 Yann Godrin warrants in December 2015. The corresponding funds were paid to Société Générale Securities Services on December 23, 2015, and forwarded to the Company in early January 2016.

## 9.4.2 Liabilities

### 9.4.2.1 Shareholders' equity

Equity was mainly affected by:

- the capital increase in December 2015,
- the exercise of share subscription warrants,
- as well as income appropriation, recording a loss of €8,860 k.

### 9.4.2.2 Non-current liabilities

This is essentially the non-current portion of lease-back commitments, repayable advances received and, to a lesser degree, pension commitments in accordance with IAS 19.

as of Dec. 31 in thousands of €	2015	2014
<b>NON-CURRENT LIABILITIES</b>		
Provisions > 1 year	100	89
Financial liabilities > 1 year	151	436
<i>o/w Repayable advances</i>	63	292
<i>o/w Lease-back</i>	88	144
Deferred tax liabilities		
Other non-current liabilities		
<b>TOTAL NON-CURRENT LIABILITIES</b>	<b>251</b>	<b>525</b>

### 9.4.2.3 Current liabilities

This balance sheet item primarily includes short-term liabilities such as those relating to supplier debts, tax and social security debts (employees and social security entities), the non-current portion of sums related to repayable advances granted by BPI France (formerly Oséo) (see Item 7.9.1 of the annex, Section 20.1) and, lastly, deferred income.

as of Dec. 31 in thousands of €	2015	2014
<b>CURRENT LIABILITIES</b>		
Provisions < 1 year	81	
Financial liabilities < 1 year	557	334

Trade and other payables	3,672	2,085
Other current liabilities	1,311	1,840
<i>o/w Tax and social security liabilities</i>	<i>1,241</i>	<i>971</i>
<i>o/w Prepaid income</i>		<i>368</i>
<i>o/w Other liabilities</i>	<i>71</i>	<i>501</i>
<b>TOTAL CURRENT LIABILITIES</b>	<b>5,622</b>	<b>4,258</b>

Total current liabilities increased significantly from 2014 to 2015, essentially due to the increase in supplier debts.

## 10 CAPITAL RESOURCES AND CASH

### 10.1 Information on the Company's capital, liquidity and capital resources

Also refer to the notes accompanying the financial statements prepared according to the IFRS standards contained in Chapter 20 of this Reference Document. At December 31, 2015, the amount of cash and cash equivalents held by the Group amounted to €45,634 k, as compared to €36,988 k at December 31, 2014.

Cash and cash equivalents include liquid assets and current financial instruments held by the Group (exclusively non-interest-bearing short-term bank deposits). These liquid assets will serve to fund the Group's business activities, notably its expenses for research and development and clinical study programs.

In addition, on December 23, 2015, the Group terminated the liquidity contract with Bryan Garnier&Co which had a management envelope of €200 k.

Between its establishment in 2004 and December 31, 2015, the Company has received the following sources of funding:

- several rounds of financing by issuing new shares in several categories: ordinary shares, Class P, U and A preferred shares for total gross proceeds of €17.7 million as of December 31, 2012,
- issue of convertible bonds for total gross proceeds of €9 million (€7 million as of December 31, 2012, and €2 million as of December 31, 2011),
- initial public offering of the Company for total gross proceeds of €17.7 million as of December 31, 2013,
- a second round of funds raised on the stock market in 2014, for total gross proceeds of €30 million,
- the granting of repayable advances by BPI France for a total of €5,711 k, of which €878 k had been received at December 31, 2015,
- the granting of non-repayable advances by BPI France totaling €2.3 million since 2005,
- payment of the research tax credit, in the total amount of €5,575 k.
- a third round of funds raised on the stock market in December 2015, for total gross proceeds of €25.4 million.

The financial status is presented below:

as of Dec. 31 in thousands of €	2015	2014
Cash & cash equivalents (a)	45,634	36,988
Current financial liabilities (b)	557	334
Non-current financial liabilities (c)	151	436
Financial debt (b+c)	708	770
Net financial debt (b) + (c) - (a)	(44,926)	(36,219)
<b>Net financial position</b>	<b>44,926</b>	<b>36,219</b>

## Capital financing

At December 31, 2015, the Company had received a total of €90.8 million during successive rounds of financing and following the Company's initial public offering.

### Financing by repayable advances

The Group did not subscribed any bank loans in the 2 financial years presented. However, during 2011, 2012, and 2013, it received €879 k out of a total of €5,711 k that have to be paid to the Company in the form of conditional advances forming the object of three contracts relating to repayable advances for innovation projects with BPI France (formerly Oséo).

The Group received no new payments in the year 2014 and 2015: only one contract is still ongoing (TEDAC) and thus in a phase of assistance payments, but the corresponding expenses allowing for new drawdowns on funds have not been reached. These payments have therefore been deferred to the next payment deadlines based on budgeted expenses incurred. The Group believes that it is within the anticipated schedule with regard to the scientific progress of the TEDAC project. The expenses incurred are less than planned in the initially submitted budget, as, in the end it was not necessary to go beyond that in order to achieve the initial steps of the project.

### Financing by research tax credit

The Group benefits from the provisions of Articles 244 B and 49 F of the French General Tax Code pertaining to the research tax credit (French CIR). Since the Group has not initiated any R&D expenditures up to granting of the marketing approval for treatments identified through clinical developments, the CIR is fully accounted for under other operating income (see Note 6.1 to Section 20.1 of this Reference Document).

## 10.2 Cash flow

Cash consumption associated with operating activities for the financial years ending December 31, 2014 and December 31, 2015 amounted to a negative flow of €7,246 k and a negative flow of €14,578 k respectively.

The table below shows the net cash flows generated by Group activities over the past two financial years:

(in K€)	31.12.2015	31.12.2014
<b>Net loss</b>	<b>(15 013)</b>	<b>(8 860)</b>
Reconciliation of net loss and the cash used for operating activities		
- Amortization and depreciation	288	277
- Increase in long term provision	20	
- Expense related to share-based payments	2 716	1 236
- Interest expenses	30	43
- Income tax expense	(3)	(20)
<b>Operating cash flow before change in working capital</b>	<b>(11 962)</b>	<b>(7 325)</b>
Increase / Decrease in inventories	32	(60)



Increase in trade and other receivables	(319)	(18)
Increase / Decrease in other current assets	(3 470)	(534)
Increase in trade and other payables	1 588	663
Decrease in other current liabilities	(528)	28
Decrease in other liabilities - non current portion	81	
<b>Change in working capital</b>	<b>(2 616)</b>	<b>79</b>
<b>Net cash flow used in operating activities</b>	<b>(14 578)</b>	<b>(7 246)</b>

The working capital requirements for business activities increased significantly in 2015 due to the Group's increased activity in both pre-clinical and clinical research, as well as the increase in overheads and general expenses. In 2015, net cash outflow for operating activities also included a €1,229 k expense to prepare the Company's initial public offering in 2015, a non-recurring increase in tax receivables in the amount of €2,315 k relating to the research tax credit for 2014, and other tax receivables for 2014 that the Company was not able to recover in 2015 due to a tax audit in progress on December 31, 2015 (see Note 6.1 to Section 20.1 of this Reference Document).

Cash consumption associated with investing activities for the fiscal years ended December 31, 2014 and December 31, 2015 amounted to €420 k and €284 k respectively. This reduction mainly reflects the adequacy of fixed assets for the Company's production plant in Lyon, its laboratory, and its other R&D facilities.

The table below shows the net cash flows over the past two fiscal years:

	31.12.2015	31.12.2014
<b>Cash flows from investing activities</b>		
Acquisition of property, plant and equipment	(49)	(26)
Acquisition of intangible assets	(220)	(396)
Acquisition of financial assets	(15)	(0)
Disposal of financial assets	-	1
<b>Net cash flow used in investing activities</b>	<b>(284)</b>	<b>(420)</b>

Cash consumption associated with financing activities for the financial years ending December 31, 2014 and December 31, 2015, amounted respectively to a positive flow of €29,542 k in 2014 and a positive flow of €23,524 k in 2015.

The table below shows the net cash flows over the past two fiscal years:

	31.12.2015	31.12.2014
<b>Cash flows from financing activities</b>		
	-	
Capital increases, net of transaction costs	23 544	29 173
Repayment of borrowings	(85)	(281)
Treasury shares	64	651

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<b>Net cash flow from financing activities</b>	<b>23 524</b>	<b>29 542</b>
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The net flows associated with financing activities result from the Company's use of the stock market to raise funds in 2014 and again in 2015.

### **10.3 Information on the borrowing requirements and funding structure**

The structure of financing received by the Group between its establishment and December 31, 2015 is summarized in Paragraph 10.1 above.

The key terms and conditions governing the repayable advances granted to the Group as of December 31, 2015, are described in Note 7.10 "Debt" in the Notes to the IFRS financial statements in Section 20.1 "Financial statements prepared in accordance with IFRS standards for the year ended December 31, 2015."

#### **10.4 Restriction on the use of capital**

The Group faces no restrictions on the availability of its capital.

#### **10.5 Sources of financing needed for the future**

The Group had an available cash flow of €45.6 million at the end of December 2015, which will cover its needs for more than one year. Other than the anticipated 2016 payments relating to reimbursement of the 2014 and 2015 CIR, which should represent an additional resource of €3.7 million, the Company has not received any new funding.

## 11 RESEARCH AND DEVELOPMENT, PATENTS AND LICENSES

### 11.1 Research and development activity

See Sections 6.7, 6.9 and 6.10 of the Reference Document for clinical development.

See Section 6.11 for Research & Development (R&D) activity.

See Section 6.2 of the IFRS annexes for the R&D costs.

### 11.2 Intellectual property

Patents and other intellectual property rights are of the utmost importance in the Group's business sector and constitute the main barrier to entry for competitors. The Group also relies on industrial secrets, and confidentiality agreements are signed to protect its products, technologies, and manufacturing process. Without prejudice to the statements made in Section 4.2.9 ("Risks related to intellectual property"), the Group's intellectual property is not, to its knowledge at the date of this Reference Document, subject to any challenge by a third party.

#### 11.2.1 Patents

##### 11.2.1.1 In its own name

As of February 29, 2016, ERYTECH Pharma's patent portfolio consisted of 13 patent families held in its own name.

Technology/products	Family	Title	Years before the next patent for any family of patents expires*	Filing date	Status
		Lysis/resealing process and device for incorporating an active ingredient in erythrocytes	2024/2030	08/05/2004	Issued in Japan Issued in Europe Issued in Australia Issued in China Issued in the United States Issued in Korea Issued in India Issued in Canada
Production process	2	Process for stabilizing suspensions of erythrocytes encapsulating the active ingredient, suspensions obtained	2033/2034	05/07/2013	Issued in France National applications filed
ERY-ASP/GRASPA®	3	Medication for the treatment of pancreatic cancer	2027/2029	12/24/2007	Issued in Europe Issued in the United States Issued in Israel Issued in Australia

<b>Technology/products</b>	<b>Family</b>	<b>Title</b>	<b>Years before the next patent for any family of patents expires*</b>	<b>Filing date</b>	<b>Status</b>
					Issued in Singapore National/regional phases for other territories
		Test for predicting neutralization of asparaginase activity	2032/2033	11/07/2008	Issued in Europe Issued in the United States Issued in Japan Issued in Australia Issued in Singapore Issued in Israel National/regional phases for other territories
		Medication for the treatment of acute myeloid leukemia	2028/2029	03/21/2012	National/regional phases initiated
		Erythrocytes containing Arginine deiminase	2026	04/25/2005	Issued in Europe, United States, Japan, China, Canada, Korea, and Australia
<b>TEDAC</b>	3	Pharmaceutical composition comprising erythrocytes encapsulating an enzyme	2034/2035	02/12/2014	PCT application filed National applications filed
		Method of treatment against cancer	2035/2036	12/31/2015	Priority application
		Composition to induce specific Immune Tolerance	2030	10/27/2009	Issued in Australia Issued in Singapore National/regional phases for other territories
<b>Immune modulation platform</b>	2	Composition and therapeutic anti-tumor vaccine	2027/2028	08/08/2007	Issued in the United States Issued in France Issued in China Issued in Australia Issued in Singapore Issued in Israel National/regional phases for other territories
<b>Other earnings</b>	3	Formulation and method for the prevention and treatment of skeletal manifestation	2028	02/13/2008	Issued in Europe Issued in Israel Other national/regional phases

Technology/products	Family	Title	Years before the next patent for any family of patents expires*	Filing date	Status
		of Gaucher's disease			
		Formulation and method for the prevention and treatment of bone metastases and other bone diseases	2028/2029	03/10/2008	Issued in Europe Issued in China Issued in Australia Issued in Singapore National/regional phases for other territories
		Composition of erythrocytes encapsulating phenylalanine hydroxylase and therapeutic use thereof	2033/2034	02/10/2013	PCT application filed

\* Does not take into account the additional protection certificates that may be obtained for the Company's patent in the United States, Europe or other countries. The expiration dates for the US patents that have not yet been issued may be adjusted.

The Company's intellectual property strategy aims to secure and perpetuate its exclusive use by filing and obtaining patents on its production process, its products and/or their therapeutic uses as well as diagnostic tests or assay methods directly related to the use of its products.

Prior to each filing, a detailed analysis of the prior art is done in order to satisfy the patentability criteria while seeking a robust and broad scope, in connection with the proposed use.

So-called main patents are those that protect the Company's key products and technologies, while the others are considered "secondary."

The "main" patents and the current stage of their process are discussed below:

#### **Patents on the production process**

- **Process patent entitled "Lysis/resealing process and device for incorporating an active ingredient in erythrocytes":**

This is the Company's main patent covering its technology for the encapsulation of therapeutic molecules. The innovation developed by ERYTECH is based on taking into account key physiological parameters of erythrocytes to obtain a reproducible product. The initial application covers both the production process, the device for its implementation as well as all directly resulting products.

This patent was issued in France, Japan, Australia, South Korea, India, and China without any significant changes being made to the claims. In Europe, the process claims had to be separated from the device claims due to inventive unit reasons. An initial European patent was thus issued for the claims covering the production process and the directly resulting products. It currently covers more than 20 countries of the European Patent Organization. The claims covering the device for the implementation of the process were included in a divisional application currently under review by the European Patent Office.

In the United States, the process claims also had to be separated from the device claims. An initial US patent has been issued for claims covering the production process, in accordance with American law

and the Patent Term Adjustment. The term of this patent has been extended by an additional five years, which means that it is protected in the United States until April 2030. The claims covering the device for the implementation of the process were included in a divisional application currently under review by the United States Patent Office.

In Canada, a patent has also been issued for claims covering the process.

This patent was licensed by the Company to Orphan Europe as part of an exclusive license and distribution agreement (*see also Chapter 22 of this Reference Document*) for the development and distribution of GRASPA® in the EU-27. This agreement covers the indications of ALL and AML.

The European patent issued was the object of opposition proceedings with the European Patent Office. Following withdrawal by the adverse claimant, the European Patent Office concluded the opposition proceedings and upheld the patent in force without any changes to the claims ([See also Section 4.2.9](#) of this Reference Document). ERYTECH was informed of the decision on February 7, 2014.

- **Process patent entitled “Process for stabilizing a suspension of erythrocytes encapsulating the active ingredient, suspensions obtained”:**

This patent application claims an improvement in ERYTECH Pharma’s encapsulation process to improve the stability of the erythrocytes suspensions obtained. This patent was issued in France and has been extended internationally by the PCT and various direct national filings.

#### **Patents on products and/or their therapeutic uses.**

- **Patent entitled “Erythrocytes containing Arginine deiminase”:**

This patent covers erythrocytes encapsulating the enzyme arginine deiminase and any related pharmaceutical compositions. Arginine deiminase encapsulated in erythrocytes is an enzyme therapy developed under the TEDAC project. This enzyme is capable of breaking down arginine and thus acting on the metabolism of certain tumor cells by depriving them of a nutrient that is essential for them.

This patent was issued in the United States, Europe, Japan, China, Canada, Korea, and Australia without significant changes to the claims. The scope obtained is therefore broad, since product claims not restricted to a particular therapeutic use are included in the claims issued.

- **Patent pertaining to a pharmaceutical composition comprising erythrocytes encapsulating an enzyme:**

This patent, filed within the context of the TEDAC project, was the object of a priority filing in France on February 10, 2014 and has been extended internationally by the PCT and various direct national filings.

- **Patent for a cancer treatment method:**

This patent application for a cancer treatment method using therapies developed by ERYTECH Pharma was filed in Europe on December 31, 2015.

- **Patent entitled “Medication for the treatment of pancreatic cancer”:**

This patent covers the use of ERY-ASP for the treatment of pancreatic cancer. This patent has been issued in Europe, the United States, Israel, Australia, and Singapore, and is under review in other territories (Japan and Canada in particular).

- **Patent entitled “Medication for the treatment of Acute Myeloid Leukemia”:**



This patent covers the use of GRASPA® for the treatment of acute myeloid leukemia. It was the subject of a priority application filed in the United States and it was extended by the PCT, plus some direct national filings.

This patent was licensed by the Company to Orphan Europe as part of an exclusive license and distribution agreement ([see also Chapter 22 of this Reference Document](#)) for the development and distribution of GRASPA® in the EU-27. The agreement covers the indications of AML.

- **Patent entitled “Composition to induce specific immune tolerance”:**

This patent application covers the technology to induce a specific immune tolerance developed by ERYTECH. The proposed scope is broad, because the application covers both a composition capable of inducing immune tolerance with respect to a therapeutic protein or peptide and a composition capable of inducing immune tolerance with respect to an autoantigen. This patent has been issued in Australia and Singapore; the application is in national/regional phases for other territories.

- **Patent entitled “Composition and therapeutic anti-tumor vaccine”:**

This patent covers a composition of erythrocytes incorporating a tumor antigen and/or adjuvant and its use as a therapeutic cancer vaccine. The proposed scope is broad because it is not limited by the nature of the antigen, the adjuvant, or their combination.

This patent has been issued in France, Australia, Israel, China, and Singapore, and is under review in other territories (Europe, Japan, and Canada in particular). This patent has also been issued for the United States.

\* \* \*

The duration of a patent is 20 years from its filing date. However, in the pharmaceutical field, supplementary protection certificates may be granted in the major industrialized countries, generally extending protection for a non-renewable term of up to five years.

The Company has a policy of regularly filing patent applications to protect its technologies, products and production process.

The Company's strategy is to systematically file priority applications in France, Europe, and/or the United States. For other countries, the Company uses a procedure known as “Patent Cooperation Treaty” (PCT) that makes it possible to validly file for more than 100 countries: PCT filing is done one year after the priority filing. The PCT application is subsequently converted into national or regional filings to cover countries or groups of countries selected according to the desired geographic coverage. Some countries not accessible by PCT may be subject to direct national filings.

With regard to intellectual property, the Company's strategy is to strengthen its leading position in the use of red blood cells for therapeutic purposes. Its portfolio of filed patents covers 13 different patent families. Of these 13 patent families, 9 are already protected by at least one issued patent.

The inventions of the Company's employees are governed by employment contracts. Upon discovery of a patentable invention, each employee agrees to reveal and recognize that the invention, made in the context of the employee's work, is the property of ERYTECH, which holds all rights. A supplemental remuneration policy for each additional invention has been implemented and a confidentiality clause is included in the employment contracts. Inventions of non-salaried consultants are governed by specific contractual provisions, as the consultants are systematically bound by confidentiality clauses and generally include waiving all rights they might have to the inventions in which they may participate.

An internal procedure ensures the proper use of laboratory notebooks so that ERYTECH's intellectual property rights can be justified if necessary and in the event there is an invention. These laboratory notebooks are regularly signed and dated by a bailiff, then stored on the Company's premises.

Scientific and technological monitoring has also been implemented at ERYTECH in order to monitor:

- scientific programs that could influence the Group's R&D programs and that could identify new opportunities;
- the emergence and development of technologies complementary to or competitive with Group technologies.


#### 11.2.1.2 Licenses

The NIH (National Institutes of Health) has granted an exclusive license to ERYTECH on intellectual property covering a diagnostic method for predicting the efficacy of L-asparaginase in a patient ([see also Chapter 22 "Major contracts" in this Reference Document](#)). This intellectual property based on developments of the National Cancer Institute includes two issued US patents (US 7,985,548 and US 9,181,552).

#### 11.2.2 Trademarks


The Company has filed the following trademarks:

TRADEMARK	DESIGNATED COUNTRIES	NO.	DATE
1 ERYtech Pharma	France	033,264,900	December 26, 2003 (Renewed)
	European Community	00 3,921,319	July 05, 2004
	Albania		
	Bosnia and Herzegovina		
	China		
	Croatia		
	Former Yugoslav Republic of Macedonia		
	Liechtenstein		
	Monaco		November 26, 2007
	Serbia		
	Switzerland		
	Australia	947,762	
	Iceland		
	Japan		
	Turkey		
	Singapore		May 14, 2008
	Belarus		
	Algeria		
	Egypt		December 18, 2013
	Georgia		
Russia			

TRADEMARK	DESIGNATED COUNTRIES	NO.	DATE		
	Ukraine				
	Montenegro				
	Norway				
	Iran				
	Republic of Korea				
	Morocco				
	Israel	226,985	February 3, 2010		
	Canada	1,387,023	March 12, 2008		
	Kosovo	KS/M/2013/1 211	December 17, 2013		
2		France	3,911,751	April 10, 2012	
		European Union	1,127,934	June 20, 2012	
		Australia			
		South Korea			
		United States			
		Israel			
		Iceland			
		Monaco			
		Russia			
		Singapore			
		Switzerland			
		Turkey			
		Montenegro			October 26, 2012
		Norway			
3	GRASPA	France	063,421,435	April 6, 2006	
		Albania	947,759	November 26, 2007	
		Bosnia and Herzegovina			
		China			
		Croatia			
		Former Yugoslav Republic of Macedonia			
		Liechtenstein			
		Monaco			
		Serbia			
		Switzerland			
		Australia			
		European Community			
		United States			
		Iceland			
		Japan			

TRADEMARK	DESIGNATED COUNTRIES	NO.	DATE			
	Republic of Korea					
	Turkey					
	Singapore			May 14, 2008		
	Russia			June 20, 2012		
	Montenegro			October 26, 2012		
	Norway					
	Belarus					
	Egypt					
	Georgia					
	Algeria			December 18, 2013		
	Morocco					
	Ukraine					
	Israel				226,992 226,993 226,994	February 3, 2010
	Canada				1,387,024	March 12, 2008
Kosovo	KS/M/2013/1 212	December 17, 2013				
4	ERYASP	France	13,397,6584	January 23, 2013		
5	Cleav'Ery System		947,760	November 26, 2007		
		Switzerland				
		European Union				
6	Oxygen'ERY	Switzerland	947,761	November 26, 2007		
		European Union				
7	Vaccin'ERY System	France	073,533,090	October 22, 2007		
		European Community	967,450	May 14, 2008		
		Switzerland				
8	ERYCAPS	France (classes 5,42,44)	073,546,157	December 21, 2007		
		France (classes 7,9,10)	164,258,547	March 21, 2016		
		Switzerland (classes 7,9,10)	164,258,547	March 21, 2016		
		European Union (classes 7,9,10)	015,251,382	March 21, 2016		
		European Community (classes 5,42,44)	972,047	July 8, 2008		
		Switzerland (classes 5,42,44)				
9	EryDexone	France	063,459,689	October 26, 2006		
10	ERYTECH Pharma Deliv'ERY System	France	073,543,340	December 10, 2007		
11	ENHOXY	France	113,819,125	March 23, 2011		

TRADEMARK	DESIGNATED COUNTRIES	NO.	DATE	
	European Union	1,110,463	February 10, 2012	
	United States			
	China			
	Switzerland			
	Australia			
	Iceland			
	Japan			
	Republic of Korea			
	Turkey			
	Israel			
	Singapore			
	Russia		June 20, 2012	
	Monaco			
12	KYTASPAR	France	144,103,802	July 8, 2014
		France	144,103,800	July 8, 2014
		European Union	013,466,123	November 17, 2014
13	ASPACELL	International: - Albania - Armenia - Azerbaijan - Belarus - Bosnia and Herzegovina - Iceland - Kazakhstan - Kyrgyzstan - Liechtenstein - Macedonia - Moldova - Montenegro - Norway - Uzbekistan - Russia - Serbia - Switzerland - Tajikistan - Turkmenistan - Turkey - Ukraine	1,235,383	December 3, 2014
		Kosovo	KS/M/2014,109	November 19, 2014
14	ERYTECH	France	164,258,540	March 21, 2016
		Switzerland		
		European Union		
15		France	164,258,544	March 21, 2016

TRADEMARK	DESIGNATED COUNTRIES	NO.	DATE
	European Union	015,251,366	

None of the Company's trademarks above are subject to a third-party trademark license, except under distribution agreements with the Teva Group and Orphan Europe, for the trademark GRASPA® (see also Chapter 22 “Major contracts” of this Reference Document).

The Company has established global monitoring of its main trademarks, namely ERYTECH Pharma® and GRASPA®.

### 11.2.3 Domain Names

The Company filed the following domain names:

Domain Name	Expiration Date
eryasp.com	November 20, 2016
erytechpharma.com	November 20, 2016
erytech.fr	May 5, 2017
ery.tech	August 25, 2016
erytech.com	July 20, 2017
erytech.eu	September 30, 2017
graspa.fr	September 23, 2016
graspa.bio	September 23, 2016
graspa.biz	September 23, 2016
graspa.eu	September 23, 2016
graspa.de	September 23, 2016
graspa.co.uk	September 23, 2016
graspa.info	September 23, 2016

## **12 TREND INFORMATION**

### **12.1 Main trends since the end of the last financial year**

See Section 20.9 "Significant change in the financial or commercial position" of this Reference Document.

### **12.2 Known trends, uncertainties, requests for commitments or reasonable events that could affect the Company's prospects**

None

## **13 FORECASTS OR ESTIMATES OF EARNINGS**

The Company does not wish to report on forecasts of earnings because the assumptions on which these forecasts would be built would include elements that are too vague as of the preparation date of this Reference Document.



## 14 ADMINISTRATIVE AND MANAGEMENT BODIES

Please note that the Company was incorporated in the form of a simplified limited company with an Executive Board and a Board of Supervisors on September 29, 2005. In a General Meeting dated April 2, 2013, the Company modified its mode of governance to the current one, that being a limited liability company with a Board of Directors.

### 14.1 Executive Officers and Directors

#### 14.1.1 Composition of the Board of Directors:

On December 31, 2015, the Company has the following directors:

Last name, first name, age	Term of office	Position
<b>Gil Beyen</b> 54 years old 3 Place des Célestins 69002 Lyon, France	1st appointed: The General meeting of April 2, 2013 (he had been chairman of the Board of Supervisors since 2012)  Term expires: The Ordinary General Meeting of 2016 voting on the financial statements for the fiscal year ending December 31, 2015.	Chairman of the Board of Directors and Chief Executive Officer
<b>Galenos SPRL</b> , represented by Sven Andreasson, 63 years old Rond Point Schuman, 6, Boîte 5 1040 Brussels, Belgium  Independent director <sup>(1)</sup>	1st appointed: The Board of Directors' meeting of April 2, 2013 (Chairman of the Supervisory Board from 2009 to 2011, Deputy Chairman of the Supervisory Board since 2011)  Term expires: The General Meeting of 2016 voting on the financial statements for the fiscal year ending December 31, 2015.	Director
<b>Philippe Archinard</b> 56 years old 47 rue Professeur Deperet, 69160 Tassin-la-Demi-Lune.  Independent director <sup>(1)</sup>	1st appointed: The General meeting of April 2, 2013 (member of the Board of Supervisors since 2005)  Term expires: The General Meeting of 2016 voting on the financial statements for the fiscal year ending December 31, 2015.	Director
<b>Martine Ortin George</b> 67 years old 9 Southern Hills Drive Skillman, NJ 08558 United States of America  Independent director <sup>(1)</sup>	1st appointed: AGM of June 17, 2014  Term expires: The General Meeting of 2017 voting on the financial statements for the fiscal year ending December 31, 2016.	Director
<b>Hilde Windels</b> 50 years old Kasteellaan 899000 GENT Belgique  Independent director <sup>(1)</sup>	1st appointed: AGM of June 17, 2014  Term expires: The General Meeting of 2017 voting on the financial statements for the fiscal year ending December 31, 2016.	Director

Last name, first name, age	Term of office	Position
<b>Luc Dochez</b> 41 years old 8 Klein Vilvoordestraat 3078 Meerbeek Belgium Independent director <sup>(1)</sup>	Date of first appointment: co-optation at the Board of Directors' meeting of March 26, 2015, ratified by the General Meeting of June 23, 2015.  Term expires: the 2016 General Meeting voting on the financial statements for the year ending December 31, 2015.	Director
<b>Yann Godfrin</b> 44 years old 8 Impasse de la Source 69300 Caluire-et-Cuire, France	1st appointed: The General Meeting of April 2, 2013 (he had been a member of the Executive Board since 2005, Chairman of the Executive board from 2005 to 2010, and Chief Executive Officer since 2010).  Term expires: January 18, 2016 following his resignation from his positions as Director and Deputy Chief Executive Officer.	Director Deputy Chief Executive Officer

(1) Independent member as defined by the Middlednext Corporate Governance Code for mid and small-cap stocks, December 2009 (see. Section **Erreur ! Source du renvoi introuvable. Erreur ! Source du renvoi introuvable.** of this Reference Document).

The professional address of Chief Executive Officer Gil Beyen, and Deputy Chief Executive Officer Jérôme Bailly is the Company headquarters at 60 avenue Rockefeller – 69008 Lyon.

The professional addresses of the other directors are those shown on the table above.

There are no family relationships between the persons listed above.

None of these people, over the course of the last five years has been:

- convicted of fraud;
- associated with a bankruptcy, seizure, or liquidation in his/her capacity as executive officer or director;
- prevented by a court from acting in a capacity as a member of a board of directors, executive board, or supervisory board of an issuer or participating in the management or conduct of business and of an issuer, and
- subject to a management prohibition; or
- the subject of indictment or official public sanction pronounced by the statutory or regulatory authorities, including by designated professional bodies.

During the financial year ended December 31, 2015, the following changes took place concerning the Board of Directors:

- Mr. Pierre-Olivier Goineau resigned from his positions as Director and Deputy Chief Executive Officer on January 11, 2015, in order to focus on other entrepreneurial projects;
- Luc Dochez was co-opted in the Board of Directors' meeting of March 26, 2015. His appointment was ratified by the shareholders at the Combined General Shareholders' Meeting of June 23, 2015 for the time remaining in the term of Pierre-Olivier Goineau, i.e. until the Shareholders' Meeting called to approve the financial statements for the year ended December 31, 2015, or no later than June 30;

Since December 31, 2015, it should be noted that Yann Godfrin resigned from his positions as Director and Deputy Chief Executive Officer, effective January 18, 2016 in order to focus on other

entrepreneurial projects. After his resignation, a consulting agreement was signed between the Company and Yann Godfrin to ensure a smooth transition. The Company has initiated his replacement.

#### 14.1.2 Composition of Senior Management:

The Chairman and Chief Executive Officer of the Company is Mr. Gil Beyen.

The Company has a Deputy Chief Executive Officer, Jérôme Bailly, the managing pharmacist.

Together, these people form the Company's Senior Management.

The biographies of the officers are presented below in Section 3.6.3.

#### 14.1.3 Other corporate duties

The executive officers and directors of the Company for the years ended December 31, 2015 hold or have also held the following offices and/or positions:

<b>Name</b>	<b>Other duties and positions held by corporate officers during the financial year ended December 31, 2015</b>	<b>Other duties performed as executive officers or other positions outside of the Company over the last five years and which have ceased as of this day</b>
<b>Gil Beyen</b>	Manager of Gil Beyen BVBA Manager of AXXIS V&C BVBA Director at Novadip SA Director at Waterleau NV Chairman of ERYTECH Pharma Inc.	Director at BIO.be
<b>Pierre-Olivier Goineau<sup>1</sup></b>	Chairman of France Biotech Secretary and Chief Financial Officer of ERYTECH Pharma, Inc. Chairman of Goineau Development & Finance (since March 2015) Chairman of eROCCA (since November 2015)	N/A
<b>Yann Godfrin<sup>2</sup></b>	N/A	Member of the Board of Supervisors for NODEA MEDICAL
<b>Galenos SPRL, represented by Sven Andreasson</b>	Director of 'Immunicum <sup>3</sup> Director at Cellastra Chairman of Cantargia AB <sup>3</sup>	Chairman and CEO of Beta-Cell NV Chairman of Unibioscreen SA Board Member of TiGenix NV Chairman of XImmune AB
<b>Philippe Archinard</b>	Director and Chairman-CEO of Transgene <sup>3</sup> TSGH's permanent representative on the board of ABL Inc. Chief Executive Officer of TSGH	Permanent representative on the Finovi Board of Directors for Lyonbiopôle

Name	Other duties and positions held by corporate officers during the financial year ended December 31, 2015	Other duties performed as executive officers or other positions outside of the Company over the last five years and which have ceased as of this day
	Permanent representative on the Board of Directors of Synergje Lyon Cancer for Lyonbiopôle Director of Biomérieux <sup>3</sup> Chairman of Lyonbiopôle Director of CPE Lyon, representative of FPUL Chairman of BioAster	
<b>Jérôme Bailly</b>	Manager of GELFRUIT SARL (France)	
<b>Martine Ortin George</b>	Manager at Global Development, Associates, Inc.	- Vice-Chairman of Pfizer Inc <sup>3</sup> . United States - Senior Vice President, GPC Biotech Inc. United States - Director, Cytomics Inc. (France)
<b>Hilde Windels</b>	- Director, VIB <sup>3</sup> - Director, Flanders Bio - Director and Chief Operating Officer at BioCartis - Director, BioCartis Group	- Director, MDX Health, - Chief Financial Officer, Pronota - Chief Financial Officer, Seps Pharma
<b>Luc Dochez</b>	Chairman and Chief Executive Officer and Director of Tusk Therapeutics SA and Tusk Therapeutics Ltd since March 2015 Executive Director Tusk Therapeutics NV Head of business at Prosensa <sup>3</sup> until January 15, 2015 Managing Director Primix Bioventures BVBA Managing Director Premis BVBA Managing Director Medilanon BVBA	CEO / Director Ovizio SA Director Arcarios BV

<sup>1</sup>Pierre-Olivier Goineau resigned from his positions at ERYTECH Pharma on January 11, 2015 (cf. supra §3.7.4.1).

<sup>2</sup>Yann Godfrin resigned from his positions at ERYTECH Pharma on January 18, 2016.

<sup>3</sup>Company listed on a regulated market.

#### 14.1.4 Experience with administrative and managerial bodies

The experience of each of the Company's executive officers and directors is described below.

- **Gil Beyen, Chairman and Chief Executive Officer:**

Gil Beyen has held the position of Chief Executive Officer of the Company since May 2013 and Chairman of the Board of Directors of the Company since August 2013. Prior to his appointment as Chief Executive Officer, he had worked with the Company since 2012 as a consultant and also served as Chairman of our Supervisory Board from August 2012 to May 2013. Gil was the Co-founder and Chief Executive Officer (CEO) of TiGenix (NYSE Euronext: TIG BB) for 12 years. Before creating TiGenix, he had directed the Life Sciences division at the international management consulting company Arthur D. Little in Brussels. He holds a master's degree in bioengineering from the University of Louvain (Belgium) and an MBA from the University of Chicago (USA).

- **Yann Godfrin, Chief Operating Officer and director (until January 18, 2016):**

Since co-founding the Company, Yann Godfrin has held the position of Scientific Director and member of the Board of Directors of the Company. He also held the position of Chief Executive Officer of the Company from 2004 to 2010. Prior to the co-founding of the company, Yann Godfrin was the R&D director of Hemoxymed Europe. He was also an industrial development consultant for BioAlliance Pharma and Hemosystem. Yann holds a doctorate in Life and Health Sciences from Université de Nantes, a degree in Biomedical Engineering from Université de Technologie de Compiègne, and a master's degree in Clinical Development of Health Products from Université de Lyon, France. He is the inventor of numerous patents and the co-author of numerous scientific publications. He is a member of several scientific societies.

- **Jérôme Bailly, Deputy Chief Executive Officer:**

Jérôme Bailly has held the position of Chief Pharmacist in the Company since 2011 and of Director of Pharmaceutical Operations since 2007. Before joining the company in 2007, Jérôme Bailly was QA/Production Manager at Skyepharma and Laboratoire Aguettant. Jérôme Bailly has a doctorate of Pharmacy and holds a Chemical Engineering degree with a concentration in Biopharmaceutical Engineering and Cell Production from École Polytechnique de Montréal.

- **Galenos, represented by Sven Andreasson, director:**

Sven Andreasson is the Director of Business Affairs at Novavax (United States) and former Chairman and Chief Executive Officer of Isconova AB (Uppsala, Sweden), Beta-Cell NV (Brussels), Active Biotech AB (Lund, Sweden), and several companies in the Pharmacia group. He has much experience in international biotechnology companies and in the pharmaceutical industry. Sven Andréasson holds a Bachelor of Science and Business Administration and Finance from the Stockholm School of Economics and Business Administration.

- **Philippe Archinard, director:**

Philippe Archinard was appointed General Manager of Transgene on December 7, 2004, after spending 15 years with bioMérieux in various positions, including management positions in the U.S. subsidiary. Philippe Archinard has been CEO of Innogenetics since March 2000. He is a chemical engineer and holds a PhD in biochemistry from Université de Lyon in addition to the Harvard Business School's Program for Management Development (PMD).

- **Martine Ortin George, director:**

A doctor of medicine, Martine George has broad experience in the United States in clinical research, medical affairs, and regulatory matters, acquired within large and small companies specialized in oncology. Until recently, Dr. George was Vice President in charge of Global Medical Affairs for Oncology at Pfizer in New York. Previously, she held the positions of Medical Director at GPC Biotech at Princeton and Head of the Oncology Department at Johnson & Johnson in New Jersey. Martine George is a qualified gynecologist and oncologist, trained in France and in Montreal. She began her career as the Department Head at Institut Gustave Roussy in France, and was a visiting professor at Memorial Sloan Kettering Cancer Centre in New York.

- **Hilde Windels, director:**

Hilde Windels has more than 20 years of experience in corporate financing, capital markets, and strategic initiatives. She is the Chief Executive Officer and Director at Biocartis, a molecular diagnosis and immunodiagnostic solutions company based in Belgium and in Switzerland. Hilde Windels was previously the Chief Financial Officer at Devgen (Euronext: DEVG) from 1999 to the end of 2008, and member of the Devgen Board of Directors from 2001 to the end of 2008. From early 2009 to mid-2011, she worked as an independent Chief Financial Officer for various private companies specialized in biotechnologies and sat on the Board of Directors of MDX Health (Euronext: MDXH) from June 2010 to the end of August 2011. Previously, she was a corporate banking services manager at ING for a region of Belgium. She has a degree in economics from Université de Louvain (Belgium).

- **Luc Dochez, director:**

Luc Dochez was Chief Business Officer and Senior Vice-President of Business Development at the Dutch company Prosensa (NASDAQ: RNA) until its recent acquisition by Biomarin. In this position, he played a key role in establishing a partnership with GSK valued at more than €500 million; he was likewise actively involved in the successful introduction of the company on NASDAQ and managed the acquisition of the company by Biomarin for an amount of \$860 million. Before Prosensa, Luc was Vice President of Business Development at TiGenix (Euronext: TIG), Director Business Development at Methexis Genomics, and consultant at Arthur D. Little.

## 14.2 Potential conflicts of interest and agreements

Related agreements are described in Section 19.2 of this Reference Document.

To the company's knowledge, there are no current or potential conflicts of interest between the duties, for the Company, and the private interests and/or duties of persons comprising the administrative, management, and senior management bodies, as referenced in Section 14.1 "Executive Officers and Directors" above.

Furthermore, to the Company's best knowledge, no agreements of any kind have been signed with shareholders, customers, suppliers or anyone else whereby a Company director or executive has been appointed.

## 15 REMUNERATION AND BENEFITS

### 15.1.1 Remuneration and in-kind benefits allocated to the Company's corporate officers for the previous financial year

The information is prepared in accordance with the Corporate Governance Code for small and mid-sized companies as published in December 2009 by Middlednext and approved by the AMF as a corporate governance standard.

The following tables are based on the AMF guidelines published on December 2, 2014 (*Position - recommandation AMF n°2014-14*),

The positions held at this date by the below-indicated persons are outlined in detail in Chapter 14 - Administrative, Management, and Supervisory Bodies of this Reference Document.

#### **Table 1: Summary of remuneration and founder subscription warrants (BSPCEs) awarded to executive officers:**

	2015 financial year:	2014 financial year:
<b>Gil Beyen – Chairman-Chief Executive Officer</b>		
Remuneration due for the year (detailed in Table 2)	€414,037	€372,268
Valuation of the options awarded during the year (detailed in Table 4)	€0	€513,960
Valuation of the performance shares awarded during the year (detailed in Table 6)		
<b>TOTAL</b>	<b>€414,037</b>	<b>€886,228</b>
<b>Pierre-Olivier Goineau – Vice Chairman and Deputy Chief Executive Officer</b>		
Remuneration due for the year (detailed in Table 2)	€9,579	€275,422
Valuation of the options awarded during the year (detailed in Table 4)	€0	€220,482
Valuation of the performance shares awarded during the year (detailed in Table 6)		
<b>TOTAL</b>	<b>€9,579</b>	<b>€495,904</b>
<b>Yann Godfrin – Deputy Chief Executive Officer</b>		
Remuneration due for the year (detailed in Table 2)	€308,852	€275,268
Valuation of the options awarded during the year (detailed in Table 4)	€0	€234,127
Valuation of the performance shares awarded during the year (detailed in Table 6)		
<b>TOTAL</b>	<b>€308,852</b>	<b>€509,395</b>



<b>Jérôme Bailly, Chief Operating Officer</b>		
Remuneration due for the year (detailed in Table 2)	€102,163	€70,085
Valuation of the options awarded during the year (detailed in Table 4)	€55,118	€39,166
Valuation of the performance shares awarded during the year (detailed in Table 6)		
<b>TOTAL</b>	<b>€157,281</b>	<b>€109,251</b>

**Table 2: Summary of remuneration of corporate officers:**

<b>Gil Beyen</b>	<b>2015 financial year:</b>		<b>2014 financial year:</b>	
	<b>Amount due</b>	<b>Amount paid</b>	<b>Amount due</b>	<b>Amount paid</b>
fixed remuneration <sup>(1)</sup>	€270,000	€270,000	€244,000	€244,000
variable remuneration <sup>(1),(2)</sup>	€135,000	€135,000	€125,600	€91,500
exceptional remuneration <sup>(1),(4)</sup>				
directors' fees				
benefits in kind <sup>(3)</sup>	€9,037	€9,037	€2,668	€2,668
<b>TOTAL</b>	<b>€414,037</b>	<b>€414,037</b>	<b>€372,268</b>	<b>€338,168</b>

<b>Pierre-Olivier Goineau</b>	<b>2015 financial year:</b>		<b>2014 financial year:</b>	
	<b>Amount due</b>	<b>Amount paid</b>	<b>Amount due</b>	<b>Amount paid</b>
fixed remuneration <sup>(1)</sup>	€5,742	€5,742	€175,783	€175,783
variable remuneration <sup>(1),(2)</sup>	-	- €	€90,000	€67,500
exceptional remuneration <sup>(1),(4)</sup>				
directors' fees				
benefits in kind <sup>(3)</sup>	€3,837	€3,837	€9,639	€9,639
<b>TOTAL</b>	<b>€9,579</b>	<b>€9,579</b>	<b>€275,422</b>	<b>€252,922</b>

<b>Yann Godfrin</b>	<b>2015 financial year:</b>		<b>2014 financial year:</b>	
	<b>Amount due</b>	<b>Amount paid</b>	<b>Amount due</b>	<b>Amount paid</b>
fixed remuneration <sup>(1)</sup>	€200,000	€200,000	€175,550	€175,550
variable remuneration <sup>(1),(2)</sup>	€100,000	€100,000	€90,000	€67,500
exceptional remuneration <sup>(1),(4)</sup>				
directors' fees				

benefits in kind <sup>(3)</sup>	€8,852	€8,852	€9,718	€9,718
<b>TOTAL</b>	<b>€308,852</b>	<b>€308,852</b>	<b>€275,268</b>	<b>€252,768</b>
<b>Jérôme Bailly</b>	<b>2015 financial year:</b>		<b>2014 financial year:</b>	
	<b>Amount due</b>	<b>Amount paid</b>	<b>Amount due</b>	<b>Amount paid</b>
fixed remuneration <sup>(1)</sup>	€90,000	€90,000	€60,755	€60,755
variable remuneration <sup>(1)(2)</sup>	€9,000	€9,000	€6,000	€5,172
exceptional remuneration				
directors' fees				
benefits in kind <sup>(4)</sup>	€3,163	€3,163	€3,331	€3,331
<b>TOTAL</b>	<b>€102,163</b>	<b>€102,163</b>	<b>€70,085</b>	<b>€69,258</b>

(1) Components of gross remuneration before taxes

(2) Variable remuneration consists of bonuses set by the Appointments and Remuneration Committee contingent on the achievement of Company objectives that are set annually (for example, Company objectives in previous years included positive outcomes of phases of clinical trials, submission of an MAA, minimum cash balance). The variable remuneration payment is proportional to the percentage of each objective actually achieved.

(3) The benefits in kind are composed of: vehicle rental, gas cards, as well as an unemployment insurance policy with the Garantie Sociale des Chefs et Dirigeants d'Entreprise (French GSC; unemployment insurance provider for corporate leaders)

(4) The benefits in kind consist of a vehicle rental

**Table 3: Attendance fees and other remuneration received by non-executive corporate officers:**

Non-executive corporate officers	Amount paid in fiscal 2015	Amount paid in fiscal 2014
<b>Luc Dochez</b>		
Attendance fees	€25,671	
Other remuneration <sup>(1)</sup>	€251,857	
<b>Sven Andréasson</b>		
Attendance fees		€1,000
Other remuneration <sup>(1)</sup>		€21,290
<b>GALENOS sprl (2)</b>		
Attendance fees	€38,000	€19,476
Other remuneration <sup>(1)</sup>	€335,208	
<b>Philippe Archinard</b>		
Attendance fees	€40,000	€20,476
Other remuneration	€335,208	€42,580
<b>Martine Ortin George</b>		

Attendance fees	€32,000	€10,024
Other remuneration <sup>(1)</sup>	€335,208	
<b>Hilde Windels</b>		
Attendance fees	€36,000	€9,024
Other remuneration <sup>(1)</sup>	€335,208	
<b>TOTAL</b>	<b>€1,764,360</b>	<b>€123,870</b>

(1) Amounts reflecting the fair value of the BSAs granted.

(2) GALENOS SPR is a company controlled by Sven Andreasson

**Table 4: Stock subscription or purchase options and other financial instruments giving rights to capital awarded during the 2015 financial year to each executive officer by the issuer and by any company of the group**

Name of executive corporate officer	Plan no. and date	Type of option (call or subscription)	Valuation of options according to the method adopted for IFRS accounts	Number of options allocated during the financial year	Exercise price for each new subscribed share	Period of exercise
Jérôme Bailly	BSPCE <sub>2014</sub> 01/22/2014	Subscription	Fair value (Black & Scholes) IFRS 7	800 in 2015	€12.25	Lapses on 01/22/2024

**Table 5: Stock subscription or purchase options exercised during the financial year by each executive corporate officer**

Name of executive corporate officer	Number and date of plan	Number of options exercised during the financial year	Exercise price
Jérôme Bailly	No. BSPCE <sub>2012</sub> Date: 8/5/2015	100 warrants (1,000 shares)	€73.62 per warrant (€7.362 per share)
Jérôme Bailly	No. BSPCE <sub>2012</sub> Date: November 16, 2015	78 warrants (780 shares)	€73.62 per warrant (€7.362 per share)
Jérôme Bailly	No. BSPCE <sub>2012</sub> Date: November 16, 2015	196 warrants (1,960 shares)	€73.62 per warrant (€7.362 per share)
Yann Godfrin	No. BSPCE <sub>2012</sub> Date: December 23, 2015	7,508 warrants (75,080 shares)	€73.62 per warrant (€7.362 per share)
TOTAL		7,882 warrants (78,820 shares)	€73.62 per warrant (€7.362 per share)

**Table 6: Performance shares allocated to each corporate officer**

Not applicable.

**Table 7: Performance shares that became available for each corporate officer**

Not applicable.

**Table 8: History of allocation of stock subscription or purchase option**

HISTORY OF ALLOCATION OF STOCK SUBSCRIPTION OR PURCHASE OPTIONS (1)				
INFORMATION ON THE SUBSCRIPTION OR CALL OPTIONS				
Date of general shareholders' meeting	BSPCE <sub>2012</sub> <sup>(1)</sup> General Meeting of 5/21/2012	BSPCE <sub>2014</sub> General Meeting of 4/2/2013	BSA <sub>2012</sub> General Meeting of 5/21/2012	BSA <sub>2014</sub> General Meeting of 4/2/2013
Date of board of directors' meeting or executive board meeting, where applicable	Executive Board 5/31/2012 Board of Directors 7/18/2012 Board of Directors 7/17/2014	Board of Directors 1/22/2014 Board of Directors 6/23/2015	Executive Board 5/31/2012 Board of Directors 7/18/2013 Board of Directors 7/17/2014 Board of Directors 4/29/2015 Board of Directors 4/31/2015	Board of Directors 1/22/2014 Board of Directors 12/4/2014 Board of Directors 6/23/2015
Total number of shares that can be subscribed or called up, <sup>(2)</sup> the number of which can be subscribed or called up by:	337,870 shares can be subscribed representing a total 33,787 warrants	195,000 shares can be subscribed representing a total 19,500 warrants	112,630 shares can be subscribed representing a total 11,263 warrants	30,000 shares can be subscribed representing a total 3,000 warrants
<i>The corporate officers</i>	277,370 shares 27,737 warrants	80,000 shares 8,000 warrants		
<i>Gil Beyen</i>	112,630 shares 11,263 warrants	60,000 shares 6,000 warrants	n/a	n/a
<i>Yann Godfrin</i>	75,080 shares 7,508 warrants.	30,000 shares 3,000 warrants <sup>(5)</sup>	n/a	n/a
<i>Jérôme Bailly</i>	14,580 shares 1,458 warrants	800	n/a	n/a
<i>GALENOS</i>	n/a	n/a	500	n/a
<i>Philippe Archinard</i>	n/a	n/a	2,554	n/a
<i>Hilde Windels</i>	n/a	n/a	1,217	n/a
<i>Martine George</i>	n/a	n/a	1,217	n/a
<i>Luc Dochez</i>	n/a	n/a	867	n/a
Starting point for exercise of options	06/05/2013 (day that the Company shares are admitted for trading on a regulated market) and/or immediately after subscription	Immediate upon subscription	06/05/2013 (day that the Company shares are admitted for trading on a regulated market) and/or immediately after subscription	Immediate upon subscription
Expiry date	5/20/2020	1/22/2024	5/20/2020	1/22/2024
Subscription or call price	€7.362 per share €73.62 per warrant	€12.25 per share €122.50 per warrant	€7.362 per share €73.62 per warrant	€12.25 per share €122.50 per warrant
Methods of exercise (where the plan includes multiple tranches)	1 warrant = 10 shares The holder must exercise a minimum of 50 warrants per exercise or all of them if he has less. The number of exercises is limited to four per year.	1 warrant = 10 shares The holder must exercise a minimum of 50 warrants per exercise or all of them if he has less. The number of exercises is limited to four per year.	1 warrant = 10 shares The holder must exercise a minimum of 50 warrants per exercise or all of them if he has less. The number of exercises is limited to four per year.	1 warrant = 10 shares The holder must exercise a minimum of 50 warrants per exercise or all of them if he has less. The number of exercises is limited to four per year.
Number of shares subscribed as of 2/29/2016 since 5/6/2013	337,870 shares subscribed i.e. 33,787 warrants	0	107,600 shares subscribed i.e. 10,760 warrants	0
Cumulative number of share subscription or call options cancelled or lapsed	0	3,000 <sup>(4)</sup>	0	0
Share subscription or call options remaining at year end <sup>(3)</sup>	174,350 shares 17,435 warrants	193,600 shares 19,360 warrants	57,380 shares 5,738 warrants	30,000 shares 3,000 warrants

<sup>(1)</sup> The General Meeting of May 21, 2012, cancelled the BSPCE<sub>Cadre2006</sub> which had been partially subscribed. The BSPCE<sub>Cadre2006</sub> were replaced by the BSPCE<sub>2012</sub>.

<sup>(2)</sup> Whether the options had been exercised or not

<sup>(3)</sup> As of December 31, 2015

<sup>(4)</sup> 3,000 BSPCE<sub>2014</sub> of the 22,500 BSPCE<sub>2014</sub> issued by the Board of Directors meeting of January 22, 2014, were converted to 3,000 BSA<sub>2014</sub> by the Board of Directors decision of December 4, 2014

<sup>(5)</sup> Of which 1,000 warrants lapsed due to his resignation on January 18, 2016.

**Table 9: Stock subscription or purchase options and founder subscription warrants (BSPCEs) granted to the top 10 non-corporate-officer employees and options exercised by them**

STOCK SUBSCRIPTION OR PURCHASE OPTIONS AND FOUNDER SUBSCRIPTION WARRANTS (BSPCEs) GRANTED TO THE TOP TEN BENEFICIARY NON-CORPORATE-OFFICER EMPLOYEES, AND OPTIONS EXERCISED BY THESE PERSONS	Total number of options allocated/ of shares subscribed or called up	Average weighted price	BSPCE <sub>2014</sub> plan	BSA <sub>2014</sub> plan
Options granted, during the fiscal year, by the issuer and any company included within the option assignment perimeter, to the ten employees of the issuer and of any company included within this perimeter, for whom the number of options thus granted is the highest (global information)	2,010	n/a	1,010	1,000
Options held in relation to the issuer and the aforesaid companies, exercised, during the fiscal year, by the ten employees of the issuer and these companies, for whom the number of options thus called up or subscribed is the highest (global information)	0	n/a	0	0

**Table 10: History of allocation of free shares**

**Not applicable.**

**Table 11: Conditions for remuneration and other benefits granted to the executive corporate officers only**

Executive corporate officers	Employment contract		Supplementary pension plan		Remuneration and benefits due or that may be due on termination or change of duties		Remuneration for a non-compete clause	
	Yes (1)	No	Yes (2)	No	Yes (3)	No	Yes (4)	No
Gil Beyen Chairman and Chief Executive Officer		X	X		X			X
Yann Godfrin Deputy Chief Executive Officer		X	X		X <sup>(5)</sup>			X
Jérôme Bailly Deputy Chief Executive Officer	X		X		X		X	

- (1) Jérôme Bailly benefited from an employment contract from November 15, 2011 until his initial appointment on December 21, 2012 as a corporate officer. He was considered, by the Supervisory Board, then by the Board of Directors, to have continued this employment contract after the aforesaid appointments, as this contract covers separate missions under his term as Head Pharmacist, missions pursuant to which he is subject to a subordination relationship.
- (2) Subscription to the supplementary pension plan with fixed contributions, within the scope of a collective pension policy stipulated by the Company with AXA. Investment in individual accounts paid for by the 5% pension contribution by employees, gross subject to deductions of 2.50% of costs, on the “Horizon” mutual funds managed by AXA.
- (3) Indemnity in an amount equal to one year of remuneration only for Mr. Bevin and Mr. Bailly (see Section 16.4 of this Reference Document).
- (4) Indemnity equal to 1/3 of the average monthly wage received during the last three months of presence at the company ERYTECH Pharma over 18 months. In addition, executive officers also benefit from a supplemental health and insurance plan and incentives (see also sections 17.4 and 19.2 of this Reference Document).
- (5) Mr. Godfrin received no severance pay or benefits upon his departure as he did not satisfy the payment conditions.

## **15.2 Amounts allocated or identified by the Company for the payment of pensions, retirement, or other benefits**

The Company has provisioned no sums to pay pensions, retirement, and other benefits to the corporate offices and/or executive officers, who also have not received severance pay or a signing bonus (see the

Special Report of the Statutory Auditors on regulated agreements and on severance benefits provided for executive corporate officers).

### **15.3 Share subscription warrants, founder subscription warrants, and other securities giving access to the share capital, assigned to directors and executive officers.**

The BSAs (share subscription warrants) and BSPCEs (founder subscription warrants) granted to non-executive or executive corporate officers are outlined in a precise list in Chapter 17.2 of this Reference Document.

### **15.4 Summary statement of transactions by executive officers and persons mentioned in Article L.621-18-2 of the Monetary and Financial Code involving shares of the Company conducted during the past financial year**

During the financial year ended December 31, 2015, the managers and persons indicated in Article L. 621-18-2 of the French Monetary and Financial Code performed the following transactions on Company securities:

- on January 13, 2015, Françoise Horand Pothirath, an executive equivalent person, sold 400 ERYTECH Pharma shares at a unit price of €30.50;
- on January 14, 2015,
  - o Yann GODFRIN, Deputy Chief Executive Officer, sold:
    - 111,687 ERYTECH Pharma shares at a unit price of €29,7951;
  - o Gil Beyen, Chief Executive Officer, sold:
    - 25,316 ERYTECH Pharma shares at a unit price of €29,7951;
- on January 15, 2015,
  - o Gil Beyen, Chief Executive Officer, sold:
    - 8,684 ERYTECH Pharma shares at a unit price of €29,0293;
  - o Yann Godfrin, Deputy Chief Executive Officer, sold:
    - 38,313 ERYTECH Pharma shares at a unit price of €29,0293;
- on February 20, 2015, Jérôme Bailly, Deputy Chief Executive Officer, sold 300 ERYTECH Pharma shares at a unit price of €27.60;
- On February 27, 2015, Françoise Horand Pothirath, an executive equivalent person, exercised 160 founder subscription warrants (BSPCE<sub>2012</sub>) at a unit price of €73.62;
- on April 9, 2015, Jérôme Bailly, Deputy Chief Executive Officer, sold:
  - 300 ERYTECH Pharma shares at a unit price of €26.08; and
  - 200 ERYTECH Pharma shares at a unit price of €27.50;
- on May 4, 2015, Jérôme Bailly, Deputy Chief Executive Officer, sold 1,000 ERYTECH Pharma shares at a unit price of €32.50;
- on May 22, 2015, Françoise Horand Pothirath, an executive equivalent person, sold 596 ERYTECH Pharma shares at a unit price of €34.11;
- on May 25, 2015, Françoise Horand Pothirath, an executive equivalent person, sold 404 ERYTECH Pharma shares at a unit price of €34.50;
- on May 27, 2015, Françoise Horand Pothirath, an executive equivalent person, sold 1,000 ERYTECH Pharma shares at a unit price of €35.00;
- on July 16, 2015, Françoise Horand Pothirath, an executive equivalent person, sold 200 ERYTECH Pharma shares at a unit price of €35.00;
- on July 21, 2015, Jérôme Bailly, Deputy Chief Executive Officer, sold 500 ERYTECH Pharma shares at a unit price of €35.00;
- on July 24, 2015, Jérôme Bailly, Deputy Chief Executive Officer, sold 500 ERYTECH Pharma shares at a unit price of €35.50;
- on August 7, 2015, Françoise Horand Pothirath, an executive equivalent person, exercised 90 founder subscription warrants (BSPCE<sub>2012</sub>) at a unit price of €73.62.



- On November 10, 2015, Jérôme Bailly, Deputy Chief Executive Officer, sold 700 shares of ERYTECH Pharma at a unit price of €29.05 and exercised 274 founder subscription warrants (BSPCE<sub>2012</sub>) at a unit price of €29.05.
- On December 23, 2015, Yann Godfrin, Deputy Chief Executive Officer, exercised 7,508 founder subscription warrants (BSPCE<sub>2012</sub>) at a unit price of €73.62.

Since December 31, 2015, the executive officers and persons stipulated in Article L.621-18-2 of the French Monetary and Financial Code have executed the following transactions on the Company's shares:

- On February 1, 2016, Philippe Archinard, director, exercised 717 share warrants (BSA<sub>2012</sub>) at a unit price of €73.62.

## 16 OPERATION OF THE ADMINISTRATIVE AND MANAGEMENT BODIES

The Company has a Board of Directors, a Management Committee, a Remuneration Committee, an Audit Committee and a Scientific and Medical Board.

### 16.1 Term of office for directors

Refer to Section 14.1.1 “Composition of the Board of Directors” in this Reference Document.

### 16.2 Service agreements binding members of the Board of Directors and Senior Management with the Company

As of the date of this Reference Document, there are no agreements binding members of the Board of Directors and Senior Management with the Company or its subsidiary ERYTECH Pharma, Inc.

### 16.3 Corporate governance, internal audit, and risk management

The Company complies with all provisions of the corporate governance code for small and mid-caps published by Middlednext in 2009 and validated as a code of reference by the AMF.

For the financial year ending December 31, 2015, in addition to the information provided in the present section, the status of application of the guidelines in the Middlednext Code is as follows:

Guidelines from the MiddleNext Code	Adopted
<b>I. Executive power</b>	
R 1: Total employment contract and term as officer	X
R 2: Definition and transparency in remuneration for executive corporate officers	X
R 3: Severance pay	X
R 4: Supplemental pension plans	X
R 5: Stock options and awards of free shares	X
<b>II. The power of “oversight”</b>	
R 6: Implementation of rules of procedure for the board	X
R 7: Professional ethics for members of the board	X
R 8: Composition of the board – Presence of independent members on the board	X
R 9: Selection of board members	X
R 10: Term for which board members are elected	X
R 11: Notice to board members	X
R 12: Implementation of committees	X
R 13: Meetings of the Board and of committees	IN PROGRESS <sup>(1)</sup>
R 14: Remuneration for directors	X
R 15: Implementation of an evaluation of work by the Board	X

<sup>(1)</sup> The Company held as many meetings of its Board of Directors and its committees as it considered necessary (see Section 16.3.2 of this Reference Document).

The Company believes that its organization and the procedures implemented (including, namely, the Board of Directors' Rules of Procedure, regularly revised by the directors in order to ensure its relevance and compliance with the Middlenext Code) make it possible to comply with almost all of the recommendations in the Code.

## 16.3.1 ISO certification

Certificate FR09/01496

The ERYTECH PHARMA management system

# ERYTECH PHARMA

60 avenue Rockefeller  
69008 Lyon  
France

has been audited and certified in accordance with the requirements of

## ISO 9001: 2008

For the following activities

Research, development, manufacturing and sale of cell based medicinal products for the site of Lyon.

**Research, development, manufacturing and sale of cell based medicinal products for the site of Lyon.**

This certificate is valid from July 30, 2012, to July 29, 2015, and remains valid until a satisfactory decision is issued based on follow-up audits  
Certification renewal date April 29, 2015  
Version 2. Certified since 2009

Authorized by



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## 16.3.2 Chairman's report on internal audits

### A. Conditions for preparing and organizing the work of the board of directors

During its meeting on May 6, 2013, the Board of Directors adopted rules of procedure that were last updated on April 25, 2014. These rules of procedure may be consulted on the Company's website. They specify the role and composition of the Board, the principles of conduct, and the obligations of the members of the Board of Directors towards the Company and the procedures for the operation of the Board of Directors and the committees, and the rules for determining the remuneration of their members. All members of the Board of Directors agree to devote the necessary time and attention to their duties. They shall inform the Board of any situations in which they may find themselves that present a conflict of interest. Furthermore, the rules of procedure incorporate current regulations pertaining to the dissemination and use of privileged information and specify that the members must abstain from engaging in transactions involving the Company's shares when they possess privileged information. All members of the Board of Directors are required to inform the Company and the AMF of any transactions involving the Company's shares that they perform, whether directly or indirectly.

After having examined the provisions of the code of corporate governance for listed companies developed by MiddleNext in December 2009, in particular the elements presented in the heading "points of vigilance," the Board of Directors, in its meeting on May 6, 2013, decided to adopt rules of procedure in which it is stated that the Company shall comply with the MiddleNext Code as a corporate code of governance for the Company.

The MiddleNext Code may be viewed at the following website:  
[http://www.middlenext.com/IMG/pdf/Code\\_de\\_gouvernance\\_site.pdf](http://www.middlenext.com/IMG/pdf/Code_de_gouvernance_site.pdf).

The Company follows the recommendations of the MiddleNext Code, except for the recommendation of the frequency of audit committee meetings as explained below. It should be noted that the recommendation relative to stock options and the allocation of free shares is not applicable by the Company, as no stock options or free shares have been allocated by the Company to its corporate officers.

#### A.1. Composition of the board:

During the financial year ended December 31, 2015, the following changes took place concerning the Board of Directors:

- Pierre-Olivier Goineau resigned from his positions as Vice Chairman, Deputy Chief Executive Officer, and Director of the Company;
- Luc Dochez was co-opted in the Board of Directors' meeting as Company director replacing Pierre-Olivier Goineau, who resigned. This appointment was ratified by the General Meeting of June 23, 2015. The term of office of Luc Dochez will expire at the end of the 2016 Ordinary General Shareholders' Meeting voting on the financial statements for the fiscal year ending December 31, 2015.

By virtue of legal provisions and of the bylaws, the Board of Directors is composed of no fewer than three directors and no more than eighteen. Directors are appointed, reappointed to their position, or removed by the Company's ordinary General Meeting. Their term of office, in accordance with Article 17 of the bylaws, is three years.

At December 31, 2015, the Board of Directors was composed of six members, i.e.:

Name	Date of appointment or co-optation	Term expires in
Mr. Gil Beyen (Chairman and Chief Executive Officer)	5/6/2013	2016
Mr. Yann Godfrin (Deputy Chief Executive Officer)	5/6/2013	2016
GALENOS SPRL, represented by Sven Andréasson	1/22/2014	2016
Mr. Philippe Archinard	5/6/2013	2016
Martine Ortin George	6/17/2014	2017
Mrs. Hilde Windels	9/17/2014	2017
Mr. Luc Dochez	3/26/2015	2016

It should be noted that the Board of Directors, at its meeting on January 10, 2016, acknowledged the resignation of Yann Godfrin from his positions as Scientific Director, Deputy Chief Executive Officer and Director.

These directors were appointed to the Board of Directors because of their knowledge of the Company's activities, their technical and general skills and abilities, as well as their aptitude to fulfill the directors' duties required for the Board.

The Company is aware of the provisions stated in the Law of January 27, 2011 pertaining to balanced representation of men and women on boards of directors. At December 31, 2015, the Company's Board of Directors was composed of four men and two women, i.e. a proportion of women greater than 20% of the members of the Board of Directors, as required by that law at the end of the first ordinary general shareholders' meeting following January 1, 2014. The Law of January 27, 2011, further requires that the proportion of men and women be at least equal to 40% at the end of the first ordinary general shareholders' meeting following January 1, 2017, or, where the Board of Directors is not composed of more than eight members, that the difference between the number of members of each gender not be greater than two.

In accordance with the MiddleNext Code, the Board of Directors includes several independent directors, GALENOS, Philippe Archinard, Martine Ortin George, and Hilde Windels, who meet the independence criteria defined by the MiddleNext Code.

The criteria specified by the MiddleNext Code make it possible to show that the members of the Board are independent, as characterized by the lack of a significant financial, contractual, or familial relationship capable of altering independent judgment, namely:

- they are neither an employee nor an executive corporate officer of the Company or a company within its group, and they have not been either of these in the last three years;
- they are not significant clients, suppliers, or bankers for the Company or its group or for which the Company or its group represent a significant share of business;
- they are not major shareholders of the Company;
- they do not have any close family connection with an officer or a major shareholder;
- they were not an auditor of the Company over the last three years.

The list of Company directors, including the positions held in other companies, is shown in chapter 13 of this Reference Document.

During the Company's Combined General Shareholders' Meeting of June 23, 2015, the total annual amount of attendance fees allocated to directors was set at €176,000, and is applicable to the current year.

The Board of Directors' meeting of January 10, 2016 approved the distribution of attendance fees in function of the regularity of the directors' attendance and of the time that they dedicated to their position during the financial year ended 2015, in accordance with the recommendations of the Remuneration Committee, which met on the same day.

#### **A.2. Frequency of meetings**

Article 19 of the bylaws states that the Board shall meet as often as the interests of the Company require.

During the year ended December 31, 2015, the Board of Directors met eleven times: January 11, March 26, April 29, June 23, July 8, August 31, September 8, September 25, October 19, October 29, and December 2.

The number of Board of Directors' meetings held during the financial year ended December 31, 2015 complies with the recommendations of the MiddleNext Code, which requires a minimum of four meetings annually.

A list of agenda items addressed in meetings of the Board of Directors during this financial year is provided below in paragraph A.6.

The attendance rate of members of the Board of Directors during the financial year ended December 31, 2015 was 91% (the rate was 87% during the financial year ended December 31, 2014).

#### **A.3. Summons of directors**

The directors were summoned with reasonable advance notice of meetings pursuant to Article 19 of the bylaws.

Pursuant to Article L.225-238 of the Commercial Code, the Statutory Auditors were given notice to appear at the meetings of the Board, which examined and approved the interim financial statements (half-year financial statements) as well as the annual financial statements.

#### **A.4. Information provided to directors**

All documents and information necessary for the directors' mission were provided to them at the same time as the notice of meeting or delivered at the beginning of each meeting of the Board of Directors.

The Board of Directors is assisted by three permanent committees whose powers and procedures are specified in the rules of procedure: The Audit Committee, the Remuneration and Appointments Committee, and the Scientific Board.

#### **A.5. Location of meetings**

The meetings of the Board of Directors take place at the headquarters or at any other location indicated in the notice of meeting, pursuant to Article 19 of the bylaws.

#### **A.6. Decisions adopted**

During the financial year recently ended, the main subjects listed below were discussed by the Board of Directors:

- The conditions for remuneration of executive officers;
- The co-optation of a new director;
- Approval of the annual budget;
- A capital increase through the issue of new shares;



- Capital increases resulting from the exercise of BSA<sub>2012</sub> and BSPCE<sub>2012</sub>;
- Capital increases resulting from the exercise of BSA<sub>2014</sub> and BSPCE<sub>2014</sub>;
- The list of beneficiaries of BSA<sub>2012</sub>;
- The list of beneficiaries of BSA<sub>2014</sub> and BSPCE<sub>2014</sub>;
- The interim financial statements and the half-year financial report;
- Professional gender equality.

#### **A.7. Meeting minutes**

Minutes of the meetings of the Board of Directors are prepared following each meeting and immediately sent to all directors. They are approved at the beginning of the following Board meeting.

#### **A.8. Evaluation by the Board of Directors**

The Chairman, once per year, shall ask the directors for an opinion about the operation and preparation of the work by the Board. During the Board of Directors' meeting of March 26, 2015, the Chairman invited members of the Remuneration and Appointments Committee to issue a reasoned opinion on these matters. On the basis of this opinion, the directors expressed themselves on October 19, 2015.

#### **A.9. Specialized committees**

ERYTECH Pharma pursues an information policy relative to corporate governance and the transparency of remuneration of all its primary corporate officers.

Accordingly, in 2007, a Scientific Board was formed and in 2008, an Audit Committee and a Remuneration and Appointments Committee were formed to assist the Supervisory Board which then became the Board of Directors in its considerations and its decisions. These committees are described in the rules of procedure, which was last updated by the Board of Directors on April 25, 2014.

The Board of Directors establishes the composition and powers of the committees which conduct their activities under its responsibility. These powers may involve delegating powers to a Committee which are expressly allocated to it by law or by the bylaws or by any other shareholder agreement enforceable as against the Company.

These Committees are purely internal to the Company. They do not have any inherent power and in particular no decision-making power. Their role is strictly advisory.

Each Committee reports on its missions to the Board of Directors.

The Board of Directors then has sole discretion to assess any follow-up it intends to make with respect to the findings presented by the Committees. Each director remains free to vote as he or she sees fit, without being bound by any studies, investigations, or reports from the Committees, or any of their recommendations.

Each Committee shall include no fewer than two members and no more than ten members. Members are appointed personally by the Board of Directors based on their experience and may not be represented. The Committees may be composed solely of directors or even include outside persons. The composition of these Committees may be modified at any time by a decision of the Board of Directors.

The term of office for the Committee members coincides with their term as directors when they are board members. The term of a Committee member may be renewed at the same time as that of the director. For Committee members who are not members of the Board of Directors, the term of office is set at one (1) year and is automatically renewable.

Committee meetings are held at the Company's headquarters or at any other location decided by the Committee Rapporteur. However if necessary, Committee meetings may be held by teleconference or videoconference.

For the correct operation of the Committees and their administrative process, the Rapporteur of each Committee:

- Draws up the agenda for each meeting according to the needs expressed by the Board of Directors;
- Formally serves notice to the members; and
- Directs discussion.

Within each Committee, the Rapporteur appoints one person who shall be tasked with writing the minutes following each meeting. The minutes shall be sent to the Chairman of the Board of Directors. The minutes shall be kept by the Company. The reports on the work and recommendations from each Committee shall be presented by the Rapporteur to the Board of Directors.

In its field of competence, each Committee issues recommendations, proposals, and opinions.

### **Confidentiality:**

Because information communicated to the Committees or to which the Committee members have access for their missions is confidential in nature, Committee members are required to adhere to the strictest confidentiality in matters pertaining to the Board of Directors with regard to any third party to a degree identical to that applicable to directors. This provision also applies to any outside persons who might be invited.

#### **A.9.1. Audit Committee**

Currently, the Audit Committee is composed of three members appointed for the duration of their terms as directors.

During the year ended December 31, 2015, the Audit Committee met three times: March 16, July 8, and September 8.

The number of meetings of the Audit Committee during the year ended December 31, 2015 is not in line with the recommendation of the MiddleNext Code, which stipulates a minimum of four annual meetings. However, the Company planned for the Audit Committee to meet at least four times in 2016, for the quarterly review of its financial results and its internal control environment.

The Audit Committee's mission is to monitor the existence and effectiveness of the Company's financial audit and risk control procedures on an ongoing basis. This committee is tasked with:

- examining the corporate and consolidated annual and interim financial statements;
- approving the relevance of the accounting methods and choices;
- verifying the relevance of financial information published by the Company;
- overseeing the implementation of internal control procedures;
- verifying the correct operation of internal controls with the assistance of internal quality audits;
- examining the schedule for internal and external audits;
- examining any subject capable of having a meaningful financial and accounting impact;
- examining the state of significant disputes;
- examining off-balance sheet commitments and risks;
- examining the relevance of risk monitoring procedures;
- examining any regulated agreements;
- directing the selection of statutory auditors, their remuneration, and ensuring their independence;
- verifying the correct performance of the statutory auditors' mission;
- establishing the rules for the use of statutory auditors for work other than auditing accounts and verifying the correct execution thereof.

The Audit Committee may conduct visits or interviews of any directors of operational or functional entities useful in the fulfilment of its mission. It can also hear from the external auditors, including without the presence of corporate officers. It may make use of outside experts with prior approval from the Board of Directors.

Currently, the members of the audit committee are:

- Hilde Windels, rapporteur and independent member;
- GALENOS, represented by Sven Andréasson, independent member (see also Section A.1 above);
- Philippe Archinard, independent member.

The experience of the members of the Audit Committee is presented in Section 13.1.4 of the Reference Document.

It is hereby specified that these three members hold specific financial and accounting competencies, as a result of their experience of nearly 25 years in the pharmaceutical industry and general management positions that they have held and still hold.

Among the points discussed during these meetings:

- The annual financial statements and the annual report for the year ended December 31, 2014;
- The interim financial statements and the interim financial report.

#### **A.9.2. Remuneration and Appointments Committee**

The Remuneration and Appointments Committee is composed of three independent members pursuant to the internal regulations:

- Hilde Windels, rapporteur and independent member,
- Philippe Archinard, independent member,
- The company Galenos, represented by Sven Andréasson and an independent member.

In the financial year ended December 31, 2015, the Remuneration and Appointments Committee met twice, on January 11 and March 6.

The experience of the members of the Remuneration and Appointments Committee is presented in Section 13.1.4 of the Reference Document.

This committee hears directors about the evaluation of the Company's performance in light of the defined goals. Additionally, and in particular, this committee performs the following duties:

- It formulates recommendations and proposals concerning (i) the various components of remuneration, pension and health insurance plans for officers and directors, and defines in particular, (ii) the procedures for establishing the variable portion of their remuneration; (iii) and formulates recommendations and proposals concerning a general policy for awarding share subscription warrants and founder subscription warrants;
- It examines the amount of attendance fees and the system for distributing them between the directors taking into account their dedication and the tasks performed within the Board of Directors;
- It advises and assists as necessary the Board of Directors in the selection of senior executives and the establishment of their remuneration;
- It assesses any increases in capital reserved to employees;
- It assists the Board of Directors when selecting new members;
- It ensures the implementation of structures and procedures to allow the application of good governance practices within the Company;
- It prevents conflicts of interest within the Board of Directors;
- It implements the Board of Directors' evaluation procedure.

The committee met twice during the year ended December 31, 2015.

Among the points discussed during these meetings:

- The conditions for remuneration of executive officers;
- The implementation of a severance package in the event of a change of control.

### **A.9.3. Scientific and Medical Board**

The members of the Scientific and Medical Board were selected because of their scientific expertise in the fields of activity engaged in and developed by the Company.

The Board is thus primarily composed of persons from outside the Company, and it meets at least once per year to evaluate, from a scientific point of view, (i) the conduct and progress of research programs conducted by the Company, (ii) the Company's development strategy, particularly given therapeutic needs and market needs and (iii) any risks that might be posed by the research and development programs of the Company's competitors.

The six members of this Board were appointed for a term of one (1) year, which is automatically renewable (except for the Deputy Chief Executive Officer in charge of scientific duties, who is the rapporteur and a member ex officio).

The members of the Scientific and Medical Board and their relationships with the Company are detailed in the table below:

Name	Connection with the Company	Member of the Scientific Board since
Dr. Yann Godfrin	Deputy Chief Executive Officer	2007 <sup>25</sup>
Dr. Iman El-Hariry	Medical Director	2016
Prof. Eric Raymond	Consultant	2009
Dr. Philip L. Lorenzi	Consultant	2010
Dr. Bridget Bax	Consultant	2012
Prof. Arthur E. Frankel	Consultant	2012
Dr. Kurt Gunter	Consultant	2012

The experience of Dr. Yann Godfrin and Dr. Iman El-Hariry are presented in Section 14.1.3 of the Reference Document.

Prof. Eric Raymond, Doctor of Medicine

Head of Medical Oncology Service, CHUV de Lausanne, Switzerland. Expert in innovative therapies against solid tumors.

Dr. Philip L. Lorenzi, Doctor of Medicine

Laboratory and Research Director at MD Anderson Cancer Centre, Houston, Texas, USA. Specializes in translational research in pharmacogenomics in the identification of biomarkers and their action mechanisms. Expert in asparagine synthetase in cancer cells.

Dr. Bridget Bax, PhD (Doctor of Sciences)

Senior researcher at the Division of Sciences of Clinical Development of the St. George Hospital and Associate Professor, Metropolitan University of London, Great Britain. Expert in metabolic diseases and enzyme therapies.

Prof. Arthur E. Frankel, Doctor of Medicine

Head of the Hematology / Oncology Division at Scott & White Cancer Institute, Texas, United States, and Professor at Texas Health Science Centre College of Medicine. He has worked on the deprivation of amino acids as a therapy against cancer.

Dr. Kurt Gunter, Doctor of Medicine

Kurt Gunter is chairman of the International Society of Cellular Therapy until 2014 and, since March 2013, has been Chief Medical Officer of Cell Medica (U.K.). Until the end of March 2013, he was head of the Department of Regenerative Medicine for Hospira Inc. in Chicago (USA). He is an expert in the development of medicine and particularly with respect to regulatory aspects. He was Acting Deputy Director at the FDA (Food and Drug Administration) of the CBER (Centre for Biologics Evaluation and Research).

**B. Internal control and risk management procedures within the Company**

**B.1. Conceptual framework for internal controls and risk management**

Reference

The Company relies on the AMF's reference framework (Recommendation No. 2010-16) pertaining to risk management and internal control mechanisms, to the AMF Recommendation No. 2010-15 of

<sup>25</sup> Until January 18, 2016

December 7, 2010 pertaining to the AMF's additional report on corporate governance, remuneration of executive officers, and internal controls for small- and mid-cap companies that use the MiddleNext Code, and to the AMF Recommendation No. 2013-17 entitled "Chairmen's Reports on Internal Control and Risk Management Procedures – Consolidated Presentation of Recommendations contained in the AMF Annual Reports."

## **B.2. Risk management**

### Goals:

- Promote achievement of the Company's objectives (see also Section B.4 below);
- Analyze and process risks identified by the Company to date and presented in Chapter 4 of this Reference Document, namely by:
  - maintaining a high level of product quality and safety;
  - protecting the Company's interests;
  - securing the Company's processes.

### Components of the mechanism:

Responsibility for risk management is held by the Chief Financial Officer and Chief Operating Officer Eric Soyer.

The risk management mechanism provides, in particular:

- analyses of risks (identification, analysis, and treatment of the risk);
  - processes and especially the Production process, as well as;
  - physical security and information systems;
  - the Company's assets and reputation.
- A risk management procedure that defines:
  - the role:
    - of the process managers;
    - of the Quality Assurance department and Chief Pharmacist.
  - direction of the mechanism, via the process of Management and ongoing Improvement and management reviews.
  - appropriate communication for its implementation by both external and internal actors.

## **B.3. Internal controls**

### Internal control objectives:

Internal control is one of the Company's mechanisms. It is intended to ensure:

- compliance with laws and regulations;
- application of the instructions and guidelines established by Senior Management;
- the correct operation of the Company's internal processes, particularly those intended to assist in the protection of its assets;
- reliability of financial information;
- and, generally speaking, contributes to the control of its activities, the effectiveness of its operations, and the efficient use of its resources.

By contributing to the prevention and control of risks of not achieving the objectives established by the Company (see also section below), the internal control mechanism plays a key role in the conduct and management of its various activities.

However, internal controls cannot provide an absolute guarantee that the Company's objectives shall be reached.

#### Components of the mechanism:

In collaboration with the Audit Committee (see also Section B.4.4 below), the responsibility for internal control is carried by the Chief Financial Officer and Chief Operating Officer, Eric Soyer.

The internal audit mechanism provides:

- an organization that includes a clear definition of responsibilities, possesses adequate skills, abilities, and resources (see also Section B.4.4 below), and relies on procedures, information systems, tools, and appropriate practices (see also Section B.4.1 below);
- the internal dissemination of relevant and reliable information (namely via an electronic document management system), the knowledge of which allows each person to exercise his/her responsibilities;
- a system intended to survey and analyze the primary identifiable risks with regard to the Company's goals and ensure the existence of procedures to manage these risks;
- control activities proportionate to the stakes inherent to each process, designed to reduce risks likely to affect the achievement of the Company's goals;
- ongoing monitoring of the internal control mechanism as well as regular examination of its operation.

#### **B.4. Scope of risk management and internal control**

##### **B.4.1. Quality System**

ERYTECH's management has always sought to offer the best possible service and the best advice in order to fully respond to the needs and requirements of hospital-based healthcare professionals. This orientation allows it to guarantee its development and its continued existence.

The application of this quality policy involves all of the company's department. It is reflected by the establishment and the tracking of shared goals.

In order to correctly implement this policy, the Company relies on its existing quality system, which is ISO 9001-certified and described in the Quality Manual.

With the goal of seeing that this policy is applied, executive officers personally commit and delegate to the Quality Assurance Department (in collaboration with the relevant departments) the implementation and monitoring of the quality system. It is directly responsible to management, and it must report on the operation of the system. It relies on process managers for efficient management of the quality system.

Management also undertakes to deploy all current resources to personally ensure the implementation and efficacy of the quality system during management reviews and meetings of the Management Committee.

The company's evolution from a research and development structure towards a structure that integrates sales requires modification of the current system to account for new client demands by striving to achieve operational excellence, with collective involvement in this undertaking.

##### **B.4.2. Financial Information**

The Company has, in particular, organized things in the following manner to limit risks from accounting and financial management:

- The Company's Senior Management, and more particularly, personnel within the Corporate Division, are attentive with regard to improving internal controls and integrating recommendations from external auditors and the Audit Committee,
- The Company has implemented several procedures to manage the Procurement process. In these procedures, the resources to prevent risks inherent to the size of the Company and which are associated with internal separation between production and supervision of financial statements have already been provided,



- The Company recruited an accounting assistant in 2015 and is planning to expand the service again in 2016.

#### **B.4.3. Actors in risk management and internal control**

##### Executive Committee:

The members of the Executive Committee are responsible for defining, driving, and monitoring the process best adapted to the situation and activity of the Company.

In this context, they monitor the commitment to the necessary corrective actions.

It is the responsibility of the Executive Committee to report to the Audit Committee on the essential characteristics of the risk management and internal control process.

The members of the Executive Committee are:

- Mr. Gil Beyen, Chief Executive Officer;
- Mrs. Iman El-Hariry, Medical Director;
- Mr. Jérôme Bailly, Deputy Chief Executive Officer and Director of Pharmaceutical Operations;
- Mr. Eric Soyer, Chief Financial Officer and Chief Operating Officer.

##### The Audit Committee:

In accordance with the internal rules established by the Board of Directors, last updated on April 25, 2014, the Audit Committee is responsible for reporting to the Board of Directors on all major risks and/or weaknesses in the internal controls such as may have a significant impact on accounting and financial information.

##### The Board of Directors:

As needed, the Board may make use of its general powers to engage in any audits and inspections it deems useful or take any other initiative it believes appropriate in the matter.

##### The internal quality auditors:

Pursuant to the PG-QUAL-004 procedure, the Company forms then designates internal auditors in order to verify that the procedures and/or processes are effective and followed.

Each year, Management defines a program for internal audits, with priority given to: activities having a direct connection to the pharmaceutical facility and patient safety.

Internal auditors are specifically responsible for reporting to the Quality Assurance department any deviation from the procedures and/or processes.

##### The Quality Assurance department:

The Quality Assurance department is responsible for reporting to Senior Management, specifically, any significant deviation from the quality policy and/or procedures and/or processes.

##### External auditors or certifying bodies or regulatory authorities:

Accordingly:

- the French Medicines Agency (ANSM), the European Medicines Agency (EMA) and the Food and Drug Administration (FDA) and;
  - ISO auditor ([\*International Organization for Standardization\*](#)); and
  - the statutory auditors;
- participate in internal control through their controls and/or audits.

#### **B.5. Areas for improvement/Outlooks for change**

In 2016, the Company will continue its efforts to improve the monitoring of risk analysis action plans and to better coordinate internal controls with risk management.

### **C. Powers of the Chief Executive Officer**

Please note that there has been no limitation made to the powers of Mr. Gil Beyen, Chief Executive Officer.

On May 6, 2013, the Board of Directors specified that the powers of Jérôme Bailly are set in accordance with Article R. 5124-36 of the Public Health Code.

Moreover, until his resignation, Yann Godfrin was more specifically in charge of duties for scientific strategy, research and preclinical and clinical development and regulatory affairs.

*Refer also to Section 13.1.2 of the Reference Document, “Composition of Senior Management.”*

### **D. Attendance at the General Meeting of Shareholders and information provided in Article L.225-100-3 of the Commercial Code**

There are no specific procedures pertaining to the shareholder participation in the General Meeting of shareholders outside of those provided in Article 27 of the bylaws.

The information referenced in Article L.225-100-3 of the French Commercial Code (concerning elements that may have an impact where there is a public takeover bid for the Company) is shown in the Section 15.4 of this Reference Document.

## **16.4 Elements capable of having an impact in the event of a public offering**

- *Capital structure of the company*

*See Section 18.1 of the Reference Document*

- *Restrictions resulting from the bylaws respecting the voting rights and transfers of shares or clauses of which the Company has been informed in application of Article L.233-11 of the Commercial Code*

*See Section 18.3 of the Reference Document*

- *Direct or indirect stakes in the capital of the Company which the Company knows under Articles L.233-7 and L.233-12 of the Commercial Code*

*See Section 18.1 of the Reference Document*

- *Parties holding any securities involving special rights of control and description thereof*

None

- *Control mechanisms provided in any system for employee shareholding, when the controller rights are not exercised by the latter*

None

- *Agreements between shareholders of which the Company is aware that may result in restrictions to transfers of shares and the exercise of voting rights*

None

- *Rules applicable to the appointment and replacement of members of the Board of Directors as well as amendment of the bylaws*

The applicable rules in this matter are found in the bylaws and comply with the law.

- *Powers of the Board of Directors, particularly the issuance or redemption of shares*

The Company shareholders' meeting on June 23, 2015, authorized the Board of Directors to:

- issue shares via capital increases in accordance with Resolutions 10, 20, 21, and 22 of the Combined General Shareholders' Meeting of June 23, 2015 (*see Section 20.1.5 of this Reference Document*); and
  - implement a program to buy back the shares of the Company pursuant to Article L. 225-209 et seq. of the Commercial Code and the market practices allowed by the AMF (*see Section 20.1.3 of this Reference Document*).
- *Agreements made by the Company that shall be amended or shall end in the event of change of control of the Company*
- The terms and conditions of the BSAs/BSPCEs plans contain provisions for early exercise, under certain conditions, in the event of a change in control of the Company.
  - Early repayment of the Repayable Advance for the TEDAC project may be required by OSEO, notably in the event of a change of control in the Company.
  - Early termination of the agreement with the TEVA Group may be requested by either party in the event of a change of control of the other party.
  - See also the section below concerning change of control packages for executive officers and employees.
- *Agreements providing for indemnities to members of the board of directors or employees if they resign or are dismissed without real or serious cause or if their employment is terminated due to a public offering*

Pursuant to the "TEPA" law and the Middledex Code of corporate governance, at its meetings of May 23, 2014 and August 31, 2015, the Board of Directors established the terms for severance packages and change of control packages awarded to the company's executive corporate officers (i.e. Gil Beyen and Jérôme Bailly).

These commitments provide:

- that should Gil Beyen leave the Company, i.e. in the event of:
  - the expiration of his term of office (except where renewal is rejected by the interested party); or
  - removal (except for removal due to serious misconduct or gross negligence as this term is understood with respect to the case law of the Labor Division of the Court of Cassation),
 the interested party may claim severance payment equal to 12 times the mean monthly remuneration (bonuses included) effectively received over the course of the 12 months preceding the removal decision or the expiration of the term of office.
- in the event of the removal of Jérôme Bailly for any reason whatsoever, except serious misconduct or gross negligence, the interested party shall be entitled to severance pay equal to six months' fixed remuneration, plus an additional three months' fixed remuneration per year

of employment with the company, up to 12 months' fixed remuneration, subject to more favorable contractual provisions.

In addition, these commitments provide that if within 12 months following a change in control of the Company (by the acquisition of more than 50% of voting rights):

- Mr. Gil Beyen:
  - is removed, (except for removal due to serious misconduct or gross negligence as this term is understood with respect to the case law of the Labor Division of the Court of Cassation),
  - resigns, provided that such resignation is the result of a refusal on his part of a proposal by the Company, its acquirer or by one of its subsidiaries of a position with less responsibility and/or lower remuneration compared to the position held before the change of control; or
  
- Mr. Jérôme Bailly:
  - is removed, except for serious misconduct or gross negligence,
  - is approved for termination under his employment contract, whether at the initiative of the Company or the employee;
  - resigns, provided that such resignation is the result of a demotion by the Company, its acquirer or by one of its subsidiaries of a position with less responsibility and/or lower remuneration compared to the position held before the change in control;

the interested party may claim severance payment equal to 12 times the mean monthly remuneration (variable remuneration included) effectively received over the course of the 12 months preceding such party's departure.

The decisions by the Board of Directors of August 31, 2015, made with respect to the procedure for regulated commitments and agreements provided under the "TEPA" law, were published in their entirety on the Company's website. The commitments will be approved by the General Shareholders' Meeting as a specific resolution pertaining to each of the executive corporate officers.

The Board of Directors decided that payment of severance packages and change of control packages is subordinate to the compliance, duly recorded by the Board of Directors at the time of or after the departure from the position, with the conditions associated with the performances of the interested party assessed with regard to those of the Company, defined on this day as being:

- compliance with the Company's expenditure budget; and
- at least one of the two following conditions:
  - at least one collaboration or licensing agreement underway;
  - at least one product in active clinical development phase by the Company.

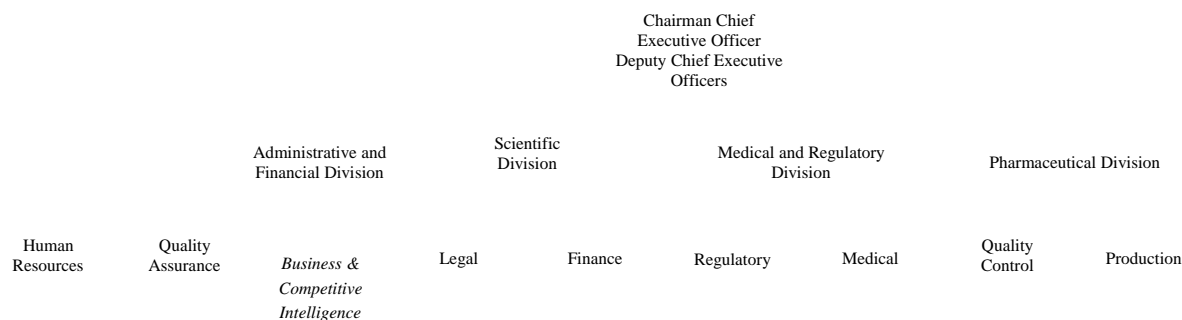
The other members of the Executive Committee (Eric Soyer and Iman El Hariry) are entitled to the same severance package as Jérôme Bailly in their employment contract, except that unlike the corporate officers, such payment is not subject to performance conditions.

## 17 EMPLOYEES

### 17.1 Personnel

See also Annex 2 of the Reference Document “Environmental, Social, and Corporate Responsibility Policy.”

#### 17.1.1 Functional organization chart



#### 17.1.2 Experience and positions of the principal managers

##### **Eric Soyer, Chief Financial Officer and Chief Operating Officer:**

Eric Soyer has over 20 years of experience in management positions in financial and operational departments of public and private companies, both new and established. Over the past eight years, he has served as Chief Financial Officer of EDAP-TMS, a Nasdaq listed company based in Lyon specializing in therapeutic ultrasound, where he was in charge of administration and finance, investor relations, legal affairs and human resources. During his last three years at EDAP-TMS, he was also Chief Executive Officer of the French subsidiary of the group, which was responsible for R&D, production and distribution for France, South America and EMEA. He previously served as Chief Financial Officer and Director of Information Systems for a leading French nursing home and care facility company, and Chief Financial Officer and Chief Legal Officer for a large French insurance company. He began his career as a financial controller within the Michelin Group. Mr. Soyer received his Executive M.B.A. from HEC Paris, an M.B.A. from University of Kansas in the United States and graduated from ESC Clermont in France.

##### **- Iman El Hariry, Chief Medical Officer:**

Iman El-Hariry, MD, PhD, is an oncologist and has over 15 years of product development experience in the biopharmaceutical industry. She served as VP Clinical Research at Syntha Pharmaceuticals in Boston, Global Head Oncology at Astellas APGD in Chicago and Group Director at GSK Clinical Oncology in London. She successfully led the development and regulatory approval of various products in Europe and the United States.

The experience and positions of the other principal executive managers are described in Section 14.1.4 above.

#### 17.1.3 Personnel distribution

The Company's workforce included 51 employees at December 31, 2015.

The Group's workforce consisted of 55 employees at December 31, 2015.

– **Changes in the Company’s workforce**

The average workforce has varied in the following proportions:

<b>Year</b>	<b>Average number of employees</b>	<b>Change</b>
<b>2004</b>	1	
<b>2005</b>	2	+100%
<b>2006</b>	8	+300%
<b>2007</b>	14	+75%
<b>2008</b>	24	+71%
<b>2009</b>	37	+54%
<b>2010</b>	41	+11%
<b>2011</b>	41	+0%
<b>2012</b>	38	-7%
<b>2013</b>	36	-5%
<b>2014</b>	38	+5%
<b>2015</b>	49	+47%

*Full-time equivalent*

– **Distribution by business segment**

At December 31, 2015, the Group’s workforce was distributed as follows:

<b>Departments</b>	<b>Number of employees</b>
<b>Business &amp; Competitive Intelligence</b>	2
<b>Clinical affairs</b>	7*
<b>Finance</b>	3.8
<b>Legal</b>	3
<b>Administration</b>	2
<b>Production</b>	14
<b>Insurance Quality</b>	2.6
<b>Preclinical</b>	16.6
<b>Regulatory</b>	2
<b>Human Resources</b>	1
<b>Grand total</b>	<b>55**</b>

*\* of which 4 employed by ERYTECH, Inc.*

*\*\* full-time equivalent.*

– Distribution by status

Status	Number
Management	28.4
Non-management	26.6
<b>Grand total</b>	<b>55**</b>

\* full-time equivalent.

#### 17.1.4 Human Resources Management

The development of human potential is of great importance for the Company. The Company must retain qualified employees who possess strong skills and abilities as ERYTECH's business is partially based on their quality, efficacy, and commitment.

The Company believes that it has good relations with its personnel.

The Company's employment contracts are controlled by the national collective-bargaining agreement in the pharmaceutical industry.

The Company has two employee representatives (one elected and one alternate) who meet with management every month.

The large majority of the Company's employees are employed on the basis of permanent contracts; however, the Company does make use of employees on fixed-term contracts, notably to satisfy the demands of periodic increases in business.

Insofar as the remuneration policy is concerned, the employment contracts may provide for, depending on the case, additional remuneration consisting of bonuses determined on the basis of goal attainment.



## 17.1.5 Organization of work time

The organization of work time at ERYTECH complies with all legal and regulatory provisions. The legal length of the workweek is 35 hours for full-time employees.

Senior executives are not covered by the laws respecting hours of work.

## 17.2 Investment stakes held by corporate officers

On the basis of the composition of the share capital and the existing diluting elements on December 31, 2015, the investment stakes held by the officers and executive officers may be summarized as follows:

	Number of shares	% capital <sup>(2)</sup>	% voting right	Type of warrants	Subscription warrants							Stoc ks opti ons
					Issue date and number of warrants	Number of warrants awarded	Number of warrants exercised	Number of warrants remaining to be exercised	Exercise price in € per new share subscribed <sup>(4)</sup>	Last date for exercise	Max number of shares tied to the number of warrants remaining to be exercised	
Gil Beyen <sup>(1)</sup>	-	-	-	BSPCE <sub>2012</sub>	05/21/12 creation of 11,263 warrants	11,263	3,400	7,863	7.362	5/20/20	78,630	N/A
				BSPCE <sub>2014</sub>	1/22/14	6,000	0	6,000	12.25	1/22/24	60,000	N/A
Yann Godfrin <sup>(1)</sup>	218,070	2.75%	3.72%	BSPCE <sub>2014</sub>	1/22/14	3,000	0	3,000 <sup>(7)</sup>	12.25	1/22/24	30,000	N/A
				BSPCE <sub>2012</sub>	5/21/12	7,508	7,508	0	7.362	5/20/20	0	N/A
Philippe Archinard <sup>(1)</sup>	8,000	0.10%	0.08%	BSA <sub>2012</sub>	5/21/12 issue of 11,263 warrants	2,554	1837	717 <sup>(6)</sup>	7.362	5/20/20	7,170	N/A
GALENOS <sup>(1)</sup>	4,500	0.06%	0.05%			1288 <sup>(5)</sup> 1717 3,005 total	1288 <sup>(5)</sup> 500	0 <sup>(1)</sup> 1217			0 <sup>(1)</sup> 12,170	
Martine Ortin George <sup>(1)</sup>	-	--	--			1217	0	1217			12,170	
Hilde Windels <sup>(1)</sup>	-	--	-			1217	0	1217			12,170	
Luc Dochez <sup>(1)</sup>						867	0	867			8,670	
Jérôme Bailly <sup>(1)</sup>	2,040	0.03%	0.02%			BSPCE <sub>2012</sub>	5/21/12	1,458			874	
				BSPCE <sub>2014</sub>	1/22/14	800	0	800	12.25	1/22/24	8,000	N/A

<sup>(1)</sup> see details of the positions currently held in Section 3.6.1. - Administration and management bodies

<sup>(2)</sup> Registered shares

<sup>(3)</sup> As delegated by the General Meeting

<sup>(4)</sup> one warrant gives the right to 10 new shares

<sup>(5)</sup> Granted to Sven Andreasson, GALENOS representative on the Company's Board of Directors

<sup>(6)</sup> Since December 31, 2015, Philippe Archinard has exercised all his 717 warrants (*see Section 14.5 of this Reference Document*), increasing the number of shares he holds to 15,170.

<sup>(7)</sup> Of which 1,000 warrants lapse due his resignation on January 18, 2016.

### 17.3 Investment stakes held by company non-corporate officers

The employees of the Company do not hold any shares under the conditions described in Article L.225-102 of the French Commercial Code.

Based on the composition of the capital and diluting elements existing on the closing date December 31, 2015, the investment stakes held by non-corporate-officer employees in a personal and individual capacity can be summarized as follows:

	Number of shares and voting rights*	% capital *	% voting right*	Subscription warrants							Stocks options
				Type of warrants	Creation date	Number allocated and not exercised***	Number subscribed and not exercised	Exercise price in € per new share subscribed	Last date for exercise	Maximum number of shares associated	
Employees who are not officers or directors	5,560	0.07%	0.06%	BSPCE <sub>2012</sub>	5/21/2012	17,435	17,435	7.362	5/20/2020	174,350	N/A
				BSPCE <sub>2014</sub>	1/22/2014	1,360	1,360	12.25	1/22/2024	13,600	N/A
				BSA <sub>2014</sub>	12/4/2014	3,000****	3,000****	12.25	12/4/2014	30,000****	N/A

\* Registered shares

\*\* See also Section 21.9.4 of the Reference Document

\*\*\* As delegated by the General Meeting

\*\*\*\* Including 2,000 warrants (20,000 shares) not yet vested

### 17.4 Profit-sharing agreement

The Company has implemented a profit-sharing agreement for the years 2014 to 2016, at the end of which a percentage (4% in 2015) of the gross annual remuneration at December 31 of each year may be distributed:

- Among the beneficiaries, in proportion to their gross remuneration and their length of employment (up to certain limits);
- Upon the achievement of performance goals. The Company is presently at a key stage in its development, with the research and clinical trials cycle entering into its final phase before a potential placement on the market. The next years will be, accordingly, decisive in achieving the objectives necessary for the culmination of many years of research, involving sustained and targeted efforts by all of its teams. The objectives may include, for example, depending on the year considered, achieving clinical and regulatory objectives and/or maintaining quality certifications.

## 18 MAJOR SHAREHOLDERS

### 18.1 Distribution of share capital and voting rights

In accordance with the provisions of Article L.233-13 of the Commercial Code, we provide you, below, with the identity of shareholders who hold a stake exceeding the threshold of 5% of the share capital and/or 5% of the voting rights. The change in share capital over the past three years is presented in Section 21.1.7 of this Reference Document.

The Company's shareholder structure as of December 31, 2015 was as follows, based on information available:

Last name, First name / Company Name	% Share capital	% Voting rights	Number of shares
FCPR AURIGA VENTURES III	12.85%	20.98%	1,018,212
RECORDATI ORPHAN DRUGS	5.44%	8.88%	431,034
Other registered shareholders with a capital holding less than 5%	5.72%	8.10%	453,234
BEARER SECURITIES	Held by the Company under the buyback program <sup>2</sup>	0.03%	2,500
	Baker Bros	9.65%	764,705
	OTHER BEARER SHARES	66.31%	5,254,926
<b>TOTAL</b>	<b>100.00%</b>	<b>100.00%</b>	<b>7,924,611</b>

<sup>2</sup> See Section 20.1.3 of this Reference Document.

The Company's shareholder structure as of February 29, 2016 was as follows, based on information available:

Last name, First name / Company Name	% Share capital	% Voting rights	Number of shares
FCPR AURIGA VENTURES III	12.84%	20.96%	1,018,212
RECORDATI ORPHAN DRUGS	5.43%	8.87%	431,034
Other registered shareholders with a capital holding less than 5%	5.80%	8.16%	460,404
BEARER SECURITIES	Held by the Company at the end of the buyback program <sup>2</sup>	0.03%	2,500
	Baker Bros	9.64%	764,705
	OTHER BEARER SHARES	66.26%	5,254,926
<b>TOTAL</b>	<b>100.00%</b>	<b>100.00%</b>	<b>7,931,781</b>

<sup>2</sup> See Section 20.1.3 of this Reference Document.

<sup>1</sup> Including, based on the latest information received from the disclosure threshold statements, 1.63% bearer shares.

<sup>2</sup> Including, based on the latest information received from the disclosure threshold statements, 3.54% bearer shares.

<sup>3</sup> Including Baker Bros., which, based on the latest information received from the disclosure threshold statements, owns 674,027 bearer shares representing a percentage of capital and voting rights of 8.51% and 6.94%, respectively.

**During the financial year ended December 31, 2015, the Company received information on the following thresholds crossed:**

- On January 14, 2015, the voting rights held by Yann Godfrin fell below the 5% disclosure threshold of the Company as a result of the sale of Company shares on the market. At that date, Yann Godfrin held 142,990 shares representing 2.08% of capital and 3.45% of voting rights;
- On May 6, 2015, the voting rights held by Pierre-Olivier Goineau fell below the 5% disclosure threshold of the Company, following an increase in the total number of voting rights in the

Company. At that date, Pierre-Olivier Goineau held 212,000 shares representing 3.08% of capital and 4.28% of voting rights;

- On May 19, 2015, the voting rights held by Idinvest Partners, acting on behalf of funds it manages, fell below the 5% disclosure threshold of the Company following an increase in the total number of the Company's voting rights. At that date, Idinvest Partners held, on behalf of the said funds, 377,582 shares representing 5.48% of shares and 4.91% of voting rights.
- On May 28, 2015, the voting rights held by Idinvest Partners, acting on behalf of funds it manages, fell below the 5% disclosure threshold of the Company following a sale of shares of the Company. At that date, Idinvest Partners held, on behalf of the said funds, 334,473 shares representing 4.86% of shares and 4.42% of voting rights.
- On December 9, 2015, the FCPI Auriga Venture III fell below the threshold of 15% of the share capital of the Company following a capital increase of the Company (prospectus approved by the AMF on December 3, 2015, under n°. 15-0614). On that date, the FCPI Auriga Venture III held 1,147,522 shares representing 14.62% of the share capital and 22.49% of the voting rights.

**Since December 31, 2015, the Company received the following threshold crossing statements:**

- On February 9, 2016, JP Morgan Asset Management, acting on behalf of clients under mandate, said it had exceeded the threshold of 5% of the share capital of the Company following the acquisition of shares of the Company on the market. On that date, JP Morgan Asset Management held, on behalf of said clients, 471,320 shares representing 5.95 % of capital and 4.86% of voting rights.

## **18.2 Major shareholders not represented on the Board of Directors**

At the date of this Reference Document, two major registered shareholders, i.e. Auriga Venture III and Recordati Orphan Drugs, were not represented on the Board of Directors.

## **18.3 Shareholder voting rights**

In the Ordinary and Extraordinary General Meetings of the Company, each share gives the right to one vote, except where there is a right to a double vote.

A double voting right is nevertheless granted, in accordance with legal conditions, to all shares fully paid up for which evidence is provided, at the latest on the second day prior to the date of the shareholders' meeting, 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 the shareholder's 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, profit, or issue premiums, the double voting right is granted, upon issue, to registered bonus shares awarded to replace existing shares already carrying double voting rights.

The double voting right will be automatically withdrawn from any share converted to a bearer share or subjected to a transfer of ownership, except where such transfer results from a succession, a sharing of the community of property between spouses, or an inter vivos gift granted by a shareholder to such shareholder's 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.

## 18.4 Control of the Company

To the Company's knowledge:

- no shareholder holds, whether directly or indirectly, a fraction of the share capital that would grant him/her/it the majority of voting rights in the Company's general meetings;
- no agreement has been formed among the shareholders so as to confer to one shareholder the majority of voting rights in the Company;
- no shareholder is able to dictate, on the basis of the voting rights that he/she/it holds, the decisions in the Company's general meetings of shareholders; and
- no shareholder has the power to name or remove the majority of members in the Company's management or oversight bodies.

Furthermore, to the Company's knowledge, no shareholder or group of shareholders directly or indirectly holds more than 40% of the voting rights in the Company, which may create a presumption of control of the Company with regard to one of the shareholders or a group of shareholders.

- Shareholders' agreement

To the Company's knowledge, there are no agreements among the shareholders.

- Concerted action

To the Company's knowledge, there is no concerted action among the shareholders.

- Agreements capable of resulting in a change in control

To the Company's knowledge, there are no agreements in place whose implementation might, at a later date, result in a change in control.

## **19 TRANSACTIONS WITH RELATED PARTIES**

All currently existing regulated agreements are mentioned in the special reports by the statutory auditor presented below.

Since preparation of the special report by the statutory auditor on to the 2015 financial year, on January 10, 2016, the Board of Directors authorized:

- an increase in the fixed and variable gross annual remuneration for Jérôme Bailly, Deputy Chief Executive Officer of the Company, pursuant to his employment contract
- the PEE (company savings scheme) and PERCO (collective plan for retirement savings) contributions of:
  - Mr. Gil Beyen, Chief Executive Officer;
  - Mr. Jérôme Bailly, Deputy Chief Executive Officer of the Company.

The annexed IFRS consolidated financial statements provide details of related parties under Section 7.11, Chapter 20.1 of this Reference Document.

### **19.1 Intra-group transactions**

#### **19.1.1 Cash pooling agreement**

During the financial year ended December 31, 2014, the Company entered into a cash pooling agreement with its subsidiary, ERYTECH Pharma Inc., and accordingly paid it \$550,000.

#### **19.1.2 Intercompany agreement**

During the financial year ended December 31, 2015, the Company also signed a service agreement with the said subsidiary (amended December 31, 2015).

Pursuant to this framework agreement, ERYTECH Pharma S.A. may provide consulting services to ERYTECH Pharma Inc. involving finance, advertising, marketing, information technology, logistics, human resources, legal, tax, environmental policy, health & safety, quality assurance, and management services. ERYTECH Pharma Inc. may also provide advice to the Company regarding regulatory and clinical medical aspects, pharmacovigilance and R&D.

These services are invoiced at actual cost plus ten (10) percent. During the financial year ended December 31, 2015, only ERYTECH Pharma S.A. provided services under this agreement. Over that period, the amount invoiced by ERYTECH Pharma S.A. to ERYTECH Pharma Inc. amounted to €34,236.13.

## 19.2 Related party transactions

### 19.2.1 Special report of the statutory auditors on regulated agreements – Financial year ended December 31, 2015

*(Free translation of a French language original)*

**Erytech Pharma S.A.**

Share capital: €792,461

#### **Statutory Auditors' special report on regulated agreements and commitments**

Dear Shareholders,

In our capacity as statutory auditor for the company, we hereby report on certain regulated agreements and commitments.

We are required to inform you, on the basis of the information that provided to us, of the terms and conditions as well as the reason justifying the benefit to the Company, of those agreements and commitments indicated to us or that we may have identified in the performance of our engagement. We are not required to comment or to whether they are beneficial or appropriate or to ascertain the existence of any agreements and commitments. It is your responsibility, in accordance with the terms of Article R.225-58 of the French Commercial Code, to evaluate the benefits resulting from these agreements and commitments prior to their approval.

In addition, we are required, where applicable, to inform you in accordance with Article R.225-31 of the French Commercial Code concerning the implementation, during the year of the agreements and commitments already approved by the General Meeting of Shareholders.

We performed those procedures which we considered necessary to comply with professional guidance issued by the national auditing board (Compagnie Nationale des Commissaires aux Comptes) relating to this type of engagement. These procedures consisted in verifying that the information provided to us is consistent with the documentation from which it has been extracted.

#### **SUBMITTED FOR APPROVAL BY THE GENERAL MEETING OF SHAREHOLDERS**

In accordance with Article L.225-40 of the French Commercial Code, we have been advised of the following agreements and commitments which received prior authorization from the Board of Directors.

#### **A - With Jérôme Bailly**

Person concerned:

❖ Jérôme Bailly, Deputy Chief Executive Officer of the Company

##### **a - Remuneration**

Nature and purpose:

Modification of the fixed gross annual remuneration in the context of Jérôme Bailly's employment contract, starting on January 1, 2015. This agreement was authorized by your Board of Directors on January 11, 2015.

Terms:



The fixed annual remuneration for Jérôme Bailly is set at €90,000, payable over 12 months. The gross remuneration paid during the 2015 financial year, variable portion included, totaled €94,163.11.

Benefit to the company:

Building the loyalty and motivation of your company's management team.

**b - Severance pay:**

Nature and purpose:

Severance pay authorized by the Board of Directors on August 31, 2015 in the event of dismissal for any reason, except for serious misconduct or gross negligence.

Jérôme Bailly may claim severance pay equal to six months' fixed compensation, plus an additional three months' fixed compensation per year of employment with the company, up to a maximum of 12 months' fixed compensation, subject to more favorable contractual provisions.

Payment of this indemnity is subject to the following performance conditions being met:

- compliance with the Company's expenditure budget, and
- at least one of the two following conditions:
  - ✓ one collaboration or licensing agreement underway;
  - ✓ one product in active clinical development phase by the Company.

Terms:

No expense was booked in this respect by the company for the 2015 financial year.

Benefit to the company:

Building the loyalty and motivation of your company's management team.

**c - Severance in the event of a change in control:**

Nature and purpose:

Severance in the event of a change in control authorized by the Board of Directors on August 31, 2015.

This severance is not cumulative with the agreement described above.

Jérôme Bailly will receive a lump-sum severance equal to 12 times the average monthly compensation (variable compensation included) effectively received over the course of the 12 months preceding his departure if in the 12 months following the change in control of your company by the acquisition of more than 50% of the voting rights, Mr. Bailly:

- is dismissed, except for serious misconduct or gross negligence or obtains a contractual dismissal, whether at the initiative of the company or the employee;
- resigns, provided that such resignation is the result of a demotion by the Company, its acquirer or by one of its subsidiaries to a position with less responsibility and/or lower remuneration compared to the position held before the change in control.

Payment of this indemnity is subject to the finding that the following performance conditions being met:

Compliance with the Company's expenditure budget and

- at least one of the two following conditions:
  - ✓ at least one collaboration or licensing agreement underway;
  - ✓ at least one product in active clinical development phase by the Company.

Terms:

No expense was booked in this respect by the company for the 2015 financial year.

Benefit to the company:

Building the loyalty and motivation of your company's management team.

**B - With Yann Godfrin**

Person concerned:

- ❖ *Mr. Yann Godfrin*, Deputy Chief Executive Officer of the Company.

**Severance in the event of a change in control:**

Nature and purpose:

Severance in the event of a change in control authorized by the Board of Directors on August 31, 2015.

This severance is not cumulative with the severance compensation agreement authorized by the Board of Directors on May 24, 2013.

Yann Godfrin will receive a lump-sum severance equal to 12 times the average monthly compensation (variable compensation included) effectively received over the course of the 12 months preceding his departure if in the 12 months following the change in control of your company by the acquisition of more than 50% of the voting rights, Mr. Godfrin:

- is dismissed, except for serious misconduct or gross negligence or obtains a contractual dismissal, whether at the initiative of the company or the employee;
- resigns, provided that such resignation is the result of a demotion by the Company, its acquirer or by one of its subsidiaries to a position with less responsibility and/or lower remuneration compared to the position held before the change in control.

Payment of this indemnity is subject to the following performance conditions being met:

- compliance with the Company's expenditure budget and
- at least one of the two following conditions:
  - ✓ at least one collaboration or licensing agreement underway;
  - ✓ at least one product in active clinical development phase by the Company.

Terms:

No expense was booked in this respect by the company for the 2015 financial year.

Benefit to the company:

Building the loyalty and motivation of your company's management team.

Mr. Yann Godfrin resigned from his positions as Director and Deputy Chief Executive Officer on January 17, 2016.

**C - With Gil Beyen**

Person concerned:

- ❖ *Mr. Gil Beyen*, Chairman of the Board of Directors and Chief Executive Officer of the Company.

## **Severance in the event of a change in control:**

### Nature and purpose:

This severance is not cumulative with the severance compensation agreement authorized by the Board of Directors on May 24, 2013.

Gil Beyen will receive a lump-sum severance equal to 12 times the average monthly compensation (variable compensation included) effectively received over the course of the 12 months preceding his departure, if in the 12 months following the change in control of your company by the acquisition of more than 50% of the voting rights, Mr. Beyen:

- is dismissed, except for serious misconduct or gross negligence or obtains a contractual dismissal, whether at the initiative of the company or the employee;
- resigns, provided that such resignation is the result of a demotion by the Company, its acquirer or by one of its subsidiaries to a position with less responsibility and/or lower remuneration compared to the position held before the change in control.

Payment of this indemnity is subject to the following performance conditions have been met:

- compliance with the Company's expenditure budget and
- at least one of the two following conditions:
  - ✓ at least one collaboration or licensing agreement underway;
  - ✓ at least one product in active clinical development phase by the Company.

### Terms:

No expense was booked in this respect by the company for the 2015 financial year.

### Benefit to the company:

Building the loyalty and motivation of your company's management team.

## **AGREEMENTS AND COMMITMENTS ALREADY APPROVED BY THE GENERAL MEETING**

### **Agreements and commitments approved during previous financial years which continued to operate during the past financial year**

In application of Article R.225-31 of the Commercial Code, we were informed that the execution of the following agreements and commitments, already approved by the General Meeting during previous financial years, continued in the past financial year.

#### **A - With Mr. Pierre-Olivier Goineau**

Person concerned:

- ❖ Mr. Pierre-Olivier Goineau, Deputy Chief Executive Officer of the Company.

#### **a - Severance pay:**

##### Nature and purpose:

Severance pay, authorized by the Board of Directors on May 24, 2013, in the event of:

- expiration of a term of office (except where renewal has been refused by the interested party),

- removal (except for removal due to serious misconduct or gross negligence as this term is understood with respect to the case law of the Labor Division of the Court of Cassation).

Mr. Pierre-Olivier Goineau may claim an indemnity equal to twelve times his average monthly remuneration (bonuses included) effectively received during the twelve months prior to the revocation decision or expiration of his term of office.

Payment of this indemnity is subject to the following performance conditions being met:

- compliance with the Company's expenditure budget, and
- at least one of the two following conditions:
  - ✓ one collaboration or licensing agreement underway;
  - ✓ one product in active clinical development phase by the Company.

Terms:

No expense was booked in this respect by the company for the 2015 financial year.

## **b - Profit-sharing agreement:**

Nature and purpose: Profit-sharing agreement

Terms:

On November 29, 2013, the Company entered into a profit-sharing agreement for the period from January 1, 2014, to December 31, 2016. On December 22, 2006, your Supervisory Board authorized the inclusion of Pierre-Olivier Goineau in a future profit-sharing agreement. The profit-sharing expense recorded in relation to the 2015 financial year had a gross value of €357.23.

## **a - Carré VIP securities management consulting contract for Société Générale Securities Services**

Nature and purpose:

Securities management contract for the company shares entered into with Société Générale for the benefit of Pierre-Olivier Goineau, authorized by the Board of Directors on March 26, 2015.

Terms:

The cost of the VIP contract for the 2015 fiscal year is €200.

Mr. Pierre-Olivier Goineau resigned from his positions as Director and Deputy Chief Executive Officer on January 11, 2015.

## **B - With Mr. Yann Godfrin**

Person concerned:

Mr. Yann Godfrin, Deputy Chief Executive Officer of the Company.

### **a) Severance pay:**

**Nature and purpose:**

Severance pay, authorized by the Board of Directors on May 24, 2013, in the event of:

- expiration of a term of office (except where renewal has been refused by the interested party),
- removal (except for removal due to serious misconduct or gross negligence as this term is understood with respect to the case law of the Labor Division of the Court of Cassation).

Mr. Yann Godfrin may claim an indemnity equal to twelve times his average monthly remuneration (bonuses included) effectively received during the twelve months prior to the revocation decision or expiration of his term of office.

Payment of this indemnity is subject to the following performance conditions being met:

- compliance with the Company's expenditure budget, and
- at least one of the two following conditions:
  - ✓ one collaboration or licensing agreement underway;
  - ✓ one product in active clinical development phase by the Company.

Terms:

No expense was booked in this respect by the company for the 2015 financial year.

**b - Profit-sharing agreement:**

Nature and purpose: Profit-sharing agreement

Terms:

On November 29, 2013, the Company entered into a profit-sharing agreement for the period from January 1, 2014, to December 31, 2016. On December 22, 2006, your Supervisory Board authorized the inclusion of Yann Godfrin in a future profit-sharing agreement. The profit-sharing expense recorded in relation to the 2014 financial year had a gross value of €1,825.92.

**c - Carré VIP securities management consulting contract for Société Générale Securities Services**

Nature and purpose:

Securities management contract for the company shares entered into with Société Générale for the benefit of Yann Godfrin, authorized by the Board of Directors on March 26, 2015.

Terms:

The cost of the VIP contract for the 2015 fiscal year is €200.

Mr. Yann Godfrin resigned from his positions as Director and Deputy Chief Executive Officer on January 17, 2016.

**C - With Mr. Gil Beyen**

Person concerned:

- ❖ Mr. Gil Beyen, Chairman of the Board of Directors and Chief Executive Officer of the Company.

**a - Severance pay:**

Nature and purpose:

Severance pay, authorized by the Board of Directors on May 24, 2013, in the event of:

- expiration of a term of office (except where renewal has been refused by the interested party),
- removal (except for removal due to serious misconduct or gross negligence as this term is understood with respect to the case law of the Labor Division of the Court of Cassation).

Mr. Gil Beyen may claim an indemnity equal to:

- twelve times his average monthly remuneration (bonuses included) effectively received during the twelve months prior to the revocation decision or expiration of his term of office, or
- the fixed annual remuneration established by the Board of Directors, in the event of revocation decided within twelve months following the appointment of Mr. Gil Beyen.

Payment of this indemnity is subject to the following performance conditions being met:

- compliance with the Company's expenditure budget, and
- at least one of the two following conditions:
  - ✓ one collaboration or licensing agreement underway;
  - ✓ at least one product in active clinical development phase by the Company.

Terms:

No expense was booked in this respect by the company for the 2015 financial year.

**a - Profit-sharing agreement:**

Nature and purpose: Profit-sharing agreement

Terms:

On November 29, 2013, the Company entered into a profit-sharing agreement for the period from January 1, 2014, to December 31, 2016. On May 24, 2013, your Board of Directors authorized the inclusion of Gil Beyen in a future profit-sharing agreement. The profit-sharing expense red in relation to the 2015 financial year had a gross value of €1,825.92.

**b - Carré VIP securities management consulting contract for Société Générale Securities Services**

Nature and purpose:

Securities management contract for the company shares entered into with Société Générale for the benefit of Gil Beyen, authorized by the Board of Directors on March 26, 2015.

Terms:

The cost of the VIP contract for the 2015 fiscal year is €200.

**D - With Mr. Jérôme Bailly**

Person concerned:

- Mr. Jérôme Bailly, Deputy Chief Executive Officer of the Company.

**Profit-sharing agreement**

Nature and purpose: Profit-sharing agreement

Terms:

On November 29, 2013, the Company entered into a profit-sharing agreement for the period from January 1, 2014, to December 31, 2016. On January 11, 2015, your Board of Directors noted that the executives are beneficiaries of this profit-sharing agreement. The profit-sharing expense recorded in relation to the 2015 financial year had a gross value of €1,825.92.

**E - With all Senior Management**

Persons concerned:

- Mr. Gil Beyen, Mr. Pierre Olivier Goineau, Mr. Yann Godfrin, Mr. Jérôme Bailly.

Nature and purpose:

The Supervisory Board, on January 24, 2013, and the Board of Directors, on May 24, 2013, authorized the company to bear the cost of certain services and expenses benefiting the Senior Management, as shown in the table attached, expressed in euros.

10/10

- Terms

Expenses recorded in the 2015 financial year	Gil Beyen	Jérôme Bailly	Pierre-Olivier Goineau	Yann Godfrin
Traditional professional health insurance APGIS (PRC)	4 062,53	1 857,84	141,94	4 022,12
Additional health insurance (VIVENS)	1 156,44	715,60	35,33	1 156,44
Unemployment insurance (GSC)				
Additional pension plan (AXA)	7 608,00	4 709,19	232,47	7 608,00
<i>Supply of a company car and fuel paid for</i>				
-Rents paid during the fiscal year	6 873,89	2 279,49	115,48	5 541,73
-Amount of fuel paid for	2 218,10	1 438,25	454,04	1 794,39
<b>TOTAL</b>	<b>21 918,96</b>	<b>11 499,31</b>	<b>979,26</b>	<b>20 122,68</b>

Mr. Pierre-Olivier Goineau resigned from his positions as Director and Deputy Chief Executive Officer on January 11, 2015.

Mr. Yann Godfrin resigned from his positions as Director and Deputy Chief Executive Officer on January 17, 2016.

## F - With all Senior Management present at December 31, 2015

Persons concerned:

- Mr. Gil Beyen, Mr. Yann Godfrin, Mr. Jérôme Bailly.

Nature and purpose:

Authorization by the Board of Directors on March 26, 2015 of an employer's contribution to the PEE and PERCO. The employer's contribution terms for the PEE and PERCO are identical to those for all employees.

Terms:

Expenses recorded in the 2015 financial year	Gil Beyen	Jérôme Bailly	Yann Godfrin
PEE	720,00	720,00	720,00
PERCO		360,00	
<b>TOTAL</b>	<b>720,00</b>	<b>1 080,00</b>	<b>720,00</b>

The statutory auditors  
Lyon, February 23, 2016

For KPMG Audit Rhône Alpes Auvergne

For RSM Rhône Alpes

Sara Righenzi de Villers  
Partner

Gaël Dhalluin  
Partner



## 19.2.2 Special report of the statutory auditor on regulated agreements – Financial year ended December 31, 2014

### **Erytech Pharma S.A.**

Headquarters: 60 avenue Rockefeller - Bâtiment Adénine - 69008 Lyon

Share capital: €688,276.10

### **Statutory Auditors' special report on regulated agreements and commitments**

Year ended December 31, 2014

Dear Shareholders,

In our capacity as statutory auditor for the company, we hereby report on certain regulated agreements and commitments.

We are required to inform you, on the basis of the information that provided to us, of the terms and conditions of those agreements and commitments indicated to us or that we may have identified in the performance of our engagement. We are not required to comment or to whether they are beneficial or appropriate or to ascertain the existence of any agreements and commitments. It is your responsibility, in accordance with the terms of Article R.225-58 of the French Commercial Code, to evaluate the benefits resulting from these agreements and commitments prior to their approval.

In addition, we are required, where applicable, to inform you in accordance with Article R.225-31 of the French Commercial Code concerning the implementation, during the year of the agreements and commitments already approved by the General Meeting of Shareholders.

We performed those procedures which we considered necessary to comply with professional guidance issued by the national auditing board (Compagnie Nationale des Commissaires aux Comptes) relating to this type of engagement. These procedures consisted in verifying that the information provided to us is consistent with the documentation from which it has been extracted.

#### **AGREEMENTS AND COMMITMENTS REQUIRING APPROVAL BY THE GENERAL MEETING**

##### **Agreements and commitments not previously authorized**

In accordance with Articles L. 225-42 et L. 823-12 of the Commercial Code, we hereby inform you that the following agreements and commitments have not been previously authorized by your Board of Directors.

It is our responsibilities to inform you of the circumstances due to which the authorization procedure was not followed.

##### **With Mr. Pierre-Olivier Goineau**

Carré VIP securities management consulting contract for Société Générale Securities Services

Person concerned: Mr. Pierre-Olivier Goineau, Chief Operating Officer of the Company.

- Nature and purpose: securities management contract for the company entered into for the 2014 financial year with Société Générale for the benefit of Pierre-Olivier Goineau, authorized by the Board of Directors on March 26, 2015.

- Terms: the cost of the VIP contract for the 2014 financial year is €200.

Mr. Pierre-Olivier Goineau resigned from his positions as Director and Deputy Chief Executive Officer on January 11, 2015.

#### **With Mr. Yann Godfrin**

##### Carré VIP securities management consulting contract for Société Générale Securities Services

Person concerned: *Mr. Yann Godfrin*, Deputy Chief Executive Officer of the Company.

- Nature and purpose: securities management contract for the company entered into for the 2014 financial year with Société Générale for the benefit of Yann Godfrin, authorized by the Board of Directors on March 26, 2015.
- Terms: the cost of the VIP contract for the 2014 financial year is €200.

#### **With Mr. Gil Beyen**

##### Carré VIP securities management consulting contract for Société Générale Securities Services

Person concerned: Mr. Gil Beyen, Chairman of the Board of Directors and General Manager of the Company.

- Nature and purpose: securities management contract for the company entered into for the 2014 financial year by Société Générale for the benefit of Gil Beyen, authorized by the Board of Directors on March 26, 2015.
- Terms: the cost of the VIP contract for the 2014 financial year is €200.

##### Tax consultancy services provided by Delsol

Person concerned: Mr. Gil Beyen, Chairman of the Board of Directors and General Manager of the Company.

- Nature and purpose: tax consultancy services provided by Delsol during the 2014 financial year for Mr. Gil Beyen's tax situation, authorized by the Board of Directors on March 26, 2015.
- Terms: the expense recorded for the 2014 financial year is €2,322.

Your company considers that these agreements fall under Article L.225-39 of the Code of Commerce and, therefore, that the pre-authorization procedure specified in Article L.225-38 of this Code does not apply to them.

#### **AGREEMENTS AND COMMITMENTS ALREADY APPROVED BY THE GENERAL MEETING**

##### **Agreements and commitments approved during previous financial years which continued to operate during the past financial year**

In application of Article R.225-31 of the Commercial Code, we were informed that the execution of the following agreements and commitments, already approved by the General Meeting in previous financial years, were pursued in the past financial year.

#### **With Mr. Pierre-Olivier Goineau**

##### 1. Severance pay:

Person concerned: Mr. Pierre-Olivier Goineau, Chief Operating Officer of the Company.

- Nature and purpose: Severance pay, authorized by the Board of Directors on May 24, 2013, in the event of:
  - expiration of a term of office (except where renewal has been refused by the interested party),

- removal (except for removal due to serious misconduct or gross negligence as this term is understood with respect to the case law of the Labor Division of the Court of Cassation).

Mr. Pierre-Olivier Goineau may claim an indemnity equal to twelve times his average monthly remuneration (bonuses included) effectively received during the twelve months prior to the revocation decision or expiry of his term of office.

Payment of this indemnity is subject to the following performance conditions being met:

- Compliance with the Company's expenditure budget, and
- at least one of the two following conditions:
  - at least one collaboration or licensing agreement underway;
  - at least one product in active clinical development phase by the Company.
- Terms: No expense was booked in this respect by the company for the 2014 financial year.

2. Profit-sharing agreement:

Person concerned: Mr. Pierre-Olivier Goineau, Chief Operating Officer of the Company.

- Nature and purpose: incentive
- Terms: on November 29, 2013, the Company entered into a profit-sharing agreement for the period from January 1, 2014, to December 31, 2016. On December 22, 2006, your Supervisory Board authorized the inclusion of Pierre-Olivier Goineau in a future profit-sharing agreement. The profit-sharing expense recorded in relation to the 2014 financial year had a gross value of €1,800.

Mr. Pierre-Olivier Goineau resigned from his positions as Director and Deputy Chief Executive Officer on January 11, 2015.

**With Mr. Yann Godfrin**

1. Severance pay:

Person concerned: *Mr. Yann Godfrin*, Deputy Chief Executive Officer of the Company.

- Nature and purpose: Severance pay, authorized by the Board of Directors on May 24, 2013, in the event of:
  - expiration of a term of office (except where renewal has been refused by the interested party),
  - removal (except for removal due to serious misconduct or gross negligence as this term is understood with respect to the case law of the Labor Division of the Court of Cassation).

Mr. Yann Godfrin may claim an indemnity equal to twelve times his average monthly remuneration (bonuses included) effectively received during the twelve months prior to the revocation decision or expiry of his term of office.

Payment of this indemnity is subject to the following performance conditions being met:

- Compliance with the Company's expenditure budget, and
- at least one of the two following conditions:
  - at least one collaboration or licensing agreement underway;
  - at least one product in active clinical development phase by the Company.
- Terms: No expense was booked in this respect by the company for the 2014 financial year.

2. Profit-sharing agreement:

Person concerned: *Mr. Yann Godfrin*, Deputy Chief Executive Officer of the Company.

- Nature and purpose: profit sharing agreement
- Terms: on November 29, 2013, the Company entered into a profit-sharing agreement for the period from January 1, 2014, to December 31, 2016. On December 22, 2006, your Supervisory Board authorized the inclusion of Yann Godfrin in a future profit-sharing agreement. The profit-sharing expense recorded in relation to the 2014 financial year had a gross value of €1,800.

### **With Mr. Gil Beyen**

#### **1. Severance pay:**

Person concerned: Mr. Gil Beyen, Chairman of the Board of Directors and General Manager of the Company.

- Nature and purpose: Severance pay, authorized by the Board of Directors on May 24, 2013, in the event of:
  - expiration of a term of office (except where renewal has been refused by the interested party),
  - removal (except for removal due to serious misconduct or gross negligence as this term is understood with respect to the case law of the Labor Division of the Court of Cassation).

Mr. Gil Beyen may claim an indemnity equal to:

- twelve times his average monthly remuneration (bonuses included) effectively received during the twelve months prior to the revocation decision or expiration of his term of office, or
- the fixed annual remuneration established by the Board of Directors, in the event of revocation decided within twelve months following the appointment of Mr. Gil Beyen.

Payment of this indemnity is subject to the following performance conditions being met:

- Compliance with the Company's expenditure budget, and
- at least one of the two following conditions:
  - at least one collaboration or licensing agreement underway;
  - at least one product in active clinical development phase by the Company.
- Terms: No expense was booked in this respect by the company for the 2014 financial year.

#### **2. Profit-sharing agreement:**

Person concerned: Mr. Gil Beyen, Chairman of the Board of Directors and General Manager of the Company.

- Nature and purpose: profit sharing agreement
- Terms: on November 29, 2013, the Company entered into a profit-sharing agreement for the period from January 1, 2014, to December 31, 2016. On May 24, 2013, your Board of Directors authorized the inclusion of Gil Beyen in a future profit-sharing agreement. The profit-sharing expense recorded in relation to the 2014 financial year had a gross value of €1,800.

### **With Mr. Jérôme Bailly**

- Person concerned: Mr. Jérôme Bailly, Chief Operating Officer of the Company.

- Nature and purpose: Modification in the fixed gross annual remuneration as part of Mr. Jérôme Bailly's employment contract, starting on January 1, 2014. This agreement was authorized by your Board of Directors on January 22, 2014.
- Terms: The fixed annual remuneration for Jérôme Bailly is set at €60,000, payable over 12 months. The gross remuneration recorded during the 2014 financial year, variable portion included, totaled €75,132.70.

#### **With all Senior Management**

- Persons concerned: Mr. Gil Beyen, Mr. Pierre Olivier Goineau, Mr. Yann Godfrin, Mr. Jérôme Bailly.
- Nature and purpose: The Board of Supervisors, on January 24, 2013, and the Board of Directors, on May 24, 2013, authorized the company to bear the cost of certain services and expenses benefiting the Senior Management, as shown in the table attached, expressed in euros.
- Terms

<b>Expenses recorded in the 2014 financial year</b>	<b>Gil Beyen</b>	<b>Jérôme Bailly</b>	<b>Pierre-Olivier Goineau</b>	<b>Yann Godfrin</b>
Traditional professional health insurance APGIS (PRC)	3,932.16	1,394.15	3,519.23	3,517.89
Additional health insurance (VIVENS)	1,096.44	504.65	1,096.44	1,096.44
Unemployment insurance (GSC)			8,562.79	8,566.02
Additional pension plan (AXA)	7,509.60	3,456.63	7,509.60	7,509.60
<i>Supply of a company car and fuel paid for</i>				
-Rents paid during the fiscal year	17,185.15	6,191.40	10,778.46	10,877.87
-Amount of fuel paid for	1,874.18	1,282.46	1,811.20	2,066.60
<b>TOTAL</b>	<b>31,597.53</b>	<b>12,829.29</b>	<b>33,277.72</b>	<b>33,634.42</b>

Mr. Pierre-Olivier Goineau resigned from his positions as Director and Deputy Chief Executive Officer on January 11, 2015.

#### **AGREEMENTS AND COMMITMENTS AUTHORIZED SINCE THE YEAR-END**

We have been informed of the following commitments which were authorized following the close of the last financial year and which were previously authorized by your Board of Directors:

#### **With all Senior Management**

- Persons concerned: Mr. Gil Beyen, Mr. Yann Godfrin, Mr. Jérôme Bailly.
- Nature and purpose: March 26, 2015 Board of Directors authorization of a PEE contribution and a PERCO contribution
- Terms: no expense was recorded for these agreements for the 2014 financial year

#### **With Mr. Jérôme Bailly**

- Person concerned: Mr. Jérôme Bailly, Chief Operating Officer of the Company.
- Nature and purpose: Modification of the fixed gross annual remuneration as part of Jérôme Bailly's employment contract, starting on January 1, 2015. This agreement was authorized by your Board of Directors on January 11, 2015.

- Terms: The fixed annual remuneration for Mr. Jérôme Bailly is henceforth set at €90,000, payable over 12 months.

**The statutory auditors  
Lyon, March 30, 2015**

**For KPMG Audit Rhône Alpes Auvergne**

**For RSM CCI Conseils**

**Sara Righenzi De Villers  
Partner**

**Gaël Dhalluin  
Partner**

## 20 FINANCIAL INFORMATION CONCERNING THE COMPANY'S EQUITY, FINANCIAL POSITION, AND RESULTS

### 20.1 Consolidated financial statements prepared in accordance with IFRS standards for the year ended December 31, 2015

#### CONSOLIDATED ANNUAL FINANCIAL STATEMENTS AT DECEMBER 31, 2015

#### CONSOLIDATED STATEMENT OF INCOME (LOSS) AND STATEMENT OF OTHER COMPREHENSIVE INCOME (LOSS)

(in thousands of €)	Notes	12/31/2015 (12 months)	12/31/2014 (12 months)
Revenues			
Other income	6.1	2,929	2,026
<b>Total operating income</b>		<b>2,929</b>	<b>2,026</b>
Research and development		(10,776)	(6,613)
General and administrative	6.2 to 6.4	(7,736)	(4,361)
<b>Total operating loss</b>		<b>(15,583)</b>	<b>(8,948)</b>
Financial income	6.5	631	142
Financial expenses	6.5	(64)	(73)
<b>Financial income (loss)</b>		<b>567</b>	<b>68</b>
<b>Loss before tax</b>		<b>(15,016)</b>	<b>(8,880)</b>
Income tax	6.6	3	20
<b>NET LOSS</b>		<b>(15,013)</b>	<b>(8,860)</b>
<b>Elements that may be reclassified subsequently to income (loss)</b>			
Foreign activities – currency translation reserve		(9)	
<b>Elements that may not be reclassified subsequently to income (loss)</b>			
Remeasurement of defined benefit liability (asset)		8	59
Tax effect		(3)	(20)
Other comprehensive income		(3)	38
<b>TOTAL COMPREHENSIVE LOSS</b>		<b>(15,017)</b>	<b>(8,822)</b>
Basic loss per share (€/share)		(2.16)	(1.51)
Diluted loss per share (€/share)		(2.16)	(1.51)



## CONSOLIDATED STATEMENTS OF FINANCIAL POSITION

ASSETS (In thousands of €)	Notes	12/31/2015	12/31/2014
<b>NON-CURRENT ASSETS</b>		<b>1,076</b>	<b>1,080</b>
Intangible assets	7.1	61	31
Property, plant and equipment	7.2	918	967
Non-current financial assets	7.3	97	82
Other non-current assets			
Deferred tax assets			
<b>CURRENT ASSETS</b>		<b>51,929</b>	<b>39,526</b>
Inventories	7.4	166	198
Trade accounts receivable	7.5	424	105
Other current assets	7.6	5,705	2,235
Cash and cash equivalents	7.7	45,634	36,988
<b>TOTAL ASSETS</b>		<b>53,004</b>	<b>40,607</b>
LIABILITIES AND SHAREHOLDERS' EQUITY (In thousands of €)		12/31/2015	12/31/2014
<b>SHAREHOLDERS' EQUITY</b>		<b>47,132</b>	<b>35,824</b>
Share capital	7.8	792	688
Premiums related to the share capital	7.8	95,931	72,427
Reserves	7.8	(34,578)	(28,431)
Net loss for the period		(15,013)	(8,860)
<b>NON-CURRENT LIABILITIES</b>		<b>251</b>	<b>525</b>
Long-term provisions	7.9	100	89
Financial liabilities - Non-current portion	7.10	151	436
Deferred tax liabilities			
Other non-current liabilities			
<b>CURRENT LIABILITIES</b>		<b>5,621</b>	<b>4,258</b>
Provisions – Current portion	7.9	81	
Financial liabilities - current portion	7.10	557	334
Trade and other payables		3,672	2,085
Other current liabilities	7.11	1,311	1,840
<b>TOTAL LIABILITIES AND SHAREHOLDERS' EQUITY</b>		<b>53,004</b>	<b>40,607</b>

## CONSOLIDATED STATEMENT OF CHANGES IN SHAREHOLDERS' EQUITY

STATEMENT OF CHANGE IN SHAREHOLDERS' EQUITY (thousands of €)	Share capital	PREMIUM S RELATED TO THE SHARE CAPITAL	Reserves	INCOME (LOSS)	Shareholders' equity
<b>12/31/2013</b>	<b>551</b>	<b>42,741</b>	<b>(21,560)</b>	<b>(8,145)</b>	<b>13,587</b>
Net loss				(8,860)	(8,860)
Remeasurement of net defined benefit liability (asset)			38		38
<b>Comprehensive income</b>			<b>38</b>	<b>(8,860)</b>	<b>(8,822)</b>
Allocation of prior period loss			(8,145)	8,145	
Issue of ordinary shares	132				132
Share premium increase		29,040			29,040
Treasury shares	5	646			651
Share-based payments			1,236		1,236
<b>12/31/2014</b>	<b>688</b>	<b>72,427</b>	<b>(28,431)</b>	<b>(8,860)</b>	<b>35,824</b>
<b>12/31/2014</b>	<b>688</b>	<b>72,427</b>	<b>(28,431)</b>	<b>(8,860)</b>	<b>35,824</b>
Net loss				(15,013)	(15,013)
Remeasurement of net defined benefit liability (asset)			6		6
Change in currency translation reserve			(9)		(9)
<b>Comprehensive income</b>			<b>(3)</b>	<b>(15,013)</b>	<b>(15,017)</b>
Allocation of prior period loss			(8,860)	8,860	
Issue of ordinary shares	104				104
Share premium increase		23,440			23,440
Treasury shares	0	64			64
Share-based payments			2,716		2,716
<b>12/31/2015</b>	<b>792</b>	<b>95,931</b>	<b>(34,578)</b>	<b>(15,013)</b>	<b>47,132</b>

## CONSOLIDATED CASH FLOW STATEMENT

(in K€)	31.12.2015	31.12.2014
<b>Net loss</b>	<b>(15 013)</b>	<b>(8 860)</b>
Reconciliation of net loss and the cash used for operating activities		
- Amortization and depreciation	288	277
- Increase in long term provision	20	
- Expense related to share-based payments	2 716	1 236
- Interest expenses	30	43
- Income tax expense	(3)	(20)
<b>Operating cash flow before change in working capital</b>	<b>(11 962)</b>	<b>(7 325)</b>
Increase / Decrease in inventories	32	(60)
Increase in trade and other receivables	(319)	(18)
Increase / Decrease in other current assets	(3 470)	(534)
Increase in trade and other payables	1 588	663
Decrease in other current liabilities	(528)	28
Decrease in other liabilities - non current portion	81	
<b>Change in working capital</b>	<b>(2 616)</b>	<b>79</b>
<b>Net cash flow used in operating activities</b>	<b>(14 578)</b>	<b>(7 246)</b>
<b>Cash flows from investing activities</b>		
Acquisition of property, plant and equipment	(49)	(26)
Acquisition of intangible assets	(220)	(396)
Acquisition of financial assets	(15)	(0)
Disposal of financial assets	-	1
<b>Net cash flow used in investing activities</b>	<b>(284)</b>	<b>(420)</b>
<b>Cash flows from financing activities</b>		
Capital increases, net of transaction costs	23 544	29 173
Repayment of borrowings	(85)	(281)
Treasury shares	64	651
<b>Net cash flow from financing activities</b>	<b>23 524</b>	<b>29 542</b>
Change in other currency cash and cash equivalents	(16)	
<b>Increase / Decrease in cash and cash equivalents</b>	<b>8 646</b>	<b>21 876</b>
Cash and cash equivalents at the beginning of the period	36 988	15 113
Cash and cash equivalents at the close of the period	45 634	36 988
<b>Increase / Decrease in cash and cash equivalents</b>	<b>8 646</b>	<b>21 876</b>
Cash paid for interest	34	31
Cash paid for income tax	-	-

# **ERYTECH PHARMA GROUP**

## **NOTES TO THE FINANCIAL STATEMENTS**

These notes are an integral part of the consolidated financial statements for the financial year ended December 31, 2015.

The financial statements were approved by the Board of Directors on February 19, 2016, and will be submitted for approval at the next General Meeting.

### **1. DESCRIPTION OF THE GROUP'S ACTIVITY**

The Group's main activity is research and development in the areas of treatment of acute leukemia and other orphan diseases through the use of its technology platform, which encapsulates active ingredients in red blood cells.

Since its creation, the Group has concentrated its efforts on:

- The development of a patented technological platform based on the encapsulation of enzymes in red blood cells, which offers an innovative approach to the treatment of acute leukemia and other solid tumors. The development of the main product, Graspas®, which began when the Group was founded, has led to the issuing of 13 patent families held in the Group's name. The Group has also implemented a patented industrial process capable of producing clinical batches of Graspas®, and capable of meeting demand in the commercialization of the product.
- The implementation of clinical programs in order to validate Graspas® initially in terms of safety of use and toxicology through a Phase I clinical study in acute lymphoblastic leukemia (ALL) in adult and pediatric patients with relapsed ALL. Based on the results obtained, the Group performed a Phase II clinical study that likewise demonstrated the safety of the product's use and its efficacy in patients older than 55 years of age with ALL. The Group completed a Phase III clinical study, at the end of which Erytech filed an application in September 2015, for approval to market Graspas® in Europe for the treatment of ALL. The Group has likewise initiated a Phase IIb study on acute myeloid leukemia (AML), as well as a Phase II study on pancreatic cancer.

The Group's business model is to develop its products up to the point of obtaining authorization for their commercialization in Europe and Israel and, as a second step, in the United States. Commercial partnerships established by ERYTECH Pharma will allow for the distribution of Graspas® in Europe and Israel. Various distribution options in the United States and the rest of the world are under review. ERYTECH Pharma has the capacity to ensure the supply of Graspas® for the first years of its sale in Europe, through its production unit in Lyon.

### **2. EVENTS CHARACTERIZING THE FINANCIAL YEAR**

#### **2.1 Company Management**

Pierre-Olivier Goineau, co-founder of the Company and Chief Operating Officer submitted his resignation from his positions within the Company at the Board of Directors' meeting of January 11, 2015.

Dr. Iman El-Hariry joined the company as Chief Medical Officer within the subsidiary Erytech Pharma Inc., based in Boston, and will be responsible for medical, clinical, and regulatory affairs. ERYTECH Pharma S.A. also strengthened its executive team by appointing Eric Soyer as Chief Financial Officer and Chief Operating Officer. Eric Soyer also replaced Pierre-Olivier Goineau as Treasurer and Secretary General of the U.S. subsidiary ERYTECH Pharma Inc.

In 2015, additional subscription warrants were allocated as follows (see Note 6.3):

- The Board of Directors' meeting on April 29, 2015, awarded 2,150 BSA2012 to the independent Board members;
- In accordance with the 2014 plan, the Board of Directors' meeting on June 23, 2015, assigned the first tranche of the plan and allocated 2,500 BSPCE2014 to employees with the status of manager within the Company, and 3,000 BSA2014 to the Chief Medical Officer based in the United States within the subsidiary ERYTECH Pharma Inc.;
- The Board of Directors' meeting on August 31, 2015, awarded 3,585 BSA2012 to the independent Board members;
- Eric Soyer was awarded 2,000 BSPCE 2014 when he was hired in September 2015.

## 2.2 Funds raised on the stock market

In December 2015, the parent company ERYTECH Pharma S.A. raised €25.44 million (excluding issue costs) on Euronext, with a total of 940,000 new shares issued in a capital increase in the form of a private placement with first-tier institutional investors in the United States and Europe, representing approximately 14% of the number of shares in circulation (post-issue).

The issue price was set at €27 per share, in accordance with Resolutions 15 and 17 of the Combined General Shareholders' Meeting on June 23, 2015. This price reflects a 3.1% discount compared to the closing price on the day before the price was set and a 4.8% discount from the weighted average of the prices of the Parent Company's shares in the last three trading sessions before the price was set.

The Company still intends to offer its shares on the US Nasdaq market once conditions are met.

## 2.3 Principal operational items

### → GRASPA® in Europe (ERYASP)

The committee of independent experts (the Data Safety Monitoring Board, or DSMB) in charge of monitoring the Phase III clinical trial of GRASPA® in adults and children experiencing a relapse of ALL met and issued a favorable opinion on the continuation of this Phase III clinical trial following the original protocol with a total of 80 patients. The company completed the Phase III trial in ALL and submitted its MA application to the EMA in September 2015. The EMA began its review on October 1, 2015.

The European Union granted orphan drug designation for AML to GRASPA®. The Company received the authorization from ANSM (French Medicine Agency) to begin a Phase IIb clinical trial in AML. ERYTECH Pharma recruited its first patient in March.

The committee of independent experts (the Data Safety Monitoring Board or DSMB) in charge of monitoring the Phase IIb clinical trial of GRASPA® in adults and children experiencing a relapse of AML met and issued a favorable opinion on the continuation of this clinical trial after evaluation of the product tolerance in the first 30 patients.

ERYTECH Pharma obtained the authorization of numerous European countries for its AML trial, enabling it to broaden the recruitment of its patients.

The Company announced the launch of a Phase 2 clinical trial of ERY-ASP™ for patients with pancreatic cancer.

The Company announced the addition of a new candidate drug to its oncology portfolio: “Affameurs de tumeurs” [Tumor starvation inducer] ERY-MET.

#### → ERYASP in the United States

The FDA granted ERYTECH Pharma the right to begin a Phase Ib trial with ERYASP™ in ALL. The main patient recruitment centers are open in: Chicago, Duke, Columbus.

The USPTO (United States Patent and Trademark Office) issued the patent protecting ERYTECH Pharma’s technology, granting it exclusivity until 2029 with the potential for extension into 2034.

- The company has filed an application for a centralized Marketing Authorization (MA) with the European Medicines Agency (EMA) for GRASPA® for the treatment of patients suffering from Acute Lymphoblastic Leukemia (ALL).
- ERYTECH Pharma was able to launch the shift to the higher dosage and change the protocol to bring about accelerated recruitment in the Phase I trial with ERY-ASP for adult ALL in the United States.
- Thirteen “double-allergic” patients treated in the context of an Expanded Access Program (EAP) in France.
- The Company confirmed the finalization of new development projects for ERY-ASP/GRASPA® in ALL with the participation of opinion leaders.
- The recruitment policy is in line with patient expectations for the European Phase IIb trial in Acute Myeloid Leukemia (AML).
- ERYTECH Pharma received positive comments from DSMB1 on the tolerance of the ERY-ASP product in the Phase II trial on pancreatic cancer.
- The Company is preparing to launch clinical trials on non-Hodgkin lymphoma.
- ERYTECH Pharma received notification of issue from the European Patent Office for a key patent covering the use of ERY-ASP for the treatment of pancreatic cancer. This patent for “Medication for the treatment of pancreatic cancer” had been submitted in late 2007 and has been issued in Australia, Israel and Singapore since that date. It should be noted that in May 2015, ERYTECH Pharma received the green light from the ANSM to begin a Phase II clinical trial with ERY-ASP for use in treating pancreatic cancer.

## **2.4 Other information**

ERYTECH Pharma S.A. has been audited by the tax authorities since October 21, 2015. This audit was still in progress as of December 31, 2015.

The Parent Company ERYTECH Pharma S.A. created its subsidiary “ERYTECH Pharma Inc.” in the USA in April 2014. As of December 31, 2015, the Group financial statements include the consolidation of the wholly owned American subsidiary.

## **3. POSTCLOSING EVENTS**

Mr. Yann Godfrin, co-founder of ERYTECH Pharma S.A. and Deputy Chief Executive Officer, submitted his resignation at the meeting of the Company’s Board of Directors on January 10, 2016.

The search for his successor has already begun. During this transition phase, Yann Godfrin will continue to support the Company's development as a consultant.

#### **4. PREPARATION BASIS**

The financial statements have been prepared according to the principle of going concern. The Group's loss-making situation is explained by the innovative nature of the products developed, therefore involving a multi-year research and development phase.

The statement of comprehensive income presents the classification of expenses and income per item, with the exception of other operating income and expenses. The comparative information is presented using an identical classification.

The Group closed its annual accounts on December 31, 2015.

The Group's consolidated financial statements for the financial year ended December 31, 2015 have been established in euros, which is the functional currency of the Company. All amounts indicated are expressed in thousands of euros, except where otherwise indicated.

#### **5. SIGNIFICANT ACCOUNTING POLICIES AND METHODS**

In application of European regulation 1606/2002 of July 19, 2002, the financial statements for the ERYTECH Pharma Group are prepared in conformity with the International Financial Reporting Standards (IFRS) published by the International Accounting Standards Board (IASB), as adopted by the European Union at the date of issue of the financial statements by the Board of Directors, as applicable at December 31, 2015.

This framework is available on the European Commission's website, at the following address: ([http://ec.europa.eu/internal\\_market/accounting/ias/index\\_fr.htm](http://ec.europa.eu/internal_market/accounting/ias/index_fr.htm)).

The accounting methods outlined below have been applied in a continuous manner to all the periods presented in the ERYTECH Pharma financial statements, after taking into account or with the exception of the new standards and interpretations described below.

##### **5.1. New standards, amendments to standards and interpretations applicable as of the financial year commencing January 1, 2015**

The accounting principles adopted for the preparation of the financial statements are those applied by the Group at December 31, 2015, with the exception of the following new standards and interpretations, which were applied for the first time as of January 1, 2015:

- IFRIC 21: "Duties or taxes": this interpretation stipulates that taxes must be recognized in accordance with the operative event as defined by law, independently of the basis of calculation. The application of this standard has no effect on the annual financial statements.
- Annual improvements to IFRS – 2011-2013 cycle: these amendments to standards are applied prospectively. The standards in question are:
  - o IFRS 3 – Business combinations. This amendment specifies that:



- The creation of any form of partnership as defined by IFRS 11 – Partnerships (i.e. joint ventures and joint operations) is excluded from the scope of IFRS 3;
- This exclusion applies only to the financial statements of joint ventures or joint operations.
- IFRS 13 – Fair value valuation. This amendment specifies that the IFRS 13 exception, which allows measuring the fair value of a set of financial assets and liabilities on a net basis, applies to all contracts covered by IAS 39 – Financial Instruments – Recognition and Measurement, or IFRS 9 – Financial Instruments, whether or not they meet the definition of financial assets or liabilities under IAS 32 – Financial Instruments – Presentation.
- IAS 40 – Investment Property. This amendment specifies that:
  - Judgment must be used to determine whether the acquisition of an investment property consists of the acquisition of an asset, of a group of assets or of a group of enterprises that falls within the scope of application of IFRS 3 – Business Combinations;
  - This judgment must be based on the provisions contained in IFRS 3 – Business Combinations.

These new texts published by the IASB had no significant impact on the Group financial statements.

## **5.2. Standards and interpretations published but not yet in force**

### **Texts not adopted by the European Union by the closing date**

The IASB has published the following standards, amendments to standards and interpretations not yet adopted by the European Union:

- IFRS 16 – Leases
- IFRS 9 – Financial Instruments
- IFRS 15 – Revenues from Contracts with Customers
- Amendment to IFRS 10 and IAS 28 – Sale or contribution of assets between an investor and an associate or joint venture partner

### **Texts adopted by the European Union on the closing date but not yet in force**

The Group has not applied in advance any of the standards and interpretations cited below, the application of which was not mandatory as of January 1, 2015:

- Amendments to IAS 1 – Meaning of “Effective IFRS”;
- Amendments to IAS 19 – Defined benefit plans, contributions from employees;
- Amendments to IAS 16 and IAS 38 – Clarification of acceptable amortization methods;
- Amendments to IFRS 11 – Recognition of acquisitions of interests in a joint venture;
- Annual improvements to the IFRS (2010-2012 and 2012-2014 cycles).

These amendments should not have a significant impact for the Group.

## **5.3. Presentation**

The statement of comprehensive income (loss) presents the classification of expenses and income by function (research and development costs, structural costs and general expenses).

The comparative information is presented using an identical classification.

The consolidated financial statements are established on the basis of the principles of going concern and consistency of accounting methods.

#### **5.4. Closing date**

The Group closed its annual accounts on December 31, 2015.

#### **5.5. Principles of consolidation**

The company ERYTECH Pharma SA (head office: 60 avenue Rockefeller, Bioparc Bat Adénine, 69008 LYON, FRANCE) holds 100% of its subsidiary, ERYTECH Pharma Inc. Headquarters: 185 Alewife Brook Parkway Ste 410, CAMBRIDGE, MA 02138, UNITED STATES). The Group's financial statements include consolidation of the American subsidiary.

Intercompany balances and transactions between Group companies have been eliminated.

#### **5.6 Translation of the financial statements of foreign subsidiaries**

The functional currency of the Company is the euro, which is also used as the presentation currency of the consolidated financial statements.

The statements of the subsidiary ERYTECH Pharma Inc. are prepared in U.S. dollars (functional currency).

The balance sheet of ERYTECH Pharma Inc. has been converted into euros using the exchange rate at the financial year-end and the income statement using the average exchange rate for the month of recognition. The corresponding translation differences are recorded in shareholders' equity.

#### **5.7 Transactions in foreign currencies**

Transactions in foreign currencies are recorded at the exchange rate in force on the transaction date. The monetary assets and liabilities denominated in these other currencies are converted at the rate in effect on the closing date. Unrealized gains and losses resulting from this conversion are recognized as income or loss for the financial year (financial results).

#### **5.8. Consolidated cash flow statement**

The cash flow statement is prepared using the indirect method and separately presents the cash flows associated with operating, investment, and financing activities.

Operating activities correspond to the company's primary income-generating activities and all the other activities that do not meet the investment or financing criteria. The Group has decided to classify grants received under this category. The cash flows associated with operating activities are calculated by adjusting the net results of variations in working capital requirements, of items with effects of a non-cash nature (amortization, impairment), of disposal gains, of calculated expenses.

Cash flows associated with investment activities correspond to cash flows associated with the purchase of assets, net of supplier debts on the assets, and with the disposal of assets and other investments.

Financing activities are operations that result in changes in the amount and composition of the shareholders' equity and borrowings of the entity. Capital increases and the obtaining or repayment of loans are classified under this category. The Group has chosen to classify the repayable 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 period's investments. The decrease in financial debt associated with leases is therefore included under the period's loan repayments.

### **5.9. Use of estimates**

The preparation of the consolidated financial statements in compliance with IFRS implies that the Group makes a certain number of estimates and uses certain assumptions that have an impact on the amounts recorded to assets or liabilities. 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 principal estimate made by the Group when preparing the financial statements applies to share-based payment (note 6.3).

## **5.10. Intangible assets**

### Intangible assets generated internally – Research and development costs

In accordance with IAS 38, “Intangible Assets,” research expenditures are accounted for in the period during which they are incurred.

An intangible asset internally generated relating to a development project is recorded as an asset if, and only if, the following criteria are met:

- Technical feasibility required to complete the development project;
- Intention to complete the project, use or sell it;
- Capacity to use the intangible asset;
- Demonstration of the probability of future economic benefits related to the asset;
- Availability of appropriate resources (technical, financial and other) to complete the project;
- Ability to reliably assess the expenditures attributable to the development project underway.

The initial measurement of the development asset is the sum of expenses sustained starting on the date on which the development project meets the above criteria. When these criteria are not met, development expenditures are accounted for in the period in which they are incurred.

According to IAS 38, “Intangible Assets,” development costs must be accounted for as intangible assets when specific conditions relating to technical feasibility, marketability and profitability are met. Considering the strong uncertainty associated with the development projects performed by the Group, these conditions will only be met when the regulatory procedures necessary for the sale of the products have been finalized. Most of the expenditures being incurred before that stage, the development costs are accounted for in the period in which they are incurred.

### Other intangible assets

The other intangible assets are recognized at their cost, decreased by the cumulated amortization and any losses in value. The amortization is calculated on a straight-line basis according to the period of the asset’s use. The useful life and the amortization method are reviewed at each year-end. All significant modifications to the anticipated use of the asset are recognized prospectively.

The other intangible assets are primarily composed of computer software and are amortized on a straight-line basis over 1 to 5 years.

An impairment is recorded where the asset's book value is greater than its recoverable value (see Note 7.1).

## **5.11. Property, plant and equipment**

Fixed assets are recorded in the balance sheet at their purchase cost, composed of their purchase price and all directly associated costs incurred to place the asset in position and in a state of operation according to the usage intended by the company’s management.

These assets are depreciated according to the straight-line method, according to their period of use.

The primary period of use adopted are as follows:

- Industrial equipment: 1 to 5 years;
- Fixtures and fittings: 3 to 10 years;

- Office equipment: 3 years;
- Furniture: 3 to 5 years.

The period of use of fixed assets, any residual values, and the depreciation method are reviewed at each year-end and, in the event of a significant change, result in a prospective revision of the depreciation plans.

In compliance with IFRS, the different components of a single fixed asset that have a different period of use or that procure economic benefits for the Company according to a different rhythm are recognized separately.

## **5.12. Impairment tests**

According to the standard IAS 36, “Impairment of Assets,” a loss in value must be recognized where the net book value is lower than the recoverable value. The recoverable value of an asset is the highest value between the fair value less disposal costs and the value in use.

The fair value less disposal costs is the amount that can be obtained from the sale of an asset in a transaction under conditions of normal competition between well-informed, consenting parties, less the disposal costs.

The value in use is the present value of estimated future cash flows anticipated from the ongoing use of an asset. The value in use is determined based on cash flows estimated based on budgets and plans, then discounted by adopting the long-term market rates after taxes that reflect the market estimates of the time value of money and the risks specific to the assets.

### Tangible and intangible assets that are depreciated or amortized

Where new events or situations indicate that the book value of certain tangible or intangible assets may not be recoverable, this value is compared to its recoverable value based on the value in use or its fair value less disposal costs. Where the recoverable value is less than the net book value of these assets, the latter is adjusted to its recoverable value and a loss in the asset value is recognized under “provisions for impairment.” The new value of the asset is thus amortized or depreciated prospectively based on the new period of the asset’s residual life.

## **5.13. Other non-current financial assets**

The valuation and recognition of financial instruments is defined by standard IAS 39 “Financial instruments: Recognition and Measurement.” The company has no derivative instrument to hedge the currency risk.

### Loans and receivables

These represent the financial assets issued or acquired by the Group which are the counterpart to a direct remittance of money, assets or services to a debtor. They are valued at amortized cost using the effective interest rate method. Long-term loans and receivables not remunerated or remunerated at a lower-than-market rate are discounted when the sums are significant. Any impairments are booked through the statement of income (loss).

### Financial assets at fair value through the income statement

A financial asset is classified as a financial asset at fair value through the income statement if it is classified as being held for transaction purposes or is designated as such when it is initially recognized. Financial assets are valued at fair value, and any resulting change, which takes into account the income from interest and dividends, is booked to the statement of income (loss). Thus, the Group can designate cash investments at fair value from inception.

#### Assets available for sale

Assets available for sale are assets which the Company intends to keep for an undefined period and which can be sold to meet liquidity needs or in response to changes in interest rates. At each accounting date, they are valued at fair value and changes in fair value are recognized in shareholders' equity.

A significant or persisting decline in value is recognized in the statement of income (loss) as an impairment.

#### Fair value of financial instruments

Valuations at fair value are detailed in accordance with the following fair value hierarchy in compliance with IFRS 7:

- Level 1: the instrument is traded on an active market;
- Level 2: the valuation relies on valuation techniques based on data that can be observed directly (price) or indirectly (price derivative);
- Level 3: at least one significant component of the fair value is based on unobservable data.

#### **5.14. Trade accounts receivable**

Customer receivables are valued at nominal value, which is equivalent to their fair value given their short-term due date. If necessary, these receivables are impaired to bring them to the estimated net realization value.

#### **5.15. Inventories**

In compliance with the IAS 2 standard for "Inventories," inventories are recognized at their cost or at their net realizable value, where this is lower. In the latter case, the loss in value is recorded under current operating income. Inventories are measured according to the FIFO method (First in First out).

#### **5.16. Cash and cash equivalents**

The item "cash and cash equivalents" in the balance sheet includes highly liquid securities for which the initial maturity is equal to or less than three months, considered equivalent to liquid assets. These investments are easily convertible into a known cash amount and are subject to a negligible risk of change in value. They are classified in assets as cash equivalents and valued at fair value through the statement of income (loss).

## **5.17. Provisions and contingent liabilities**

A provision is recognized where the Group has a current or implicit legal obligation resulting from a prior 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 discharge the obligation. The portion of a provision estimated as payable in less than one year is recorded under current liabilities, and the balance under non-current liabilities. The provisions are discounted where the impact is significant.

Provisions notably include:

- obligations for retirement indemnities;
- provisions for disputes.

Disclosure is made in the detailed notes on any contingent assets and liabilities where the impact is significant, except where the probability of occurrence is low.

### Provisions for retirement indemnities - defined benefit plans

In compliance with IAS 19, “Employee Benefits,” within the scope of defined benefit plans, the post-employment benefits and other long-term benefits are measured every year using the projected unit credit method. According to this method, each service period gives rise to an additional unit of rights to benefits, and each of these units is measured separately to obtain the final commitment. This final commitment is then discounted.

These calculations primarily include:

- an estimate of the date of payment of the benefit;
- a financial discount rate;
- an inflation rate;
- assumptions regarding salary increases, personnel turnover rates and mortality rates.

The primary actuarial assumptions adopted at December 31, 2015, are described in note 7.9.

The positive or negative actuarial differences include the effects, on the commitment, of a change in calculation assumptions as well as adjustments to the commitment linked to experience. In compliance with the standard IAS 19 “Post-employment benefits [employee benefits],” the Group recognizes these actuarial differences under other items of the comprehensive income for post-employment benefits.

The provision that appears on the balance sheet on a specific line represents the total commitment at the closing date, adjusted, as applicable, for the cost of past services. The cost of prior services associated with a change in the plan are recognized in the statement of income (loss).

The expense for the period, composed of the cost of services rendered and the financial expense of accretion, constitutes an operating expense.

### Provisions for risks

Provisions for risks represent commitments resulting from disputes and other risks, the payment dates and amounts of which are uncertain.

The amount recognized in the consolidated financial statements as provision for risks represents the best estimate of the costs necessary to resolve the dispute.

## **5.18. Measurement and recognition of financial liabilities**



### Financial liabilities at the amortized cost

Loans and other financial liabilities are initially measured at their fair value, and then at the amortized cost, calculated using the effective interest method (“EIM”).

The transaction costs directly attributable to the acquisition or issue of a financial liability decrease this financial liability. These costs are then actuarially amortized over the lifetime of the liability, based on the EIM.

The EIM is the rate that equalizes the flow anticipated from future cash outflows at the current net book value of the financial liability, with a view to deducting its amortized cost.

### Liabilities at fair value through the statement of income (loss)

The liabilities at fair value through the statement of income (loss) are measured at their fair value.

## **5.19. Lease agreements**

At the beginning of an agreement, the Group determines whether the agreement is, or contains, a lease agreement. The Group’s lease agreements are recognized pursuant to IAS 17, which distinguishes finance lease agreements and operating leases.

### Finance lease agreement:

A lease agreement is considered as being a finance lease where it transfers to the borrower substantially all the risks and benefits inherent in ownership of the asset. The other contracts are considered as being operating lease agreements.

The assets held within the scope of a finance lease are recognized in the balance sheet assets and liabilities at their fair value at the start of the contract or, where this is lower, at the discounted value of the minimum payments on the lease. These assets are then depreciated over the duration of the lease or the anticipated use of the asset, whichever is shorter.

### Operating lease:

Other leases are classified as operating leases and are not recorded in the Group balance sheet. The payments made under operating leases are recognized on a straight line basis over the term of the lease. The benefits received from the lessor are an integral part of the net total of lease expenses and are recognized as a deduction to expenses over the term of the lease. Commitments related to operating leases (note 9) represent the minimum future fixed payments calculated over the term in which the lease cannot be terminated.

## **5.20. Share capital**

The share capital is presented as equity. The cost of capital transactions that are directly attributable to the issuance of new securities or options is deducted from funds received for the issue at their net after-tax value.

## **5.21. Share-based payments**

In compliance with IFRS 2, the benefits granted to certain employees in the form of share-based payments are measured at the fair value of the instruments granted.

This remuneration can take the form of either equity or cash instruments.

Share call and subscription options are granted to directors and to certain employees of the Group.

In compliance with IFRS 2, “Share-Based Payment,” the fair value of the options is determined on the grant-date.

To determine their value, the Group uses the Black & Scholes mathematical model. This allows them to take into account the characteristics of the plan (exercise price, period of exercise), the market data at the time of grant (risk-free rate, volatility, expected dividends), and recipient behavior assumptions. Changes in value subsequent to the grant-date have no effect on this initial measurement.

The value of options is notably a function of their expected lifetime. This value is recorded under personnel expenses using the straight-line method between the grant date and the maturity date (vesting period), with a direct contra-entry in the shareholders’ equity.

## **5.22. Other income**

### Grants

ERYTECH Pharma benefits from public financing from local, state or EU organizations that cover all or part of the research and development on specific projects or subjects. This assistance can be in the form of subsidies or conditional advances.

The other income from activities includes income relating to grants. The grants are initially recognized at their fair value under deferred income, where a reasonable assurance exists that they will be received and the Group will comply with the conditions attached to these grants.

They are then recognized as income according to the expenses incurred on the closing date pursuant to IAS 20. As a result, subsidies to be received can be recognized if the subsidy contract is signed, but the subsidies have not yet been received.

### Conditional advances

Conditional advances are repayable only if the research and development projects they are financing are successful. They are recognized as long-term debt according to IAS 20. The payments and reimbursements of conditional advances are presented under cash flows related to financing activities in the consolidated statement of cash flows.

### Research tax credit

Certain research and development expenses give the right in France to a tax credit recognized at the end of the financial year in which the expenses have been recognized and the tax credit requested. When it has not been used by being offset against a tax expense, the tax credit may be paid to the Company depending on the tax rules in effect. The research tax credit, which is classified as public assistance under IAS 20, is recorded to the statement of income (loss) under “Other operating income.”

The Company has not yet received the 2014 Research Tax Credit (Crédit d’Impôt Recherche-CIR) as of December 31, 2015, in the amount of €1,524k; the receivable in the balance sheet at December 31, 2015, therefore corresponds to the CIR for 2015 and the balance from 2014.

### Partnership with Orphan Europe

Within the context of its partnership agreement with Orphan Europe on the development of AML, the Group re-invoices, with no margin, certain clinical costs incurred and invoiced to the Group by external providers.

In application of IAS 18, the Group estimates that, within the context of this partnership, it acts as agent insofar as concerns external costs re-invoiced, in that:

- The Group does not have the primary responsibility for supplying goods or services, as the majority of the services are provided by third parties, the largest of which, CRO (the company that manages the clinical trials) invoices Orphan Europe directly. The Group is only directly invoiced for the associated services.
- The Group does not bear the inventory risk.
- The Group has no ability to determine prices, as all external costs are invoiced to the nearest euro, without margin, and it does not absorb any change in price made by the suppliers.
- The Group bears a credit risk not considered to be significant.

Consequently, the re-invoicing of these external costs to Orphan Europe is presented as a decrease in the corresponding expenses sustained by the Group. For 2015, the amount of external costs re-invoiced within the scope of this partnership totaled €341,443.

Within the context of this same agreement, the Group also re-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. These re-invoiced internal costs are recognized by the Group as other operating income from ordinary activities. They total €340,959 for the 2015 financial year.

### **5.23. Financial results**

Financial income:

- income from interest on cash and cash equivalents;
- foreign exchange gains.

Other expenses consist of:

- other costs paid to the banks on financial transactions;
- foreign exchange losses;
- the impact of investment securities;
- interest expenses on financial debt (cost of gross financial debt includes the financial costs and the issue costs on the financial debts) composed of loans and other financial debts (notably overdrafts and debts on financial leases).

### **5.24. Taxes**

#### Current taxes

Considering the level of tax losses that can be carried forward, no tax expense is owing.

#### Deferred taxes

Deferred taxes are calculated for all the time-based differences between the book value of an asset or a liability and its tax value, save for the exceptions established under standard IAS 12.

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 time-based 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 using of 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 balance sheet under non-current assets and liabilities.

The parent company 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 is based on property rental values and which can, where applicable, have a ceiling at a percentage of the value added is recognized under operating expenses;
- the corporate value added contribution meets, based on the Group's analysis, the definition of an income tax as established under IAS 12.2 ("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 Group 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 time-based differences existing at year end, with a contra-entry of a net expense in that year's statement of income (loss). Where applicable, this deferred tax expense is presented on the line "taxes." For the moment, the parent company does not pay the CVAE.

## **5.25. Earnings per share**

The Group presents the basic earnings per share and the diluted earnings per share.

The basic earnings per share are calculated by dividing the Group's net results by the weighted average number of shares in circulation during the financial year.

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.

Diluted earnings are identical to basic earnings when the result for the financial year is a loss (potential shares are not taken into account as their effect would be anti-dilutive).

## **5.26. Segment reporting**

In accordance with IFRS 8 "Operating Segments," reporting by operating segment is derived from the internal organization of the Group's activities; it reflects management's viewpoint and is established

based on internal reporting used by the chief operating decision maker (the Chairman - CEO) to implement the allocation of resources and to assess performance.

The company conducts its activities exclusively in research and development in the fields of treatment for acute leukemia and other orphan diseases, none of which has currently been commercialized. Most of its activities are located in France. Therefore, the Company has decided to use only one operating segment in establishing and presenting its financial statements.

## 5.27. Off-balance sheet commitments

The Group has defined and implemented monitoring for its off-balance sheet commitments in order to gain information about their nature and purpose. This monitoring pertains to information relative to the following commitments given:

- personal guarantees (guarantees, endorsements, and bonds),
- security interests (mortgages, pledges, and sureties),
- operating leases, purchase and investment commitments,
- other commitments.
- contracts signed with CROs (contract research organizations) and hospitals as part of clinical studies.

## 6. NOTES RELATIVE TO THE CONSOLIDATED STATEMENT OF INCOME LOSS

### 6.1 Other income

The other operating income is composed of the following:

<b>(in K€)</b>	<b>31.12.2015</b>	<b>31.12.2014</b>
Research tax credit	2 219	1 524
Subsidies	368	271
Other income	341	231
<b>Operating income</b>	<b>2 929</b>	<b>2 026</b>

The other income was primarily generated by the research tax credit, the grants associated with the pre-clinical research programs in partnership with BPI France.

The “Other income” totaling €341k in 2015 represents the sum of the internal costs sustained by the Group within the scope of the AML study, and re-invoiced to the company Orphan Europe to this end. The other external costs associated with this clinical trial were re-invoiced to Orphan Europe with no margin, and do not appear under income from activities, but are deducted from the associated expenses.

The increase in the research tax credit and subsidies at December 31, 2015, compared to December 31, 2014, is due to the increase in the research and development activity between the two periods.

The grant recognized in income for the 2015 financial year corresponds to the use of the €992k advance for the TEDAC project received at the inception of the project. The Company did not receive a new grant for the TEDAC project on June 30, 2015 (end date of key stage 3), despite the request to BPI in accordance with the contract. BPI asked the Company to make a new request on June 30, 2016.

As a result, and despite the project's progress, no subsidy to be received was recorded as at December 31, 2015, in light of the uncertainty surrounding receipt of the grant.

## 6.2 Details of expenses by item

31/12/2015 in K€	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	607	56	547	3	2 593	3 200
Depreciation and amortization	250	26	224	-	120	369
<b>Total</b>	<b>10 810</b>	<b>3 575</b>	<b>6 779</b>	<b>456</b>	<b>7 702</b>	<b>18 512</b>

31/12/2014 in K€	Research and development expenses	of which other R&D expenses	of which clinical studies	of which Intellectual Property	General and administrative expenses	Total
Consumables	424	252	172	-	28	452
Rental and maintenance	495	217	278	-	291	785
Services, subcontracting and fees	2 959	356	2 187	416	1 045	4 004
Personnel expenses	2 443	1 351	1 017	75	2 368	4 811
Other	71	35	33	3	601	672
Depreciation and amortization	222	32	190	-	28	250
<b>Total</b>	<b>6 613</b>	<b>2 244</b>	<b>3 875</b>	<b>493</b>	<b>4 361</b>	<b>10 974</b>

The €4,163k increase in research and development costs is mainly due to:

- The increase in external services of €1,516k mainly related to the development of the TEDAC project
- The €1,534k increase in personnel costs (see note 6.3).

The €3,375k increase in overheads and general expenses is primarily due to:

- The €1,977k increase in external services related mainly to the initial public offering project on NASDAQ.
- The BSA2014 allocated to directors during the financial year for a value of €1,593k.
- Partially offset by lower personnel costs of €741k (see note 6.3).

## 6.3 Personnel costs

The personnel costs are broken down as follows:

31/12/2015 in K€	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	301	1 124
Social security expenses	920	427	468	25	429	1 349
<b>Total personnel expenses</b>	<b>3 977</b>	<b>1 506</b>	<b>2 384</b>	<b>87</b>	<b>1 627</b>	<b>5 603</b>

31/12/2014 en K€	Frais de recherche et développement	dont Autres Frais de Recherche et développement	dont Etudes cliniques	dont Propriété intellectuelle	Frais de structure et généraux	Total général
Wages and salaries	1 408	733	632	43	1 051	2 459
Share-based payments	384	284	89	11	852	1 236
Social security expenses	651	335	296	20	464	1 115
<b>Total personnel expenses</b>	<b>2 443</b>	<b>1 351</b>	<b>1 017</b>	<b>75</b>	<b>2 368</b>	<b>4 811</b>

The €792k increase in personnel costs is mainly due to the increase in payroll of the subsidiary ERYTECH Inc. for €300k and of ERYTECH Pharma S.A. for €670k following the increase in the workforce.

#### 6.4 Share-based payment (IFRS 2)

Share options have been allocated to the managers, to certain employees, as well as to members of the Board of Directors in the form of share subscription warrants (“BSA”) or founder subscription warrants (“BSPCE”).

##### 6.4.1 “2012 Plan”

In the context of the BSA<sub>2012</sub> plans, the Board of Directors’ meeting on April 29, 2015 and August 31, 2015 awarded 2,150 and 3,585 BSA<sub>2012</sub>, respectively, to the directors without vesting conditions.

##### 2,150 BSA awarded on April 29, 2015

The main assumptions used to determine the fair value of these instruments are:

- The price of the underlying asset: €31.19 representing the market price on the date of the Board meeting;
- Risk-free rate: -0.07% (according to the zero coupon government bond rates curve);
- Anticipated dividends: zero;
- Volatility: 20.5% based on the historical volatility observed on the NextBiotech index;
- Anticipated maturity: 2.5 years.

The fair value of the warrants awarded in 2015 under the 2012 plan was valued at €512k and in the absence of vesting conditions was fully recorded in the statement of income (loss) for the 2015 financial year (as overheads and general expenses).

##### 3,585 BSA awarded on August 31, 2015

The main assumptions used to determine the fair value of these instruments are:

- The price of the underlying asset: €37.52 representing the market price on the date of the Board meeting;
- Risk-free rate: -0.08% (according to the zero coupon government bond rates curve);
- Anticipated dividends: zero;
- Volatility: 22.55% based on the historical volatility observed on the NextBiotech index;
- Anticipated maturity: 2.36 years.

The fair value of the warrants awarded in 2015 under the 2012 plan was valued at €1,081k and in the absence of vesting conditions was fully recorded in the statement of income (loss) for the 2015 financial year (overheads and general expenses).

At the end of 2015, the share subscription warrants for the 2012 plan were broken down as follows:

Types of securities	BSPCE <sub>2012</sub>	BSA <sub>2012</sub>
Number of warrants that the Company is authorized to issue for all types of warrants	45,050	
Number of warrants granted	33,788	10,760
Number of warrants exercised	16,352	5,525
Date of General Meeting	May 21, 2012	



<b>Exercise price per new share subscribed</b>	€7,362
<b>Final date for exercising warrants</b>	May 20, 2020
<b>Parity</b>	1 warrant for 10 shares
<b>General conditions of exercise</b>	The warrants may be exercised as of their vesting date.
<b>Maximum number of new shares that can be issued</b>	231,730

#### **6.4.2 “2014 Plan”**

##### **2014 Allocation**

On January 22, 2014, the Board of Directors used the delegation granted by the Combined General Shareholders’ Meeting of April 2, 2013, to make a free allocation of 12,000 BSPCE<sub>2014</sub> to the Group’s directors, including 6,000 to Gil Beyen, Chief Executive Officer, and 3,000 each to Pierre-Olivier Goineau and Yann Godfrin, Deputy Chief Executive Officers. One-third of the warrants are vested per year. Given this condition of service, these warrants are allocated gradually, over a three-year vesting period.

In the event of a beneficiary's departure from the Group for any reason whatsoever, the beneficiary shall retain the warrants to which he subscribed prior to his departure. However, in the event of a beneficiary’s departure from the Group for any reason whatsoever prior to the subscription of the warrants to which he is entitled, those warrants have been forfeited and may be reallocated to the person who replaces the individual who leaves the Company.

Following the departure of Pierre-Olivier Goineau in January 2015, 2,000 BSPCE of the 3,000 initially allocated were not granted. They were granted to his replacement, Eric Soyer, on September 1, 2015.

Following the departure of Yann Godfrin in January 2016, 1,000 BSPCE of the 3,000 initially allocated were not granted.

The primary assumptions used to determine the fair value of the BSPCE<sub>2014</sub> granted to executive officers are:

- The price of the underlying asset: €12.77 representing the market price on the date of the Board meeting;
- Risk-free rate: between 1.31% and 1.60% depending on the tranches (according to the zero coupon government bond rates curve);
- Anticipated dividends: zero;
- Volatility: 18.98% based on the historical volatility observed on the NextBiotech index;
- Anticipated maturity: between 5.6 and 6.7 years in function of the tranches allocated.

The residual fair value of the plan was valued at €118k. This expense is distributed gradually over the remaining duration of the plan in compliance with IFRS 2 (“graded vesting method”). An expense of €66k was recorded for this purpose under personnel expenses at December 31, 2015, and divided between R&D staff costs (€13k) and administrative personnel costs (€53k). The fair value was revised to take into account the departures of Pierre-Olivier Goineau in 2015 and Yann Godfrin in January 2016.

##### **2015 Allocations**

2,500 BSPCE awarded on June 23, 2015

Under the BSPCE<sub>2014</sub> plans, on June 23, 2015, the Board of Directors granted 2,500 BSPCE<sub>2014</sub> each to 25 employees without vesting conditions.

The main assumptions used to determine the fair value of the BSPCE<sub>2014</sub> awarded to employees are:

- The price of the underlying asset: €37.52 representing the market price on the date of the Board meeting;
- Risk-free rate: between 0.21% and 0.40% depending on the tranches (according to the zero coupon government bond rates curve);
- Anticipated dividends: zero;
- Volatility: Volatility: between 19.59% and 20.75% based on historical volatilities observed on the NextBiotech index;
- Anticipated maturity: between 4.3 and 5.3 years based on the tranches allocated.

The residual fair value of the plan was valued at €517k. In the absence of vesting conditions, the expense was fully recognized as personnel costs at December 31, 2015, and was broken down, based on the award to the beneficiaries, into R&D personnel costs, for €425k, and administrative personnel costs, for €92k.

### 3,000 BSA awarded on June 23, 2015

Following the recruitment of the Chief Medical Officer at ERYTECH Pharma Inc., the Board of Directors granted her 3,000 BSA<sub>2014</sub>. One thousand warrants vested immediately and the remaining 2,000 vest, in two equal amounts, over the following two years.

The main assumptions used to determine the fair value of the BSA<sub>2014</sub> awarded to the Chief Medical Officer are:

- The price of the underlying asset: €32.75 representing the market price on the date of the Board meeting;
- Risk-free rate: between 0.21% and 0.40% depending on the tranches (according to the zero coupon government bond rates curve);
- Anticipated dividends: zero;
- Volatility: between 19.59% and 20.75% based on historical volatilities observed on the NextBiotech index;
- Anticipated maturity: between 4.3 and 5.3 years according to the tranches allocated.

The fair value of the BSA<sub>2014</sub> plan was estimated at €622k. An expense will be recognized gradually over a 2-year period in compliance to IFRS2. An expense of €385k was recognized under personnel expenses (R&D personnel expenses) at December 31, 2015.

### 2,000 BSPCE awarded on September 1, 2015

After the hiring of a new Chief Financial Officer to replace Pierre-Olivier Goineau, the remaining 2,000 BSPCE<sub>2014</sub> were granted to him under the same vesting conditions as his predecessor.

The primary assumptions used to determine the fair value of the BSA<sub>2014</sub> allocated to the Chief Financial Officer are:

- Underlying price: €35.44;
- Risk-free rate: between 0.24% and 0.33% depending on the tranches (according to the zero coupon government bond rates curve);
- Anticipated dividends: zero;
- Volatility: between 20.37% and 21.55% based on historical volatilities observed on the NextBiotech index;
- Expected Maturity: 4.55 years for the first tranche and 5.05 years for the second tranche.

The fair value of the BSPCE<sub>2014</sub> plan was estimated at €468k. An expense will be gradually recorded over the residual vesting period in accordance with IFRS 2. An expense of €156k was recorded to this end under personnel expenses (overheads and general expenses only) at December 31, 2015.

At the end of 2015, the share subscription warrants for the 2014 plan were broken down as follows:

Types of securities	BSPCE <sub>2014</sub>	BSA <sub>2014</sub>
Number of warrants that the Company is authorized to issue for all types of warrants	22,500	
Number of warrants granted	13,500	3,000
Number of warrants exercised	140	0
Date of the Board of Directors meeting	January 22, 2014	
Exercise price per new share subscribed	€12.250	
Final date for exercising warrants	January 22, 2024	
Parity	1 warrant for 10 shares	1 warrant for 10 shares
General conditions of exercise	The warrants may be exercised as of their vesting date.	
Maximum number of new shares that can be issued	223,600	

## 6.5 Amortization and depreciation expense

(in K€)	31.12.2015	31.12.2014
R&D	26	32
Clinical studies	224	190
Intellectual property	-	-
General and administrative	120	28
<b>Total accumulated amortization and depreciation</b>	<b>369</b>	<b>250</b>

## 6.6 Financial income (loss)

(in K€)	31.12.2015	31.12.2014
Interests on leases	(5)	(7)
Other finance expenses	(59)	(67)
<b>Total finance expense</b>	<b>(64)</b>	<b>(73)</b>
Income from disposal of short term investments	524	141
Other finance income	107	1
<b>Total finance income</b>	<b>631</b>	<b>142</b>
<b>Total finance income</b>	<b>567</b>	<b>68</b>

Financial income primarily corresponds to the interest accrued on short-term deposits. Other financial expenses correspond to exchange losses recognized on current transactions.

## 6.7 Income tax

in K€	31.12.2015	31.12.2014
Deferred tax (assets)	-	-
Deferred tax (liabilities)	-	-
<b>Total net deferred tax</b>	<b>-</b>	<b>-</b>

## Tax proof

in K€	31.12.2015	31.12.2014
Loss before tax	(15 016)	(8 880)
Theoretical tax expense or income	5 170	3 057
Current year loss not capitalized	(5 001)	(3 145)
CICE (employment and competitiveness tax credit)	18	15
Research tax credit	764	525
Share-based compensation expense	(935)	(426)
Change in tax rate	(7)	
Other differences	(6)	(6)
<b>Effective tax (loss)/income</b>	<b>3</b>	<b>20</b>

The losses that can be carried forward were capitalized only in the amount of the deferred tax liabilities.

The amount of tax losses carried forward at December 31, 2015, totaled €59 million.

## 7 NOTES RELATIVES TO THE CONSOLIDATED STATEMENT OF FINANCIAL POSITION

### 7.1 Intangible assets

in K	31.12.2014	Increase / Acquisitions	Decrease / Disposal	31.12.2015
<b>Other intangible assets</b>				
Gross amount	135	49	-	184
Accumulated depreciation	(104)	(18)	-	(122)
<b>Net value</b>	<b>31</b>	<b>30</b>		<b>61</b>

### 7.2 Property, plant and equipment

in K	31.12.2014	Increase / Acquisitions	Decrease / Disposal	31.12.2015
<b><u>Property, plant and equipment held under finance leases</u></b>				
<b>Laboratory equipment</b>				
Gross amount	974			974
Accumulated depreciation	(753)			(753)
<b>Net value</b>	<b>221</b>			<b>221</b>
<b>Assets under construction</b>				
	-			-
<b><u>Property, plant and equipment</u></b>				
<b>Plant, equipment and tooling</b>				
Gross amount	617	110		727
Accumulated depreciation	(346)	(157)		(504)
<b>Net value</b>	<b>271</b>			<b>223</b>
<b>General equipment, fixtures and fittings</b>				
Gross amount	959	120		1 079
Accumulated depreciation	(636)	(98)		(733)
<b>Net value</b>	<b>323</b>			<b>345</b>
<b>Office equipment and computers</b>				
Gross amount	76	59		134
Accumulated depreciation	(36)	(15)		(51)
<b>Net value</b>	<b>40</b>			<b>83</b>
<b>Assets under construction</b>				
	112	29	(98)	44
<b>TOTAL</b>				
<b>Gross amount</b>	<b>2 738</b>	318	(98)	2 958
<b>Accumulated depreciation</b>	<b>(1 771)</b>	(270)	-	(2 041)
<b>Net value</b>	<b>967</b>	<b>48</b>	<b>(98)</b>	<b>918</b>

### 7.3 Non-current financial assets

in K€	31.12.2015	31.12.2014
Deposits	97	82
<b>Total other non-current financial assets</b>	<b>97</b>	<b>82</b>

### 7.4 Inventories

in K€	31.12.2015	31.12.2014
Deposits	97	82
<b>Total other non-current financial assets</b>	<b>97</b>	<b>82</b>

### 7.5 Trade accounts receivable

(in K€)	31.12.2015	31.12.2014
Trade receivables	424	105
<b>Trade and other receivables</b>	<b>424</b>	<b>105</b>

Trade receivables primarily represent the receivable related to the re-invoicing to Orphan Europe of the 2012-10 AML clinical trial. The payment was made in January 2016

### 7.6 Other current assets

in K€	31.12.2015	31.12.2014
Research tax credit	3 743	1 524
Tax receivables (e.g VAT) and other receivables	1 190	494
Cash to be received from bank related to exercise of warrants	553	-
Prepayments	220	217
<b>Other current assets</b>	<b>5 705</b>	<b>2 235</b>

The Company is undergoing a tax audit since November 2015. Consequently, the tax receivables were not paid at December 31, 2015, i.e. the 2014 research tax credit (CIR) for €1,524k and the other tax receivables primarily related to the VAT to be recovered.

The cash to be received from bank related to exercise of warrants for €553k at December 31, 2015, represent the exercise of 7,508 warrants by Yann Godfrin. The amount was paid by Société Générale Securities Services in January 2016.



## 7.7 Cash and cash equivalents

in K€	31.12.2015	31.12.2014
Cash and cash equivalents	45 634	36 988
Bank overdrafts	-	-
<b>Total cash and cash equivalents</b>	<b>45 634</b>	<b>36 988</b>

The cash position is composed of the following items:

- At 12/31/2015:

- €20,181k in current accounts,
- €25,453k in short-term deposits with 3 banking institutions, with maturities of 1 month to 3 years, but available without penalty subject to a 32 days' notice.

- At 12/31/2014:

- €3,001k in money market funds,
- €1,988k in current accounts,
- €32,000k in short-term deposits with 3 banking institutions, with maturities of 1 month to 3 years, but available without penalty subject to 32 days' notice.

1 month to 3 years, but available without penalty subject to 32 days' notice.

### Liquidity agreement

Under the liquidity agreement related to the shares of ERYTECH Pharma, entrusted to Bryan, Garnier & Co, the following appeared in the liquidity account on December 23, 2015, the contract termination date:

- 2,500 shares in ERYTECH Pharma;
- €351k in cash.

Note that in the interim consolidated financial statement as at June 30, 2015, the amounts shown in the liquidity account were identical.

It should be noted that €600,000 in cash had initially been paid into the liquidity account before this was reduced to €200,000 in cash on March 25, 2014.

Following the termination of the liquidity agreement effective December 23, 2015, Bryan, Garnier & Co returned the sum of €351k to ERYTECH Pharma. ERYTECH Pharma also retained in its securities portfolio the 2,500 treasury shares. These shares will be used for a future employee share allocation.

ERYTECH Pharma does not intend to establish a new liquidity contract in the immediate future.

## 7.8 Shareholders' equity

At December 31, 2014, the capital of the parent company was comprised of 6,882,761 shares, fully paid up, with a nominal value of 0.1 euro.

Following new funds raised on the Euronext stock exchange in December 2015 and the exercise of subscription warrants, the share capital was increased to 7,924,611 shares with a par value of €0.1.

Nature of transactions	Number of Shares
<b>Balance as of January 1, 2015</b>	<b>6,882,761</b>
Exercise of share warrants	101,850
Issuance of new shares on Euronext	940
<b>Total as of December 31, 2015</b>	<b>7,924,611</b>

The costs of issuance for the new shares on the stock exchange, which totaled €2,592k were recorded against the share premium.

This involves mainly banking commissions, legal fees, and auditors' fees.

At December 31, 2015, the Company held 2,500 treasury shares at an average price of €28.40, or €71k (4,500 shares at an average price of €28.00, or €126k at December 31, 2014).

### Basic earnings per share and diluted earnings per share

in K€	31.12.2015	31.12.2014
Net loss	(15 013)	(8 860)
Weighted number of shares for the period	6 957 654	5 874 794
<b>Basic loss per share (€/share)</b>	<b>- 2,16</b>	<b>- 1,51</b>
<b>Diluted loss per share (€/share)</b>	<b>- 2,16</b>	<b>- 1,51</b>

At December 31, 2015, the 455,330 potential shares that could be issued within the context of exercising warrants issued were not taken into consideration in the calculation of the diluted earnings, as their effect would be anti-dilutive.

## 7.9 Provisions

The provisions for risks and expenses can be broken down as follows

in K€	31.12.2015	31.12.2014
Retirement indemnity provision	100	89
Provision for disputes	81	-
<b>Total</b>	<b>181</b>	<b>89</b>

The regime for retirement indemnities applicable at ERYTECH Pharma is defined by the collective agreement for the pharmaceutical industry.

The Group recognizes actuarial differences under other items of 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.

The company settled the dispute over the GR-SIL subsidy with BPI France for €81k and the residual repayment advances for €23k. The reimbursement in the amount of €104k was made in January 2016.

The calculation assumptions for measuring the provision concerning employees are as follows:

	31.12.2015	31.12.2014
Discount rate	2,03%	1,49%
Wage increase	2%	2%
Social welfare contribution rate	Non cadre 44%	Non cadre 44%
Age of retirement	Cadre 54%	Cadre 54%
Mortality table	65 - 67 ans	65 - 67 ans
	INSEE 2014	INSEE 2014

The breakdown of provisions is as follows:

in K€	Opening	Other *	Provisions	Unused Reversals	Used Reversals	Closing
<b>Period from 01.01 to 31.12.2015</b>						
Retirement indemnity provision	89	8	20			100
Provision for disputes	-		81			81
<b>Net closing balance</b>	<b>89</b>	<b>8</b>	<b>101</b>	<b>-</b>	<b>-</b>	<b>181</b>
<b>Période du 01.01 au 31.12.2014</b>						
Retirement indemnity provision	117	(59)	30			89
Provision for disputes	-					-
<b>Net closing balance</b>	<b>117</b>	<b>(59)</b>	<b>30</b>	<b>-</b>	<b>-</b>	<b>89</b>

\* The "other movement" correspond to actuarial differences

\* The "Other movements" correspond to actuarial differences recognized.

## 7.10 Debt

### Debt by type

in K€	31.12.2015	31.12.2014
Liabilities related to leases	144	220
Bank overdrafts	-	-
Conditional advances	563	549
Convertible bonds	-	-
Loans	-	-
<b>Total financial liabilities</b>	<b>708</b>	<b>770</b>

## Debt by maturity

in K€	2015		
	Less than one year	More than one year	TOTAL
Liabilities related to leases	56	88	144
Bank overdrafts			-
Conditional advances	501	63	563
Convertible bonds			-
Loans			-
<b>Total financial liabilities</b>	<b>557</b>	<b>151</b>	<b>708</b>

in K€	2014		
	Less than one year	More than one year	TOTAL
Liabilities related to leases	76	144	220
Bank overdrafts			-
Conditional advances	258	292	549
Convertible bonds			-
Loans			-
<b>Total financial liabilities</b>	<b>334</b>	<b>436</b>	<b>770</b>

The conditional advances from public authorities relates to contracts with BPI FRANCE. The Group has three contracts related to conditional advances with BPI FRANCE Innovation. These advances are not interest-bearing and are 100% repayable (nominal value) in the event of technical and/or commercial success.

Within the IFRS framework, the fact that a conditional advance does not require an annual interest payment is certain 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 OAT) increased by an estimated credit spread is considered to be a grant received from the State. These grants are recognized 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 at less than one year is recorded under financial debts - current portion.

Since its creation, the Group has received 3 advances from BPI FRANCE, repayable under certain conditions, the main terms of which are presented below:

- **BPI FRANCE / PANCREAS**

The first conditional advance, granted by BPI FRANCE, for a total amount of €735,000, concerns the program for the “development of a new treatment against pancreatic cancer through the administration of allogenic red blood cells incorporating L-asparaginase.”

This conditional advance was received in 3 phases:

- €294,000 upon signature of the agreement (paid in 2008)
- €294,000 upon calls for funds (paid in 2010)

- balance upon completion of work after acceptance of the finalization program by BPI France (paid in 2011).

The repayment of this conditional advance will be made according to a fixed payment schedule that will end no later than 6/30/2016.

The Group has undertaken to repay the entire conditional advance according to the following payment schedule:

- €100,000 by June 30, 2013
- €150,000 by June 30, 2014
- €225,000 by June 30, 2015
- €260,000 by June 30, 2016

As of December 31, 2015, the payment due on June 30, 2015 had not been made due to an ongoing dispute with BPI over another conditional advance which led to BPI blocking the progress of this project.

- **BPI FRANCE FEDER**

The second conditional advance, granted by BPI FRANCE FEDER, which provided for a total amount of €135,000 relates to a program for the “preclinical validation of the encapsulation of interfering RNA for therapeutic use in red blood cells, particularly to limit inflammation of the cirrhotic liver and/or prevent the development of hepatocellular carcinomas.”

This conditional advance was received in 4 phases:

- €40,500 upon signature of the agreement (paid in 2009)
- €40,500 upon calls for funds (paid in 2010)
- €27,000 upon calls for funds
- balance upon completion of work with acceptance of the finalization of the program by BPI France.

The Group has received €81,000 from BPI FRANCE/FEDER under this program. As the work corresponding to the FEDER assistance is currently terminated, the Group will not receive the last two payments of €27k.

The repayment of this conditional advance will be made according to a fixed payment schedule that will end no later than June 30, 2016.

The Group has undertaken to repay the entire conditional advance according to the following payment schedule:

- €7,500 by September 30, 2013
- €7,500 by December 31, 2013
- €7,500 by March 31, 2014
- €7,500 by June 30, 2014
- €9,250 by September 30, 2014
- €9,250 by December 31, 2014
- €9,250 by March 31, 2015
- €9,250 by June 30, 2015
- €14,000 by September 30, 2015

The company repaid the entire amount of the conditional advance of €23k in January 2016 (representing to balance). It also repaid the corresponding subsidy of €81k to settle the dispute with BPI France.

- **BPI FRANCE / TEDAC**

Conditional advance provided by BPI FRANCE in the context of the TEDAC project 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)
- the remainder upon calls for funds when key milestones are reached.

The Group undertakes to repay BPI France initially:

- a) a sum of €5,281,000 upon achieving a cumulative amount of 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 is achieved,
  - €750,000 at the latest on June 30 of the second year,
  - €1,500,000 at the latest on June 30 of the third 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, where the cumulative sales reach €60 million, the Group undertakes to pay BPI France a sum of 2.5% of the sales generated by the products developed within the project, limited to a total amount of €15 million over 15 years.

#### **7.11 Other liabilities**

<b>in K€</b>	<b>31.12.2015</b>	<b>31.12.2014</b>
Taxation and social security	1 241	971
Deferred revenue	-	368
Other payables	71	501
<b>Total other current liabilities</b>	<b>1 311</b>	<b>1 840</b>

The decrease in deferred income corresponds to the recognition of the subsidy received for the TEDAC project. As the project advanced, the subsidy was recognized in full in 2015.

#### **7.12 Related parties**

Gil Beyen and Yann Godfrin are the Chief Executive Officers of the Company; Jérôme Bailly is the chief pharmacist of the Company and Deputy Chief Executive Officer. Eric Soyer replaced Pierre-Olivier Goineau as treasurer and secretary of the U.S. subsidiary. The other related parties are the members of the Board of Directors.

The remuneration of managers and other members of senior management during the financial year was as follows.

<b>in K€</b>	<b>12/31/2015</b>	<b>12/31/2014</b>
--------------	-------------------	-------------------

<b>Gross total compensation</b>	<b>1,144</b>	<b>973</b>
<b>Share-based payments</b>	<b>1,994</b>	<b>1,084</b>
<b>Total</b>	<b>3,138</b>	<b>2,057</b>

The Group has no further related parties.



## 7.13 Financial instruments recorded in the balance sheet and effect on results

31/12/2015 in K€		Carrying amount on the statement of financial position	Fair value through P&L	Loans and receivables	Debt at amortized cost	Fair value
Non-current financial assets	➤ (1)	97		97		97
Trade receivables		424		424		424
Other current assets	➤ (1)	5 705		5 705		5 705
Cash and cash equivalents	➤ (2)	45 634	45 634			45 634
<b>Total financial assets</b>		<b>51 860</b>	<b>45 634</b>	<b>6 226</b>	<b>-</b>	<b>51 860</b>
Financial liabilities - Non-current portion	➤ (1)	151			151	151
Financial liabilities - Current portion	➤ (1)	557			557	557
Trade payables & related accounts	➤ (1)	3 672			3 672	3 672
<b>Total financial liabilities</b>		<b>4 380</b>	<b>-</b>	<b>-</b>	<b>4 380</b>	<b>4 380</b>
31/12/2014 in K€		Carrying amount on the statement of financial position	Fair value through P&L	Loans and receivables	Debt at amortized cost	Fair value
Non-current financial assets	➤ (1)	82		82		82
Trade receivables		105		105		105
Other current assets	➤ (1)	2 235		2 235		2 235
Cash and cash equivalents	➤ (2)	36 988	36 988			36 988
<b>Total financial assets</b>		<b>39 410</b>	<b>36 988</b>	<b>2 421</b>	<b>-</b>	<b>39 410</b>
Financial liabilities - Non-current portion	➤ (1)	436			436	436
Financial liabilities - Current portion	➤ (1)	334			334	334
Trade payables & related accounts	➤ (1)	2 085			2 085	2 085
<b>Total financial liabilities</b>		<b>2 854</b>	<b>-</b>	<b>-</b>	<b>2 854</b>	<b>2 854</b>

(1) The book value of these assets and liabilities is a reasonable approximation of their fair value.

(2) Fair value at level 2

## 8 MANAGEMENT OF FINANCIAL RISKS

The main risks to which the company is exposed are liquidity risk, foreign exchange rate risk, interest rate risk and credit risk.

### Foreign exchange rate risk

The Group uses the euro as its functional currency within the context of its information and financial communications activity. However, a significant portion, about of 15% of its operating expenses, is denominated in US dollars (agency office in Boston, 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 cooperation around tests and clinical projects in the United States).

To date, the Group has not opted to use active hedging techniques, and does not use derivative instruments to this end. Unfavorable exchange rate fluctuations between the euro and the dollar that are difficult to predict could affect the financial position of the Company.

This dependency will increase, as the Group will perform clinical trials in the USA and, in the longer term, sell on this market.

Expenses in US Dollars totaled \$3,149,196 during the 2015 financial year.

The EUR/USD rate fell considerably at the period end, reaching \$1.0887 per €1 at December 31, 2015.

The exchange rate differences are not significant for the periods presented.

### Liquidity risk

The Group has been structurally loss generating since its creation. The net cash flows associated with the Group's operating activities were respectively -€15 million at December 31, 2015 and -€7.2 million at December 31, 2014.

Historically, the Group has financed its growth by strengthening its shareholders' equity in the form of capital increases and the issue of convertible bonds. The capital increase associated with its introduction on the stock market in May 2013, as well as the transaction renewed in 2014 and 2015, enables the Group to ensure its business continuity.

The remaining contractual maturities of financial liabilities are broken down as follows (including interest payments):

in K€	2015			
	Carrying amount	Contractual cash flows		
		Total	Less than one year	One to Five years
Loans				
Conditional advances	563	(570)	(507)	(63)
Liabilities related to leases	144	(149)	(59)	(91)
Convertible bonds				
Bank overdrafts				
Trade payable and related accounts	3 672	(3 672)	(3 672)	
<b>Total</b>	<b>4 380</b>	<b>(4 392)</b>	<b>(4 238)</b>	<b>(153)</b>

in K€	2014			
	Carrying amount	Contractual cash flows		
		Total	Less than one year	One to Five years
Loans				
Conditional advances	549	(580)	(258)	(323)
Liabilities related to leases	220	(230)	(81)	(149)
Convertible bonds		-		
Bank overdrafts		-		
Trade payable and related accounts	2 085	(2 085)	(2 085)	
<b>Total</b>	<b>2 854</b>	<b>(2 895)</b>	<b>(2 423)</b>	<b>(472)</b>

### Interest rate risk

The Group has little exposure to interest rate risk. Such exposure would involve monetary fund investments in foreign currencies and short-term deposit accounts. The change in interest rates has a direct impact on the rate of return on investment and cash flows generated.

The Group has no borrowings or credit. The repayment of conditional advances from BPI France is not subject to interest rate risk.

### Credit risk

Credit risk arising from the Company's cash and cash equivalents is not significant in view of the quality of the financial institutions contracting with the Group.

### Fair value risk

The fair value of instruments traded on an active market that are classified as available for sale is based on market rates at December 31, 2015. The market prices used by the Group for valuing financial instruments are close to the market price on the date of valuation. The nominal value, minus depreciation, of receivables and payables is considered the best approximation of the fair value of those items.

### Inflation risk

We do not believe that inflation could have a material effect on our business, financial conditions, or results of operations. If our costs were to be subject to inflationary changes, it is possible that we would not be able to pass on a significant increase in costs.

## 9 OFF-BALANCE SHEET COMMITMENTS

### Clinical trials

The costs associated with clinical trials are recognized as expenses as and when they are incurred.

The remainder of the costs to be incurred until the end of the clinical trial are monitored as off-balance sheet commitment. The tables below summarize only ongoing clinical trials for which a contractual commitment was made by the Company.

**As of December 31, 2015**  
(amounts in €'000)

Clinical trial name	Budget balance	Comment
---------------------	----------------	---------

2012/09	768	Recruitment begun
2012/10	-	No off-balance sheet commitment
2013/03	3,693	Recruitment begun
<b>Total</b>	<b>4,461</b>	

**As of December 31, 2014**  
**(amounts in €'000)**

<b>Clinical trial name</b>	<b>Budget balance</b>	<b>Comment</b>
2012/09	1,014	Recruitment not begun
2012/10	-	No off-balance sheet commitment
2013/03	4,526	Recruitment not begun
<b>Total</b>	<b>5,540</b>	

The off-balance sheet commitments relating to operating leases total €885k and essentially correspond to the lease of buildings. The maturities on these expenses are as follows:

Less than 1 year: €322k  
Between 1 year and 5 years: €563k  
More than 5 years: €0

## **10 AUDITORS' FEES**

For the 2015 financial year, the auditor fees totaled:

- within the scope of its legal term of office: €119 k, excluding out-of-pocket expenses,
- within the scope of the capital increase by the parent company: €40 k
- in the context of the Nasdaq IPO project: €277 k

## 20.2 Financial statements prepared (French standards) for the year ended December 31, 2015

### Assets

Period from 01/01/15 to 12/31/15

ERYTECH PHARMA

Published on 02/02/16

HEADINGS	GROSS	Amortization	Net (N) 12/31/2015	Net (N-1) 12/31/2014
UNCALLED SHARE CAPITAL				
<b>INTANGIBLE ASSETS</b>				
Start-up costs				
Development costs				
Licences, patents and similar rights	183,554	122,399	61,155	30,951
Business goodwill				
Other intangible assets				
Advances and payments on intangible assets				
<b>TOTAL intangible assets:</b>	<b>183,554</b>	<b>122,399</b>	<b>61,155</b>	<b>30,951</b>
<b>TANGIBLE FIXED ASSETS</b>				
Land				
Buildings				
Plant, equipment and industrial tooling	727,039	425,739	301,300	271,059
Other tangible assets	1,213,179	784,450	428,728	362,806
Assets under construction	14,962		14,962	112,480
Advances and deposits	29,326		29,326	
<b>TOTAL tangible assets:</b>	<b>1,984,506</b>	<b>1,210,190</b>	<b>774,316</b>	<b>746,345</b>
<b>INVESTMENTS</b>				
Investment in companies accounted for using the equity method				
Other investments	1		1	1
Receivables relating to participating interests				
Other investments				
Loans				
Other long-term financial investments	167,781		167,781	458,923
<b>TOTAL investments:</b>	<b>167,782</b>		<b>167,782</b>	<b>458,924</b>
<b>NON-CURRENT ASSETS</b>	<b>2,335,842</b>	<b>1,332,589</b>	<b>1,003,253</b>	<b>1,236,220</b>
<b>INVENTORY AND WORKS IN PROGRESS</b>				
Raw materials and supplies	165,889		165,889	198,356
Inventory of in-process goods				
Inventory of in-process services				
Inventory of intermediate and finished goods				
Inventory of goods for resale				
<b>TOTAL inventory:</b>	<b>165,889</b>		<b>165,889</b>	<b>198,356</b>
<b>RECEIVABLES</b>				
Advances and payments on account				
Trade accounts receivable and associated accounts	457,936		457,936	104,870
Other receivables	1,630,929		1,630,929	2,128,962
Called-up share capital, not paid				
<b>TOTAL receivables:</b>	<b>2,088,865</b>		<b>2,088,865</b>	<b>2,233,832</b>
<b>MISCELLANEOUS CASH AT BANK AND IN HAND</b>				
Marketable securities				3,000,583
Cash at bank and in hand	45,493,612		45,493,612	33,654,518
Prepayments	202,581		202,581	216,779
<b>TOTAL miscellaneous cash at bank and in hand:</b>	<b>45,696,193</b>		<b>45,696,193</b>	<b>36,871,880</b>
<b>CURRENT ASSETS</b>	<b>47,950,947</b>		<b>47,950,947</b>	<b>39,304,069</b>
Debt issuance costs to be spread out				
Bond redemption premiums				
Translation difference - debit balance				
<b>GRAND TOTAL</b>	<b>50,286,790</b>	<b>1,332,589</b>	<b>48,954,200</b>	<b>40,540,288</b>

## Liabilities

ERYTECH PHARMA

Period from 01/01/15 to 12/31/15  
Published on 02/02/16

HEADINGS	Net (N) 12/31/2015	Net (N-1) 12/31/2014
<b>NET FINANCIAL POSITION</b>		
Individual or share capital including paid 792,461	792,461	688,276
Issuance, merger, contribution premiums, etc.	94,749,614	71,375,715
Revaluation difference including equity method difference		
Legal reserve		
Reserves required by articles of association or contract		
Regulated reserves		
Other reserves		
Reserves brought forward	(36,058,170)	(28,774,932)
<b>FY Profit (loss)</b>	<b>(11,801,131)</b>	<b>(7,283,237)</b>
<b>TOTAL net financial position:</b>	<b>47,682,775</b>	<b>36,005,821</b>
INVESTMENT SUBSIDIES		
REGULATED PROVISIONS		
<b>SHAREHOLDERS' EQUITY</b>	<b>47,682,775</b>	<b>36,005,821</b>
Proceeds from the issuance of equity securities		
Conditional advances	570,857	580,107
<b>OTHER SHAREHOLDERS' EQUITY</b>	<b>570,857</b>	<b>580,107</b>
Provisions for liabilities	81,000	
Provisions for charges		
<b>PROVISIONS FOR LIABILITIES AND CHARGES</b>	<b>81,000</b>	
<b>DEBT</b>		
Convertible bonds		
Other bonds		
Bank loans and overdrafts	16,181	
Miscellaneous other loans and advances		
<b>TOTAL debt:</b>	<b>16,181</b>	
ADVANCES AND DEPOSITS RECEIVED ON CONTRACTS		
<b>OTHER LIABILITIES</b>		
Trade payables and related accounts		2,096,901
Taxation and social security liabilities	536,355	988,430
Liabilities on fixed assets and related		
Other liabilities	67,033	500,593
<b>TOTAL miscellaneous debt:</b>	<b>603,388</b>	<b>3,585,925</b>
DEFERRED INCOME		368,436
<b>DEBT</b>	<b>619,569</b>	<b>3,954,360</b>

## Income Statement (Part One)

ERYTECH PHARMA

Period from 01/01/15 to 12/31/15  
Published on 02/02/16

HEADINGS	France	Export	Net (N) 12/31/2015	Net (N-1) 12/31/2014
Sale of goods purchased for resale				
Production of goods sold				
Services sold	682,403	34,236	716,639	791,853
<b>Net sales</b>	<b>682,403</b>	<b>34,236</b>	<b>716,639</b>	<b>791,853</b>

Production taken to inventory				
Production capitalized				
Operating subsidies			368,436	271,231
Reversals of provisions and depreciation, transfer of expenses			34,687	39,754
Other income			6	10,294
<b>OPERATING INCOME</b>			<b>1,119,767</b>	<b>1,113,132</b>

<b>EXTERNAL EXPENSES</b>				
Purchases of goods for resale [including customs duties]				
Change in inventory of goods for resale				
Purchases of raw materials and other consumables			1,017,411	613,929
Change in inventory [raw materials and consumables]			32,467	(60,118)
Other purchases and external expenses			9,910,097	5,866,460
<b>TOTAL external expenses:</b>			<b>10,959,991</b>	<b>6,420,271</b>
<b>TAXES (OTHER THAN CORPORATION TAX)</b>			110,986	66,537
<b>EMPLOYEE EXPENSES</b>				
Wages and salaries			2,707,422	2,359,456
Social security charges			1,464,009	1,211,628
<b>TOTAL employee expenses:</b>			<b>4,171,431</b>	<b>3,571,084</b>
<b>PROVISIONS FOR OPERATIONS</b>				
Depreciation expenses of non-current assets			210,120	151,645
Impairment expense of non-current assets				
Expenses related to reserves on current assets				
Expenses related to provisions for liabilities and charges			81,000	
<b>TOTAL operating expenses:</b>			<b>291,120</b>	<b>151,645</b>
<b>OTHER OPERATING EXPENSES</b>			201,702	88,250
<b>OPERATING EXPENSES</b>			<b>15,735,230</b>	<b>10,297,787</b>
<b>OPERATING PROFIT (LOSS)</b>			<b>(14,615,463)</b>	<b>(9,184,655)</b>



## Income Statement (Part Two)

ERYTECH PHARMA

Period from 01/01/15 to 12/31/15  
Published on 02/02/16

HEADINGS	Net (N) 12/31/2015	Net (N-1) 12/31/2014
<b>OPERATING PROFIT (LOSS)</b>	<b>(14,615,463)</b>	<b>(9,184,655)</b>
Allocated profit or transferred loss		
Loss borne or profit transferred		
<b>FINANCIAL INCOME</b>		
Financial income from investments		
Income from other securities and receivables from non-current assets		
Other interest and similar income	531,585	317,545
Reversals of provisions and transfers of expenses		100,607
Foreign exchange gains	94,184	605
Net proceeds from the disposal of marketable securities	988	513
	<b>626,758</b>	<b>419,270</b>
<b>FINANCIAL EXPENSES</b>		
Financial expenses for amortization and provisions		
Interest and similar expense	27	499
Foreign exchange losses	32,625	24,867
Net expense from the disposal of marketable securities		
	<b>32,652</b>	<b>25,367</b>
<b>NET FINANCIAL INCOME (LOSS)</b>	<b>594,106</b>	<b>393,903</b>
<b>EARNINGS BEFORE INCOME TAX</b>	<b>(14,021,357)</b>	<b>(8,790,751)</b>
<b>EXCEPTIONAL INCOME</b>		
Non-recurring income on revenue transactions	5,262	201
Non-recurring income on capital transactions		
Reversals of provisions and transfers of expenses		
	<b>5,262</b>	<b>201</b>
<b>EXCEPTIONAL EXPENSES</b>		
Non-recurring expenses on revenue transactions	211,	15,605
Non-recurring expenses on capital transactions		770
Non-recurring expenses for amortization and provisions	352	
	<b>563</b>	<b>16,375</b>
<b>EXCEPTIONAL PROFIT(LOSS)</b>	<b>4,699</b>	<b>(16,174)</b>
Employee profit-sharing		
Income taxes	(2,219,406)	(1,523,688)
<b>TOTAL INCOME</b>	<b>1,751,786</b>	<b>1,532,603</b>
<b>TOTAL EXPENSES</b>	<b>13,549,039</b>	<b>8,815,841</b>
<b>PROFIT OR LOSS</b>	<b>(11,797,253)</b>	<b>(7,283,237)</b>

Notes to the balance sheet prior to allocation of the loss, characterized by:

- total assets in €:	€53,439,644.20
- sales in €:	€716,638.66
- net loss in €:	(€11,797,253.71)

The financial year was 12 months, covering the period from 01/01/2015 to 12/31/2015.

The notes and tables presented below form an integral part of the annual financial statements.

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## **1 EVENTS CHARACTERIZING THE FINANCIAL YEAR**

Pierre-Olivier Goineau, co-founder of the Company and Chief Operating Officer, submitted his resignation from his positions within the Company at the Board of Directors' meeting of January 11, 2015.

Dr. Iman El-Hariry joined the company as Chief Medical Officer within the subsidiary Erytech Pharma Inc., based in Boston, and will be responsible for medical, clinical and regulatory affairs.

ERYTECH Pharma S.A. also strengthened its executive team by appointing Eric Soyer as Chief Financial Officer and Chief Operating Officer. Eric Soyer also replaced Pierre-Olivier Goineau as treasurer and secretary general of the U.S. subsidiary ERYTECH Pharma Inc.

In financial year 2015, additional subscription warrants were awarded as follows:

- The Board of Directors' meeting on April 29, 2015, granted 2,150 BSA2012 to the independent Board members;
- In accordance with the 2014 plan, the Board of Directors' meeting on June 23, 2015, assigned the first tranche of the plan and granted 2,500 BSPCE2014 to employees with the status of manager within the Company, and 3,000 BSA2014 to the Chief Medical Officer based in the United States within the subsidiary ERYTECH Pharma Inc.;
- The Board of Directors' meeting on 8/31/2015, granted 3,585 BSA2012 to the independent Board members;
- Eric Soyer was granted 2,000 BSPCE 2014 when he was hired in September 2015.

ERYTECH Pharma S.A. is subject to an audit by the tax authorities since October 21, 2015. This audit was still in progress as of December 31, 2015.

In December 2015, the parent company ERYTECH Pharma S.A. raised €25.4 million (excluding costs of issuance) on Euronext, with a total of 940,000 new shares issued in a capital increase in the form of a private placement with first-tier institutional investors in the United States and Europe, representing approximately 14% of the number of shares outstanding (post-issue).

The issue price was set at €27 per share, in compliance with resolutions no. 15 and 17 of the Combined General Shareholders' Meeting of June 23, 2015. This price reflects a 4.8% reduction as compared to the weighted average of the parent company's share price in the last five trading sessions prior to establishing the price.

- The company has filed an application for a centralized Marketing Authorization (MA) with the European Medicines Agency (EMA) for GRASPA® for the treatment of patients suffering from Acute Lymphoblastic Leukemia (ALL).
- ERYTECH Pharma S.A. was able to launch the shift to the higher dosage and change the protocol to speed up recruitment in the Phase I trial with ERY-ASP for adult ALL in the United States.
- Thirteen “double-allergic” patients were treated in the context of an Expanded Access Program (EAP) in France.
- The Company confirmed the finalization of new development projects for ERY-ASP/GRASPA® in ALL with the participation of opinion leaders.
- The recruitment policy is in line with patient expectations for the European Phase IIb trial in Acute Myeloid Leukemia (AML).
- ERYTECH Pharma S.A. received positive comments from DSMB1 on the tolerance of the ERY-ASP product in the Phase II trial on pancreatic cancer.
- The Company is preparing to launch clinical trials on non-Hodgkin lymphoma.
- ERYTECH Pharma S.A. received notification of issue from the European Patent Office for a key patent covering the use of ERY-ASP in the treatment of pancreatic cancer. This patent for “Medication for the treatment of pancreatic cancer” had been submitted in late 2007 and has been issued in Australia, Israel and Singapore since that date. It should be noted that in May 2015, ERYTECH Pharma received a green light from the ANSM to begin a Phase II clinical trial with ERY-ASP for use in treating pancreatic cancer. The Company has continued to expand its patent portfolio.

## **2 SIGNIFICANT POSTCLOSING EVENTS**

Mr. Yann Godfrin, co-founder of ERYTECH Pharma S.A. and Deputy Chief Executive Officer, submitted his resignation at the meeting of the Company’s Board of Directors on January 10, 2016.

The search for his successor has already begun. During this transition phase, Yann Godfrin will continue to support the Company’s development as a consultant.

## **3 GOING CONCERN**

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 of:

- going concern,
- continuity of accounting methods from one year to the next,
- independence of financial years,

and in accordance with the general rules for the preparation and presentation of annual financial statements.

## **4 ACCOUNTING PRINCIPLES AND METHODS**

### **4.1 General principle and conventions**

The annual financial statements were prepared and presented in accordance with the accounting rules in effect in France, in compliance with the principle of prudence and the independence of financial years, and with the assumption of going concern.

The method adopted for measuring the items recorded in the accounts is the historical cost method.

The accounting conventions were applied in compliance with the provisions of the Code of Commerce, the accounting decree of November 29, 1983, as well as CRC Regulations no. 2000-06, no. 2004-06, and no. 2002-10, and of ANC Regulation no. 2014-03 of June 5, 2014 relative to the general chart of accounts.

## **4.2 Consistency of methods**

No changes in accounting regulations or accounting methods took place during the financial year ended December 31, 2015.

## **4.3 Other accounting principles**

The main accounting principles used are as follows:

### **INTANGIBLE ASSETS**

The intangible assets are measured at their historic cost or at their production cost.

R&D costs are recognized based on the following method in the research phase:

- No intangible assets resulting from research can be recognized;
- Research expenses (or expenses for the research phase of an internal project) must be recognized as expenses as and when they are incurred;
- Intangible assets are recognized if, and only if, the Company can demonstrate:
  - \* technical feasibility,
  - \* the intention and ability to complete the asset or sell it,
  - \* how the intangible asset will generate probable future economic benefits,
  - \* the availability of resources to complete development, use or sell the intangible asset,
  - \* the ability to reliably evaluate the expenses attributable to the intangible asset or during its development.

Development costs must be accounted for as intangible assets when specific conditions relating to technical feasibility, marketability and profitability are met. Considering the strong uncertainty associated with the development projects performed by the Company, these conditions will be met only when the regulatory procedures necessary for commercializing the products have been finalized. As most of the expenditures have been incurred before that stage, the development costs are accounted for in the period in which they are incurred.

The balance of the research and development asset is zero on the balance sheet. Not all of the criteria for recognition under intangible fixed assets have been met, and the corresponding expenses have therefore been recorded as operating expenses. The method adopted will be to capitalize development costs if and when marketing authorization (MA) is obtained.

### **PROPERTY, PLANT AND EQUIPMENT**

The tangible fixed assets are measured at their purchase cost (purchase price and accessory costs, excluding costs for the purchase of assets) or at their production cost.

The depreciation is calculated according to the straight-line or decreasing charge method in function of anticipated useful life:

- Concessions, software, patents 1 to 10 years

- Technical facilities	3 to 10 years
- Industrial equipment and tools	1 to 5 years
- Office equipment and furnishings	3 to 5 years

## **INVESTMENTS, OTHER LONG-TERM INVESTMENTS, AND INVESTMENT SECURITIES**

The gross value is composed of the purchase cost excluding accessory expenses. Where the recoverable value is lower than the gross value, a provision for impairment is recorded for the difference.

## **INVENTORIES**

Inventories are measured according to the FIFO method.

The gross value of merchandise and supplies includes the purchase price and the accessory expenses.

Manufactured products are valued at their production cost, including consumption and direct and indirect production expenses, the depreciation of assets involved in production. The cost of the under-activity is excluded from the value of inventories.

An inventory reserve, equal to the difference between the gross value determined based on the above-indicated methods and the spot price or the realizable value less the proportional sales costs, is recorded when this gross value is greater than the other value given.

## **RECEIVABLES**

Receivables are valued at their nominal value. A reserve is recorded when the realisable value is lower than the book value.

## **RECOGNITION OF SUBSIDY INCOME**

Subsidy income is recognized as soon as it is granted.

According to the matching principle, the corresponding expenses incurred are taken into account and, where applicable, a portion of the subsidy is recorded under “deferred revenues” where the subsidy agreement explicitly stipulates the expenses that must be incurred. Vice-versa, an accrual is recorded where the expenses incurred allow for recognition of a portion of the grant to be received.

The company therefore records a deferred income corresponding to the portion of the subsidies received corresponding to expenses not incurred. As of December 31, 2015, all subsidies had been recognized and no deferred income was recorded.

## **CONDITIONAL ADVANCES**

The advances received from the State generally contain a portion in grants for which repayment is not required, and a portion repayable in the event of technical or commercial success, classified as conditional advances.

Conditional advances are presented in the balance sheet under the item “Other shareholders’ equity” where a doubt exists regarding the technical or commercial success.

A public subsidy is recorded in accrued income in the period the costs for the program are incurred either to compensate for the expenses or losses already incurred, or in the form of immediate financial support to the Company with no related future costs.

## **CLINICAL TRIALS**

The costs associated with clinical trials are recognized as expenses as and when they are incurred.

The remainder of the costs incurred leading up to the end of the clinical trial are monitored off-balance sheet.

## **PROVISIONS**

A provision for risks and liabilities is recorded where an item has a negative economic value for the entity, which translates into an obligation in relation to a third party for which it is probable or certain that it will result in an outflow of resources to the benefit of this third party, without an at least equivalent compensation anticipated by this third party.

## **TRANSACTIONS WITH RELATED PARTIES THAT HAVE NOT BEEN CONCLUDED UNDER NORMAL MARKET CONDITIONS**

Over the financial year, share options were allocated to the directors, certain employees, and members of the Board of Directors in the form of share subscription warrants (“BSA”) or founder subscription warrants (“BSPCE”). This information is detailed in the note “Warrants.”

An intercompany agreement was signed by the company with its U.S. subsidiary, ERYTECH Pharma Inc. It provides for the re-invoicing of expenses paid by ERYTECH Pharma S.A. for expenses incurred by ERYTECH Pharma Inc. and paid by ERYTECH Pharma S.A. A mark-up (margin) of 10% is applied via an amendment to the intercompany agreement (see Note 19.1.2).

## **PENSION AND RETIREMENT COMMITMENTS**

The company has signed no special agreements relating to retirement commitments. These commitments are therefore limited to the contractual retirement indemnity. No provision for liabilities was recognized in relation to this financial year.

The method adopted is the projected unit credit method (or the accrual of rights method).

The technical assumptions used are the following:

Age of retirement: 65-67 years

Average turnover (non-management), high turnover (management)

Evolution of wages: management and non-management at 2%

INSEE 2014 mortality table

Discount rate: IBOXX Corporates AA rate of 2.03% at December 2015

Employer contribution rate adopted: 50% (non-management) and 54% (management and directors).

## TAX CREDIT FOR COMPETITION AND EMPLOYMENT (“CREDIT D'IMPOT POUR LA COMPETITIVITE ET L'EMPLOI” - CICE)

The tax credit for competition and employment (CICE) is a tax benefit for companies with employees and is equivalent to a decrease in their social security contributions.

The CICE must be offset against the corporate tax due for the year in which the remuneration taken into account for calculation of the CICE was paid.

According to the ANC [French accounting standards authority] guidelines, the Company recognizes the CICE as a credit in the sub-account dedicated to account 64 “Personnel expenses.”

## 5 ADDITIONAL INFORMATION ON THE BALANCE SHEET

### INTANGIBLE ASSETS

The amount of research costs recognized as expenses for the financial year and not capitalized total €8,169,096.

### NON-CURRENT FINANCIAL ASSETS

The Company terminated the liquidity agreement with the Bryan Garnier firm on December 23, 2015.

As a result of this, the Company received €351,101 in cash and 2,500 ERYTECH Pharma shares that will be used for a future employee share allocation. These 2,500 shares are recognized as treasury shares.

The other financial assets are composed of deposits & sureties for €97,056.

The company holds, in equity securities, 100% of the capital of the subsidiary ERYTECH Pharma Inc., i.e., US\$1 valued at €0.73.

The company's investments can be summarized as follows:

	Capital	Reserves before allocation of earnings	Share of capital held (as %)	Book values of securities held		Loans and advances made by the company and not yet repaid	Amount of pledges and securities given by the company	Sales (excluding VAT) for previous year	Earnings (profit or loss for the previous year)	Dividends received by the company during the year	Comments
				Gross	Net						
<b>A - DETAILED INFORMATION ON SUBSIDIARIES AND INVESTMENTS</b>											
1. Subsidiary (+50% of the capital held by the company) - ERYTECH PHARMA Inc.	0.73	0.00	100.00	0.73	0.73	80,847.28	0.00	0.00	-108.72	0.00	
2. Investments (10 to 50% of the capital held by the company)											
<b>B - GENERAL INFORMATION ABOUT OTHER SUBSIDIARIES AND INVESTMENTS</b>											
<b>1. Subsidiaries not shown in A</b>											
1. French											
2. Foreign											
<b>2. Investments shown in A</b>											
1. French											
2. Foreign											





**Fixed assets**  
ERYTECH PHARMA

Period from 01/01/15 to 12/31/15  
Published on 02/02/16

HEADINGS	Gross value start of year	Increases by re-evaluation	Acquisitions contributions, creation, transfers	
INTANGIBLE ASSETS				
Start-up and development costs				
Other intangible assets	134,975		48,579	
<b>TOTAL intangible assets:</b>	<b>134,975</b>		<b>48,579</b>	
TANGIBLE FIXED ASSETS				
Land				
Buildings on own ground				
Buildings on someone else's ground				
General facilities construction				
Technical installations and industrial tooling	617,457		109,582	
Fixtures and fittings	958,845		119,994	
Transport equipment				
Office equipment, computers and furniture	75,656		58,684	
Recoverable packaging and other				
Assets under construction	112,480		14,962	
Advances and deposits			29,326	
<b>TOTAL tangible assets:</b>	<b>1,764,438</b>		<b>317,586</b>	
INVESTMENTS				
Investment in companies counted using the equity method				
Other participating interests	1			
Other investments				
Loans and other long-term financial investments	458,923		25,459	
<b>TOTAL investments:</b>	<b>458,924</b>		<b>25,459</b>	
<b>GRAND TOTAL</b>	<b>2,358,337</b>		<b>366,165</b>	
HEADINGS	Decreases by wire transfer	Decreases by disposals placed out of service	Gross value end of fiscal year	Legal re-evaluations
INTANGIBLE ASSETS				
Start-up and development costs				
Other intangible assets			183,554	
<b>TOTAL intangible assets:</b>			<b>183,554</b>	
TANGIBLE FIXED ASSETS				
Land				
Buildings on own ground				
Buildings on someone else's ground				
General facilities construction				
Technical installations and industrial tooling			727,039	
Fixtures and fittings			1,078,839	
Transport equipment				
Office equipment, computers and furniture			134,340	
Recoverable packaging and other				
Assets under construction	112,480		14,962	
Advances and deposits			29,326	
<b>TOTAL tangible assets:</b>	<b>112,480</b>		<b>1,984,506</b>	
INVESTMENTS				
Investment in companies counted using				
Other participating interests			1	
Other investments				
Loans and other long-term financial		316,601	167,781	
<b>TOTAL investments:</b>		<b>316,601</b>	<b>167,782</b>	

GRAND TOTAL	112,480	316,601	2,335,842	
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# Amortization

ERYTECH PHARMA

Period from 01/01/15 to 12/31/15  
Published on 02/02/16

POSITIONS AND TRANSACTIONS IN THE FISCAL YEAR				
FIXED ASSETS SUBJECT TO AMORTIZATION	Start of FY amount	Increases provisions	Decreases reversals	Amount end of fiscal year
INTANGIBLE ASSETS				
Start-up and development costs				
Other intangible assets	104,025	18,375		122,399
<b>TOTAL intangible assets:</b>	<b>104,025</b>	<b>18,375</b>		<b>122,399</b>
TANGIBLE FIXED ASSETS				
Land				
Buildings on own ground				
Buildings on someone else's ground				
General facilities construction				
Technical installations and industrial tooling	346,398	79,341		425,739
Fixtures and fittings	635,854	97,553		733,406
Transport equipment				
Office equipment, computers and furniture	35,841	15,203		51,044
Recoverable packaging and other				
<b>TOTAL tangible assets:</b>	<b>1,018,093</b>	<b>192,097</b>		<b>1,210,190</b>
<b>GRAND TOTAL</b>	<b>1,122,117</b>	<b>210,472</b>		<b>1,332,589</b>

BREAKDOWN OF PROVISIONS FOR DEPRECIATION FOR THE FISCAL YEAR			
FIXED ASSETS SUBJECT TO AMORTIZATION	Straight-line depreciation	Declining balance depreciation	Amortization - exceptional
INTANGIBLE ASSETS			
Start-up and development costs			
Other intangible assets			
<b>TOTAL intangible assets:</b>			
TANGIBLE FIXED ASSETS			
Land			
Buildings on own ground			
Buildings on someone else's ground			
General facilities construction			
Technical installations and industrial tooling			
Fixtures and fittings			
Transport equipment			
Office equipment, computers and furniture			
Recoverable packaging and other			
<b>TOTAL tangible assets:</b>			
Acquisition costs for participating interests			

GRAND TOTAL			
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## Details of changes in Inventory and work in progress

ERYTECH PHARMA

Period from 01/01/15 to 12/31/15

Published on 02/02/16

HEADINGS	At the end of fiscal year	At the start of fiscal year	Change in inventories	
			Increases	Decreases
<b>Goods for resale</b>				
Inventory resold				
Goods for resale				
<b>Supplies</b>				
Supplies inventory				
Raw materials	79,010	122,936		43,926
Other supplies	86,879	75,420	11,459	
<b>TOTAL I</b>	<b>165,889</b>	<b>198,356</b>		<b>32,467</b>

<b>Production</b>				
Intermediate goods				
Finished goods				
By-products				
<b>TOTAL II</b>				

<b>Work in progress - production</b>				
Goods				
Work				
Studies				
Delivery of services				
<b>TOTAL III</b>				

**PRODUCTION TAKEN TO INVENTORY (or production taken out of inventory)**

**II + III**

The line “Raw materials” relates to the inventory of products dedicated to the production of batches for clinical usage.

The line “Other supplies” concerns the inventory of products dedicated to pre-clinical research.

## Statement of Due Dates for Receivables and Liabilities

ERYTECH PHARMA

Period from 01/01/15 to 12/31/15  
Published on 02/02/16

STATEMENT OF RECEIVABLES	Gross amount	Due within 1 year	Due in more than 1 year
<b>NON-CURRENT ASSETS</b>			
Receivables relating to investments			
Loans			
Other long-term financial investments	167,781	70,725	97,056
<b>TOTAL non-current assets:</b>	<b>167,781</b>	<b>70,725</b>	<b>97,056</b>
<b>CURRENT ASSETS</b>			
Disputed trade receivables			
Other trade receivables	457,936	457,936	
Receivables representing shares loaned or delivered as collateral			
Personnel and associated accounts			
Social Security and other social organizations			
French State - Income taxes	3,743,094	3,743,094	
French State - Value added tax	1,025,711	1,025,711	
French State - Taxes (other than corporation tax)	95,650	95,650	
French State - Miscellaneous			
Group and partners	1,046,802	1,046,802	
Sundry debtors	120,000	120,000	
<b>TOTAL current assets:</b>	<b>6,489,193</b>	<b>6,489,193</b>	
<b>PREPAYMENTS</b>	219,581	219,581	

<b>GRAND TOTAL</b>	<b>6,876,555</b>	<b>6,779,499</b>	<b>97,056</b>
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STATEMENT OF LIABILITIES	Gross amount	Due within 1 year	Due between 1 & 5 years	Due in more than 5 years
Convertible bonds / Other bonds				
With lending institutions:				
- 1 yr maximum from inception				
- over 1 year from inception	16,181	16,181		
Miscellaneous other loans and advances				
Trade payables and related accounts	3,778,063	3,778,063		
Personnel and associated accounts	543,382	543,382		
Social Security and other bodies	508,136	508,136		
Income taxes				
Value added tax	70,617	70,617		
Guaranteed bonds				
Taxes (other than corporation tax)	56,274	56,274		
Liabilities on fixed assets and related accounts				
Group and partners				
Other liabilities	67,033	67,033		
Debt representing borrowed shares				
Accrued income				

<b>GRAND TOTAL</b>	<b>5,039,685</b>	<b>5,039,685</b>		
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## RESEARCH TAX CREDIT

The Company has benefited, since its creation in 2004, from the research tax credit (Crédit d'Impôt Recherche - CIR) as defined in Article 244, c B I of the French General Tax Code.

It is recognized in the income statement, net of income tax expense, with a tax receivable contra-entry.

The amount of the company's CIR for the last three financial years totaled:

- 2015: €2,219,406
- 2014: €1,523,688
- 2013: €1,366,356

## TAX CREDIT FOR COMPETITION AND EMPLOYMENT ("CREDIT D'IMPOT POUR LA COMPETITIVITE ET L'EMPLOI" - CICE)

The company benefits from a tax credit for competition and employment (CICE) created under Article 66, Law no. 2012-1510 of December 29, 2012, the amending finance law for 2012.

The amount for 2015 totaled €52,814.70 and was recorded as a deduction to salary expenses, with a tax receivable contra-entry in the balance sheet.

Following the tax audit initiated by the tax authorities, the 2014 tax credit for competitiveness and employment (CICE) has not yet been received.

## OTHER DEBTORS

Other debtors represent credits notes to be received from suppliers that have provided services for which the Company will be reimbursed for a portion of the expenses.

## CASH AND CASH EQUIVALENTS

The Company's cash position totaled €45,477,430, of which €25,053,893 was placed in short-term deposits :

- €4,000,000, with Société Générale, 1-month maturity tacitly renewable,
- €16,000,000, with Banque Populaire, 18-month maturity, available on demand,
- €5,053,893, with Banque CIC, 18-month maturity, available on demand.

The cash position was therefore divided based on the following categories:

Current accounts	€20,024,406.00
Short-term deposits	€25,053,893.00
Accrued interest	€399,131.08
<b>Total</b>	<b>€45,477,430.08</b>

## Deferred income and expenses

Period from 01/01/15 to 12/31/15  
Published on 02/02/16

ERYTECH PHARMA

HEADINGS	Expenses	Income
Operating expenses or income	219,581	
Financial expenses or income		
Exceptional expenses or income		
<b>TOTAL</b>	<b>219,581</b>	

The prepaid expenses primarily notes to maintenance contracts, as well as lease agreements on equipment and buildings.

## Accrued income

Period from 01/01/15 to 12/31/15  
Published on 02/02/16

ERYTECH PHARMA

AMOUNT OF ACCRUED INCOME INCLUDED IN THE FOLLOWING BALANCE SHEET ITEMS	Amount
<b>Non-current financial assets</b>	
Receivables relating to investments	
Other long-term financial investments	
<b>Receivables</b>	
Trade accounts receivable and associated accounts	
Personnel	
Social security and similar	
French State	95,650
Miscellaneous accrued income	
Other receivables	120,000
<b>Marketable securities</b>	
<b>Cash at bank and in hand</b>	
<b>TOTAL</b>	<b>215,650</b>

## Composition of Share Capital

ERYTECH PHARMA

Period from 01/01/15 to 12/31/15  
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SHARE CLASSES	Number	Face value
1 - Shares or stock composing the share capital at start of the fiscal year	6 882 761	0,1
2 - Shares or stock issued during the fiscal year	1 041 850	0,1
3 - Shares or stock repaid during the fiscal year		
4 - Shares or stock comprising the share capital at the end of the fiscal year	7 924 611	0,1

The Company issued 940,000 new shares on the Euronext stock exchange in December 2015.

The exercise of BSA<sub>2012</sub> and BSPCE<sub>2012</sub> created 101,850 new shares during the financial year. In addition, the exercise of BSPCE<sub>2014</sub> created 1,400 new shares during the year.

### Statement of changes in shareholders' equity (in euros, French standards)

	Number of shares	Share Capital	Issue premium	Reserves & carry forward	FY profit (loss)	Regulated provisions	Total Capital and Reserves
Balance as of December 31, 2014	6,882,761	€688,276.10	€71,375,714.50	(€28,774,932.38)	(€7,283,237.00)	- €	€36,005,820.94
Allocation of 2014 earnings				(€7,283,237.00)	€7,283,237.00		
Bond interest capitalization							
Bond conversions							
Issuance of new shares	940,000	€94,000.00	€25,286,000.00				
Costs associated with issuance of shares			(€2,658,578.07)				
Share warrants & Founder's warrants conversion	101,850	€10,185.00	€746,477.90				
FY profit (loss) 2015					(€11,801,131.27)		
Balance as of December 31, 2015	7,924,611	€792,461.10	€94,749,614.33	(€36,058,169.38)	(€11,801,131.27)	- €	€47,682,774.78

## **CONDITIONAL ADVANCES**

Since its creation, the Group has received 3 advances from BPI FRANCE, repayable under certain conditions.

The conditional advances, totaling €570,857, are presented below as at 12/31/2015:

- **BPI FRANCE / PANCREAS**

The first conditional advance, granted by BPI FRANCE, for a total amount of €735,000, concerns the program for the “development of a new treatment against pancreatic cancer through the administration of allogenic red blood cells incorporating L-asparaginase.”

This conditional advance was received in 3 phases:

- €294,000 upon signature of the agreement (paid in 2008)
- €294,000 upon calls for funds (paid in 2010)
- balance upon completion of work after acceptance of the finalization of the program identified by BPI FRANCE (paid in 2011).

The repayment of this conditional advance will be made according to a fixed payment schedule that will end no later than 6/30/2016.

ERYTECH Pharma S.A. has undertaken to repay the entire conditional advance according to the following payment schedule:

- €100,000 by June 30, 2013
- €150,000 by June 30, 2014
- €225,000 by June 30, 2015
- €260,000 by June 30, 2016

As of December 31, 2015, the payment due on June 30, 2015 had not been made due to an ongoing dispute with BPI over another conditional advance, which led to BPI blocking the progress of this project.

- **BPI FRANCE FEDER**

The second conditional advance, granted by BPI FRANCE FEDER, 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.”

This conditional advance was received in 4 phases:

- €40,500 upon signature of the agreement (paid in 2009)
- €40,500 upon calls for funds (paid in 2010)
- €27,000 upon calls for funds
- balance upon completion of work with acceptance of the finalization of the program by BPI FRANCE.

ERYTECH Pharma S.A. has received €81,000 from BPI FRANCE/FEDER under this program. As the work corresponding to the FEDER assistance is currently completed, ERYTECH Pharma S.A. will not receive the last two payments of €27k.



The repayment of this conditional advance will be made according to a fixed payment schedule that will end no later than June 30, 2016.

ERYTECH Pharma S.A. has undertaken to repay the entire amount of the conditional advance according to the following payment schedule:

- €7,500 by September 30, 2013
- €7,500 by December 31, 2013
- €7,500 by March 31, 2014
- €7,500 by June 30, 2014
- €9,250 by September 30, 2014
- €9,250 by December 31, 2014
- €9,250 by March 31, 2015
- €9,250 by June 30, 2015
- €14,000 by September 30, 2015

ERYTECH Pharma S.A. repaid the entire amount of the conditional advance of (€23k) of the advance in January 2016 (representing to balance). It also repaid the corresponding subsidy of €81k to settle the dispute with BPI France.

- **BPI FRANCE / TEDAC**

Conditional advance provided by BPI FRANCE in the context the TEDAC project 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)
- the remainder upon calls for funds when key milestones are reached.

ERYTECH Pharma S.A. undertakes to reimburse BPI FRANCE initially:

- c) a sum of €5,281,000 upon achieving a cumulative amount of 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 is achieved,
  - €750,000 at the latest on June 30 of the second year,
  - €1,500,000 at the latest on June 30 of the third year,
  - €2,531,000 at the latest on June 30 of the fourth year,
- d) 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, where the cumulative sales reach €60 million, ERYTECH Pharma S.A. undertakes to pay BPI France a sum of 2.5% of the sales generated by the products developed within the project, limited to a total amount of €15 million over 15 years.

## Provisions recognized on the Balance Sheet

Period from 01/01/15 to 12/31/15  
Published on 02/02/16

ERYTECH PHARMA

HEADINGS	Start of FY amount	Increases, allocations	Decreases reversals	Amount end of fiscal year
Prov. for restoration of raw material deposits Provisions for investment Provisions for price increases Tax depreciation Inc. exceptional increases of 30% Tax provisions for locating abroad prior to 1.1.1992 Tax provisions for locating abroad performed after 1.1.1992 Provisions for facilities loans Other regulated provisions				
<b>REGULATED PROVISIONS</b>				
Provisions for disputes. Provisions for guarantees made to clients Provisions for losses on futures markets Provisions for fines and penalties Provisions for foreign exch. losses Prov. for pensions and similar obligat. Provisions for taxes Prov. for building renovation Provisions for major maint. and large-scale revisions Provisions for soc. sec. and tax charges for vacation pay Other prov. for liabilities and charges		81,000		81,000
<b>PROV. FOR LIABILITIES AND CHARGES</b>		<b>81,000</b>		<b>81,000</b>
Prov. on intangible assets Prov. for tangible assets Prov. for blocked securities accounted for using the equity method. Prov. for investments Prov. for other non-current financial assets Provisions for inventory and work in progress Provisions for trade receivables Other provisions for depreciation				
<b>PROVISIONS FOR DEPRECIATION</b>				
<b>GRAND TOTAL</b>		<b>81,000</b>		<b>81,000</b>

The Company recorded a provision of €81,000 for a dispute relating to a subsidy received for the GR-SIL project.

After the closing date, the Company settled the BPI France dispute regarding the GR-SIL subsidy of €81k and refundable advances of €23k. The reimbursement of €104k was made in January 2016.

## Expenses to be paid

ERYTECH PHARMA

Period from 01/01/15 to 12/31/15  
Published on 02/02/16

AMOUNT OF EXPENSES TO BE PAID INCLUDED IN THE FOLLOWING BALANCE SHEET ITEMS	Amount
Accounts payables and associated accounts	497,597
Social security and similar	750,695
Miscellaneous	
Other payables	67,033
<b>TOTAL</b>	<b>1,315,325</b>

## **6 ADDITIONAL INFORMATION RELATING TO THE INCOME STATEMENT**

### **Sales**

By way of reminder, in 2012, the Company signed an exclusive distribution agreement for its product in the indication of acute lymphoblastic leukemia with Orphan Europe.

The Company likewise entered into a contract with the Recordati Group to financially support the clinical trial of GRASPA AML 2012 01-in AML, in the amount of €5 million.

Therefore, the Company continues to re-invoice without margin, on a monthly basis, the costs for the trial which totaled €682,402 for 2015.

Amounts re-invoiced are recorded in sales.

### **Operating subsidy**

The subsidy recognized in income for the 2015 financial year corresponds to the use of the €992k advance for the TEDAC project received at the project inception. The Company did not receive a new subsidy for the TEDAC project on June 30, 2015 (end date of key stage 3), despite the request to BPI in accordance with the contract. BPI asked the Company to make a new request on June 30, 2016. As a result, and despite the project's progress, no subsidy to be received was recorded at December 31, 2015 in light of the uncertainty surrounding receipt of the subsidy.

### **Remuneration of executive officers**

The total gross compensation paid to executive corporate officers was €894,453.

The securities held giving the right to a future portion of the share capital are presented in the detailed table "Subscription warrants."

## DEFERRED TAX EFFECTS

	Amount
FY profit (loss)	(€11,797,253)
Income tax	(€2,219,406)
Loss before tax	(€14,016,659)
Loss Before income tax and special tax effects	(€14,016,659)
Taxable income (loss) for the financial year	(€16,552,035)
Deficits to be carried forward from the previous financial year	€43,130,417
Total deficits remaining to be carried forward	€59,682,452

## INCOME TAX

### BREAKDOWN OF TAX BETWEEN CURRENT INCOME (LOSS) AND EXCEPTIONAL PROFIT (LOSS)

	Amount	Current income (loss)	Exceptional Profit (loss)
FY profit (loss)	(€11,797,253)	(€11,801,952)	€4,699
Income tax	(€2,219,406)	(€2,219,406)	
Earnings before tax	(€14,016,659)	(€14,021,358)	€4,699

The income tax amount corresponds to the research tax credit. Its basis corresponds to research costs excluded from exceptional profit (loss).

## 7 OTHER INFORMATION

### Clinical trials

The costs associated with clinical trials are recognized as expenses as and when they are incurred.

The remainder of the costs incurred leading up to the end of the clinical trial are monitored off-balance sheet. The tables below summarize only ongoing clinical studies for which a contractual commitment was made by the Company.

#### As of December 31, 2015 (amounts in €'000)

Clinical trial name	Budget balance	Comment
2012/09	768	Recruitment begun
2012/10	-	No off-balance sheet commitment
2013/03	3,693	Recruitment begun
<b>Total</b>	<b>4,461</b>	

#### As of December 31, 2014 (amounts in €'000)

Clinical trial name	Budget balance	Comment
2012/09	1,014	Recruitment not begun
2012/10	-	No off-balance sheet commitment
2013/03	4,526	Recruitment not begun
<b>Total</b>	<b>5,540</b>	

## **Retirement indemnity**

Based on the Company data, and the actuarial assumptions used, i.e., primarily a gross discount rate of 2.03%, the total commitment for retirement indemnities measured at 12/31/2015 amounts to 100,241 euros.

No provision for liabilities was recognized in relation to this financial year.

## **Commitment to executive officers**

By way of reminder, on May 24, 2013, the Board of Directors authorized severance indemnities for benefit of:

- Mr. Gil Beyen. This commitment stipulates that, in the event of Mr. Beyen's departure from the company, i.e., in the event of:
  - o expiry of his mandate (save where renewal is rejected by Mr. Beyen) or
  - o revocation (except due to serious misconduct or gross negligence, as understood pursuant to case law resulting from the corporate chambers of the Court of Cassation),Mr. Beyen may claim an indemnity equal to:
  - o twelve times his average monthly remuneration (bonuses included) effectively received during the twelve months prior to the revocation decision or expiry of his term of office, or
  - o the fixed annual remuneration established by the Board of Directors, in the event of revocation decided within twelve months following the appointment of Mr. Beyen.
  
- Mr. Yann Godfrin. This commitment stipulates that, in the event of Mr. Godfrin's departure from the company, i.e., in the event of:
  - o expiry of his mandate (save where renewal is rejected by Mr. Godfrin) or
  - o revocation (except due to serious misconduct or gross negligence, as understood pursuant to case law resulting from the corporate chambers of the Court of Cassation),Mr. Godfrin may claim an indemnity equal to twelve times his average monthly remuneration (bonuses included) effectively received during the twelve months prior to the revocation decision or expiry of his term of office. Mr. Godfrin resigned as Chief Executive Officer at the Board of Directors meeting on January 10, 2016.

Within the context of his resignation, we specify that Pierre-Olivier Goineau did not receive any indemnities.

## **Auditors' fees**

For the 2015 financial year, the external auditor fees paid totaled:

- within the scope of its legal term of office: €118,750, excluding out-of-pocket expenses,
- in relation to the capital increase: €40,000,
- in the context of the NASDAQ IPO project: €276,387.

## Subscription warrants

Share options have been allocated to the directors, to certain employees, as well as to members of the Board of Directors in the form of share subscription warrants (“BSA”) or founder subscription warrants (“BSPCE”).

### – “2012 Plan”

At the end of 2015, the share subscription warrants for the 2012 plan were broken down as follows:

Types of securities	BSPCE <sub>2012</sub>	BSA <sub>2012</sub>
Number of warrants that the Company is authorized to issue for all types of warrants	45,050	
Number of warrants granted	33,788	10,760
Number of warrants exercised	16,352	5,525
Date of General Meeting	May 21, 2012	
Exercise price per new share subscribed	€7,362	
Final date for exercising warrants	May 20, 2020	
Parity	1 warrant for 10 shares	
General conditions of exercise	The warrants may be exercised as of their vesting date.	
Maximum number of new shares that can be issued	231,730	

Under the BSA<sub>2012</sub> plans, the Board of Directors meetings of April 29, 2015 and August 31, 2015 allocated, respectively, 2,150 and 3,585 BSA<sub>2012</sub> to the directors.

### – “2014 Plan”

#### 2014 Allocation

On January 22, 2014, the Board of Directors used the delegation granted by the Combined General Shareholders’ Meeting of April 2, 2013 to make a free allocation of 12,000 BSPCE<sub>2014</sub> to the Group’s directors, including 6,000 to Gil Beyen, Chief Executive Officer, and 3,000 each to Pierre-Olivier Goineau and Yann Godfrin, Chief Operating Officers. One-third of the warrants are vested per year. Given this condition of service, these warrants are allocated gradually, over a three-year vesting period.

In the event of a beneficiary's departure from the Group for any reason whatsoever, the beneficiary shall retain the warrants to which he subscribed prior to his departure. However, in the event of a beneficiary’s departure from the Group for any reason whatsoever prior to the subscription of the warrants to which he is entitled, those warrants have been forfeited and may be reallocated to the person who replaces the individual who leaves the Company.

Following the departure of Pierre-Olivier Goineau in January 2015, 2,000 BSPCE of the 3,000 initially allocated were not granted. They were granted to his replacement, Eric Soyer, on September 1, 2015.

Following the departure of Yann Godfrin in January 2016, 1,000 BSPCE of the 3,000 initially allocated were not granted.



## **2015 Allocations**

Under the BSPCE<sub>2014</sub>/BSA<sub>2014</sub> plans, on June 23, 2015, the Board of Directors granted, respectively, 2,500 BSPCE<sub>2014</sub> to employees and 3,000 BSA<sub>2014</sub> to the newly-hired Chief Medical Officer.

Following the hiring of the new Financial Officer replacing Pierre-Olivier Goineau, the remaining 2,000 BSPCE<sub>2014</sub> were granted to him under the same vesting conditions as those applied to his predecessor.

At the end of 2015, the share subscription warrants for the 2014 plan were broken down as follows:

<b>Types of securities</b>	<b>BSPCE<sub>2014</sub></b>	<b>BSA<sub>2014</sub></b>
<b>Number of warrants that the Company is authorized to issue for all types of warrants</b>	22,500	
<b>Number of warrants granted</b>	13,500	3,000
<b>Number of warrants exercised</b>	140	0
<b>Date of the Board of Directors meeting</b>	January 22, 2014	
<b>Exercise price per new share subscribed</b>	€12,250	
<b>Final date for exercising warrants</b>	January 22, 2024	
<b>Parity</b>	1 warrant for 10 shares	1 warrant for 10 shares
<b>General conditions of exercise</b>	The warrants may be exercised as of their date of vesting. Warrants not exercised by January 22, 2024 will automatically be canceled.	
<b>Maximum number of new shares that can be issued</b>	223,600	

## **Personal training account**

In the context of the individual right to training established by Law 2004-391 of May 4, 2004 relative to life-long professional training, as of 12/31/2015, the number of total training hours relating to the rights acquired and not exercised was 2,988.58 hours.

It should be noted that, in accordance with:

- Law no. 2014-288 of March 5, 2014 relative to professional development, jobs, and social democracy,
- Decree no. 2014-1120 of October 2, 2014 relative to methods of funding and mobilizing the CPF (personnel training account),

The CPT mechanism replaced the individual right to training (formerly DIF) as of January 1, 2015.

## Leasing-purchase agreements

Period from 01.01.18 to 12.31.15

ERYTECH PHARMA

This table includes the R&D and Production equipment financed by lease.

The furthest maturity is December 2018.

HEADINGS	Land	Buildings	Facilities, equipment, and tooling	Other	Total
Original value				973,877	973,877
Depreciation:					
- totals from prior financial years				752,747	752,747
- allocations from the financial year				77,850	77,850
<b>TOTAL</b>				<b>143,280</b>	<b>143,280</b>

RENTAL COSTS PAID:					
- totals from prior financial years				843,262	843,262
- allocations from the financial year				80,757	80,757
<b>TOTAL</b>				<b>924,019</b>	<b>924,019</b>

RENTAL COSTS REMAINING TO BE PAID:					
- up to one year				58,815	58,815
- from one year up to five years				90,666	90,666
- over five years					
<b>TOTAL</b>				<b>149,481</b>	<b>149,481</b>

RESIDUAL VALUE					
- up to one year				143,279	143,279
- from one year up to five years				3,009	3,009
- over five years					
<b>TOTAL</b>				<b>146,288</b>	<b>146,288</b>

Amount covered by the financial year					
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Note: Lease concessions					81,105
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## Average staff

ERYTECH PHARMA

Period from 01/01/15 to 12/31/15  
Published on 02/02/16

STAFF	Staff employee	Personnel provided to the company
Management	20	
Mid management and technicians		
Employees	29	
Laborers		
<b>TOTAL</b>	<b>49</b>	

During the financial year, the company hired 12 employees and 6 employees left.

## Financial commitments

Period from 01.01.15 to 12.31.15

ERYTECH PHARMA

COMMITMENTS MADE	Amount
Discounted notes not yet matured	
Deposits and guarantees	
Pension, retirement, and compensation commitments	100,241
Other commitments made:	

<b>TOTAL</b>	<b>100,241</b>
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COMMITMENTS RECEIVED	Amount
Deposits and guarantees and securities	
Other commitments received:	1,812,000

<b>TOTAL</b>	<b>1,812,000</b>
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The Recordati commitment on the GRASPA-AML study contractually totals €5,293,000 and was valued at €1,812,000 at the end of 2015, the difference corresponding to 2013, 2014 and 2015 re-invoicing.

### **Market risk**

ERYTECH Pharma S.A. uses the euro as its functional currency within the context of its information and financial communications activity. However, a significant portion, of about 15% of its operating expenses, is denominated in US dollars (agency office in Boston, 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 cooperation around tests and clinical projects in the United States).

To date, ERYTECH Pharma S.A. has not opted to use active hedging techniques, and does not use derivative instruments to this end. Unfavorable exchange rate fluctuations between the euro and the dollar that are difficult to predict could affect the financial position of the Company.

This dependency will increase, as the Company, through its subsidiary ERYTECH Pharma Inc., will perform clinical trials in the USA and, in the longer term, sell on this market.

Expenses in US Dollars totaled \$3,149,196 during the 2015 financial year.

The EUR/USD rate fell considerably at the period end, reaching \$1.0887 per €1 at December 31, 2015.

The exchange rate differences are not significant for the periods presented.

## 20.3 Statutory auditors' report on the consolidated financial statements prepared in accordance with IFRS standards for the year ended December 31, 2015

*This is a free translation into English of the statutory auditors' report on the consolidated financial statements issued in French and is provided solely for the convenience of English-speaking users.*

*The statutory auditors' report includes information specifically required by French law in such reports, whether modified or not. This information is presented below the audit opinion on the consolidated financial statements and includes an explanatory paragraph discussing the auditors' assessments of certain significant accounting and auditing matters. These assessments were considered for the purpose of issuing an audit opinion on the consolidated financial statements taken as a whole and not to provide separate assurance on individual account balances, transactions, or disclosures.*

*This report also includes information relating to the specific verification of information given in the Group's management report.*

*This report should be read in conjunction with, and construed in accordance with, French law and professional auditing standards applicable in France.*

### **Erytech Pharma S.A.**

**Headquarters: 60 avenue Rockefeller - Bâtiment Adénine - 69008 Lyon**

**Share capital: €792,461**

### **Auditors' Report on the consolidated financial statements**

**Year ended December 31, 2015**

Dear Shareholders,

In compliance with the assignment entrusted to us by your annual general meeting, we hereby report to you for the year ended December 31, 2015 on:

- the audit of the accompanying consolidated financial statements of Erytech Pharma S.A.;
- the justification of our assessments;
- the specific verifications required by law.

The consolidated financial statements have been approved by the Board of Directors. Our role is to express an opinion on these consolidated financial statements based on our audit.

### **OPINION ON THE CONSOLIDATED FINANCIAL STATEMENTS**

We conducted our audit in accordance with professional standards applicable in France; 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. An audit involves performing procedures, using sampling techniques or other methods of selection, to obtain audit evidence about the amounts and disclosures in the consolidated financial statements. An audit also includes evaluating the appropriateness of accounting policies used and the reasonableness of accounting estimates made, as well as the overall presentation of the consolidated financial statements. We believe that the audit evidence we have obtained is sufficient and appropriate to provide a basis for our audit opinion.

In our opinion, the consolidated financial statements give a true and fair view of the assets and liabilities and of the financial position of the Group as at 31 December 2015 and of the results of its operations for the year then ended in accordance with International Financial Reporting Standards as adopted by the European Union.

## JUSTIFICATION OF OUR ASSESSMENTS

In accordance with the requirements of article L.823-9 of the French Commercial Code (*Code de commerce*), we bring to your attention the following matter.

### Other income

Note 5.22 “Other income” in the notes to the consolidated financial statements outlines the accounting rules and methods regarding revenue recognition and the recognition of subsidy-related income.

As part of our assessment of the accounting rules and principles that the group applied, we verified the appropriate nature of the accounting methods indicated above and the information provided in the notes to the financial statements and we verified their correct application.

These assessments were made as part of our audit of the consolidated financial statements taken as a whole, and therefore contributed to the opinion we formed which is expressed in the first part of this report.

## SPECIFIC VERIFICATION

As required by law we have also verified, in accordance with professional standards applicable in France, the information presented in the group's management report..

We have no matters to report as to its fair presentation and its consistency with the consolidated financial statements.

The statutory auditors

Lyon, February 23, 2016

Lyon, February 23, 2016

KPMG Audit Rhône Alpes Auvergne  
French original signed by

RSM Rhône-Alpes  
French original signed by

Sara Righenzi de Villers  
*Partner*

Gaël Dhalluin  
*Partner*

## 20.4 Statutory auditors' report on the corporate financial statements for the year ended December 31, 2015

*This is a free translation into English of the statutory auditor's report on the financial statements issued in French and it is provided solely for the convenience of English-speaking users. The statutory auditor's report includes information specifically required by French law in such reports, whether modified or not. This information is presented below the audit opinion on the financial statements and includes an explanatory paragraph discussing the auditor's assessments of certain significant accounting and auditing matters. These assessments were considered for the purpose of issuing an audit opinion on the financial statements taken as a whole and not to provide separate assurance on individual account balances, transactions, or disclosures.*

*This report also includes information relating to the specific verification of information given in the management report and in the documents addressed to shareholders.*

*This report should be read in conjunction with, and construed in accordance with, French law and professional auditing standards applicable in France.*

### **Erytech Pharma S.A.**

**Headquarters: 60 avenue Rockefeller - Bâtiment Adénine - 69008 Lyon**

**Share capital: €792,461**

### **Statutory auditors' Report on the Financial Statements**

**Year ended December 31, 2015**

Dear Shareholders,

In performance of the assignment entrusted to us by the annual general meeting, we hereby report to you, for the year ended December 31, 2015, on:

- the audit of the accompanying financial statements of Erytech Pharma S.A.;
- the justification of our assessments;
- the specific verifications and information required by law.

These financial statements have been approved by the Board of Directors. Our role is to express an opinion on these financial statements based on our audit.

### **OPINION ON THE ANNUAL FINANCIAL STATEMENTS**

We conducted our audit in accordance with professional standards applicable in France; those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit involves performing procedures, using sampling techniques or other methods of selection, to obtain audit evidence about the amounts and disclosures in the financial statements. An audit also includes evaluating the appropriateness of accounting policies used and the reasonableness of accounting estimates made, as well as the overall presentation of the financial statements. We believe that the audit evidence we have obtained is sufficient and appropriate to provide a basis for our audit opinion.



In our opinion, the financial statements give a true and fair view of the assets and liabilities and of the financial position of the Company as at December 31, 2015 and of the results of its operations for the year then ended in accordance with French accounting principles.

## JUSTIFICATION OF ASSESSMENTS

In accordance with the requirements of article L.823-9 of the French Commercial Code (*Code de commerce*), we bring to your attention the following matter.

Note “4.3 Recognition of income from subsidies” in the notes to the financial statements presents the accounting methods and rules pertaining to the accounting of subsidies.

As part of our assessment of the accounting rules and principles that the company applied, we verified the appropriate nature of the accounting method indicated above and the information provided in the notes to the financial statements and we verified their correct application.

These assessments were made as part of our audit of the financial statements, taken as a whole, and therefore contributed to the opinion we formed which is expressed in the first part of this report.

## SPECIFIC VERIFICATIONS AND INFORMATION

We have also performed, in accordance with professional standards applicable in France, the specific verifications required by French law.

We have no matters to report as to the fair presentation and the consistency with the financial statements of the information given in the management report of the Board of Directors, and in the documents addressed to shareholders with respect to the financial position and the financial statements.

Concerning the information given in accordance with the requirements of article L.225-102-1 of the French Commercial Code ("Code de commerce") relating to remunerations and benefits received by the directors and any other commitments made in their favour, we have verified its consistency with the financial statements or with the underlying information used to prepare these financial statements and, where applicable, with the information obtained by your Company from companies controlling your Company or controlled by it. Based on this work, we attest the accuracy and fair presentation of this information.

In accordance with French law, we have verified that the required information concerning the identity of the shareholders has been properly disclosed in the management report.

Lyon, February 23, 2016

KPMG Audit Rhône Alpes Auvergne  
French original signed by

Sara Righenzi de Villers  
*Partner*

Lyon, February 23, 2016

RSM Rhône-Alpes  
French original signed by

Gaël Dhalluin  
*Partner*

## 20.5 Date of last financial information

December 31, 2015

## 20.6 Table of five-year results (Erytech Pharma S.A., corporate financial statements in accordance with French accounting standards)

	12/31/2011	12/31/2012	12/31/2013	12/31/2014	12/31/2015
<b>CAPITAL AT YEAR-END</b>					
No. of common shares existing	315,355	315,355	5,558,952 ***	6,882,761	7,924,611
No. of priority dividend shares existing	315,355	315,355	5,558,952 ***	6,882,761	7,924,611
Maximum no. of future shares to be created					
- by conversion of bonds	67,916 *	135,833 *	-		
- through exercise of subscription right	172,876 **	244,855	22,736	452,180	455,330
<b>TRANSACTIONS AND RESULTS</b>					
Revenues ex. tax			483,964	791,853	716,639
Income before taxes, employee profit-sharing and amort., deprec. and provisions	(6,605,757)	(2,149,309)	(7,592,464)	(8,755,887)	(13,729,417)
Income taxes	(798,967)	(812,570)	(1,366,656)	(1,523,688)	(2,219,406)
Employee profit-sharing for the year					
Income after taxes, employee profit-sharing and amort., deprec. and provisions	(5,983,691)	(2,011,394)	(6,478,994)	(7,283,237)	(11,801,131)
Distributed earnings					
<b>EARNINGS PER SHARE</b>					
Income after taxes, employee profit-sharing but before amort., deprec. and provisions	(18.41)	(4.23)	(1.12)	(1.05)	(1.45)
Income after taxes, employee profit-sharing and amort., deprec. and provisions	(18.97)	(6.38)	(1.17)	(1.06)	(1.49)
Dividend distributed to each share					
<b>PERSONNEL</b>					
Average number of salaried employees during the year	41	38	36	38	49
Amount of payroll for the year	1,847,841	1,718,300	2,504,423	2,402,291	2,707,422
Amount of payments for employee benefits for the years	833,826	827,736	1,164,033	168,792	1211,628

## 20.7 Dividend distribution policy

### 20.7.1 Dividends paid during the last three financial years.

None

### 20.7.2 Dividend distribution policy.

No plan exists to initiate a dividend policy in the short term, given the Company's stage of development.

## **20.8 Legal and arbitration proceedings**

At the registration date of this Reference Document, no government, legal, or arbitration proceedings existed, including any proceedings of which the Company has knowledge, that are suspended or with which it is threatened, such as will have or had during the last 12 months a significant effect on the financial position, activity, or results of the Company and/or of its subsidiary.

## **20.9 Significant change in the financial or commercial position**

To the knowledge of the Company, no significant changes have taken place in the Company's financial or commercial position since December 31, 2015.

## **20.10 Report on the economic and financial results (annual financial statements prepared in accordance with French accounting standards)**

Revenues excluding tax amounted to €716,639 resulting from the re-invoicing, without margin, of the GRASPA-AML clinical trial to Orphan Europe/Recordati Group, compared with €791,852 in 2014.

Total operating income was €1,119,767 versus €1,113,132 for the previous financial year. This increase is associated with the recognition of the operating grants in connection with progress of the TEDAC project.

Operating expenses for the financial year totaled €15,735,230 compared with €10,297,787 for the previous financial year, a change of 52.8%. This change in operating expenses is due to a very significant increase in external purchases and expenses tied to the clinical and preclinical developments of ERY-ASP/GRASPA®, and personnel costs.

The operating result was a loss of €14,615,463, versus a loss of €9,184,655 for the previous financial year, representing a change of +59.1%.

The average number of employees was 49, up from 38 the previous financial year, a change of +11 people, because of the strong growth of the Company.

Financial income was €594,106, versus €393,903 for the previous financial year, primarily resulting from the performance of investments in term deposits.

The current result before tax for the financial year was a loss of €14,021,357 compared with a loss of €8,790,751 for the previous financial year, a change of +59.55%.

In consideration of the preceding information,

- the exceptional income of €4,699 versus -€16,174 for the previous financial year,
- the research tax credit of €2,219,406.

The result for the financial year was a loss of €11,797,253 compared with a loss of €7,283,237 the previous financial year, a change of 62%.

As of December 31, 2015, the Company's balance sheet total was €53,439,644 compared with €40,540,288 for the previous financial year, a change of +32%.

## **20.11 Income allocation**

The Shareholders' Meeting will be asked to approve the annual financial statements (balance sheet, income statement and notes) as they are presented to you, and to allocate the loss of €11,797,253 to the "retained earnings" account.

Based on this allocation, the Company shareholders' equity will amount to €47,752,858.

### 20.12 Luxury expenditures and non-deductible expenses

The financial statements for 2015 include expenses of €25,942 corresponding to non-tax deductible expenditures.

Consequently, the tax sustained by reason of these expenditures and expenses totals €8,647.

### 20.13 Information on payment timeframes

The breakdown, at the end of the last two financial years, of the balance of debts to suppliers, by due date:

2015 financial year:

PAST DUE	TOTAL
< 1 month	58,903
1 ≥ 3 months	4,063
3 ≥ 6 months	- 41,170
> 6 months	- 10,320
<b>TOTAL =</b>	<b>€11,476</b>
DUE	TOTAL
< 1 month	1,992,689
1 ≥ 3 months	710,874
3 ≥ 6 months	646
> 6 months	560,065
<b>TOTAL =</b>	<b>€3,264,274</b>

In other words, a total of €3,275,750 for trade payables item.

2014 financial year:

PAST DUE	TOTAL
< 1 month	345,332
1 ≥ 3 months	187,552
3 ≥ 6 months	107,799
> 6 months	28,088
<b>TOTAL =</b>	<b>€668,771</b>
DUE	TOTAL
< 1 month	1,224,565
1 ≥ 3 months	33,266
3 ≥ 6 months	-
> 6 months	-
<b>TOTAL =</b>	<b>€1,257,832</b>

In other words, a total of €1,926,603 for trade payables item.

## 21 ADDITIONAL INFORMATION

### 21.1 Share capital

#### 21.1.1 Amount of subscribed capital

At December 31, 2015, the share capital, fully paid-up, totaled €792,461.10, divided into 7,924,611 common shares each with a par value of €0.10, all of the same class.

#### 21.1.2 Shares not representing the capital

None

#### 21.1.3 Acquisition of shareholder equity by the Company

The Company's Combined General Shareholders' Meeting of June 23, 2015, modified as follows the authorization given to the Board of Directors by the Combined General Shareholders' Meeting of June 17, 2014 to implement a buyback program of Company shares, according to the provisions of Article L.225-209 of the French Commercial Code and the French Autorité des Marchés Financiers General Regulations.

Maximum number of shares that can be repurchased: 5% of the number of shares constituting the Company's share capital at the performance date of these buybacks, as calculated in conformity with applicable legislative and regulatory provisions, it being nevertheless specified that the maximum number of shares held after these buybacks cannot exceed 10% of the capital.

Objectives of the shares share repurchase:

- Awarding shares to employees or corporate officers of the Company and French or foreign companies or groups that might be associated with it in the conditions and following the terms provided by law, particularly in the context of employee profit sharing in the results of the company's expansion, employee shareholder plans, or company savings plans, the stock options plan, or by way of the award of bonus shares;
- Retaining the shares for the purpose of using them for payment or exchange, namely as part of external growth operations, complying with recognized market practice by the AMF and within the limits provided by Article L.225-209 of the French Commercial Code;
- Assuring liquidity of the market for shares by way of one or more providers of investment services acting independently, in the context of a liquidity contract, pursuant to a professional ethics charter recognized by the AMF, it being noted that the number of shares used to calculate the aforementioned 10% limit corresponds to the number of shares purchased, after deducting the number of shares resold during the term of this authorization;
- Reducing the Company's share capital in application of the Eighth Resolution of this General Meeting of Shareholders if adopted;
- Delivering shares, when there is an exercise of rights associated with securities giving access to shares by any means, whether immediately or over time; and
- Implementing any market practice which might be recognized by law or by the AMF.

Maximum purchase price: ninety (90) euros (excluding purchase costs), it being specified that, in the event of a capital transaction, such as one involving incorporation of reserves and award of bonus shares, or share splits or reverse splits, or even changes of the nominal value of shares, this price will be consequently adjusted.

During the fiscal year ended December 31, 2015, this buyback program was used exclusively within the scope of a liquidity agreement with an objective of stimulating trading or liquidation of the Company shares, stipulated with the company Bryan Garnier as investment service provider.

	January 1, 2014 to December 31, 2014	January 1, 2015 to December 23, 2015
Securities purchased	167,345	52,181
Nominal share value	€0.10	
Average share price	€19,487	€28,239
Total amount paid for acquisition of securities	€3,261,099.75	€1,473,538.94
Shares sold	215,780	54,181
Nominal share value	€0.10	
Average share price	€18,129	€28,378
Total amount received for the sale of shares	€3,911,775.10	€1,537,537.31

The amount of the trading fees was €3,011.23 for financial year 2015 versus €7,223.09 for the year ended 2014.

Following the termination of the liquidity contract, effective December 23, 2015, Bryan, Garnier & Co returned the sum of €351,101.16 to the Company. At December 31, 2015, the Company held 2,500 treasury shares in its portfolio (0.03% of the share capital).

ERYTECH Pharma does not intend to establish a new liquidity contract in the immediate future.

#### 21.1.4 Other securities giving access to the capital

All the securities giving access to the Company's capital and in circulation at December 31, 2015, are described in the table below:

##### **Founder subscription warrants (“BSPCE”) and share subscription warrants (“BSA”)**

Types of securities	BSPCE <sub>2012</sub>	BSA <sub>2012</sub>	BSPCE <sub>2014</sub>	BSA <sub>2014</sub>
Number of warrants that the company is authorized to issue	33,787	11,263	19,500	3,000
Maximum number of warrants not yet exercised	17,435	5,235	13,360	3,000
Number of warrants awarded	33,787	10,760	13,500	3,000
Date of General Meeting	May 21, 2012		April 2, 2013	

<b>Warrant subscription price</b>	€0.00	
<b>Exercise price per new share subscribed</b>	€7,362	€12.25
<b>Final date for exercising warrants</b>	May 20, 2020	January 22, 2024
<b>Exchange ratio</b>	1 warrant for 10 shares	
<b>General conditions of exercise</b>	<p>Warrant holders can only exercise their subscribed warrants upon the occurrence of a firm, definitive transaction involving the initial listing of Company shares for trading on a regulated or unregulated stock market, in France or the European Union, or a foreign securities exchange:</p> <ul style="list-style-type: none"> <li>(i) on one single occasion, or</li> <li>(ii) on multiple occasions, within a limit of twice a year and at least 100 warrants.</li> </ul> <p>Upon the occurrence of one of the following transactions:</p> <ul style="list-style-type: none"> <li>(i) acceptance, by shareholders representing at least sixty-six point sixty seven percent (66.67%) of the shares constituting the Company's capital, of a firm, definitive buyback offer pertaining to control of the Company (as pursuant to Article L.233-3 of the French Commercial Code);</li> <li>(ii) the signing of a merger agreement providing for absorption of the Company;</li> </ul> <p>warrant holders can exercise all the warrants they hold.</p> <p>The securities to which the warrants give rights are common shares.</p> <p>Each warrant will give the right to ten (10) shares in the Company's share capital.</p> <p>The new shares resulting from the exercise of founder's share warrants (BSPCEs) shall form the object of periodic requests for admission for trading on the regulated market NYSE Euronext.</p>	<p>The BSPCE<sub>2014</sub> can be exercised:</p> <ul style="list-style-type: none"> <li>- on a single occasion or;</li> <li>- except in the event of an M&amp;A operation, at most four (4) times per year, and for the exercise of a minimum of fifty (50) founder's share warrants (BSPCE<sub>2014</sub>).</li> </ul> <p>By way of exception, the possibility of early exercise has been established in the event of (i) a change in control as pursuant to Article L.233-3(1) of the French Commercial Code, or (ii) a merger of the Company, without conditions on minimum threshold or frequency.</p> <p>The securities to which the warrants give rights are common shares.</p> <p>Each warrant will give the right to ten (10) shares in the Company's share capital.</p> <p>The new shares resulting from the exercise of founder's share warrants (BSPCEs) shall form the object of periodic requests for admission for trading on the</p>

			regulated market Euronext.	NYSE
<b>Number of shares issued</b>	163,520	55,250	1,400	0
<b>Maximum number of new shares that can be issued relating to warrants granted but not exercised*</b>	174,350	52,350	133,600	30,000
<i>Of which the maximum number of shares that can be exercised by:</i>	<i>Yann Godfrin</i>	0	n/a	30,000**
	<i>Jérôme Bailly</i>	5,840	n/a	800
	<i>Gil Beyen</i>	78,630	n/a	60,000
<b>Maximum dilution of shares and % resulting from the exercise of warrants</b>	390,300 shares, i.e., a maximum dilution of approximately 4.93%***			

\* *Post division of the nominal value of Company shares*

\*\* *Due to his resignation on January 18, 2016, 10,000 shares from 1,000 BSPCE<sub>2014</sub> lapsed*

\*\*\* *Based on the exercise of all diluting instruments and not yet exercised (i.e., the BSA and BSPCE) and a share capital of €792,461.10*

At the date of the Reference Document, no “guarantee of value” (ratchet) share subscription warrants exist any longer. The previously outstanding 233,855 warrants were canceled by the General Shareholders’ Meeting of April 2, 2013.

### 21.1.5 Authorized capital not issued

The General Shareholders’ Meeting of June 23, 2015 delegated to the Company’s Board of Directors the power to issue securities in the proportions and for the amounts summarized in the table below.

<b>Date of General Meeting</b>	<b>Nature of authorization</b>	<b>Maximum nominal amount of capital increase or issue of securities representing debt securities resulting from the issue</b>	<b>Cumulative ceiling</b>	<b>Duration</b>	<b>Use</b>	<b>Maximum nominal amount remaining</b>
6/23/2015	Capital increase to remunerate contributions in kind, granted outside of a public exchange offer (9 <sup>th</sup> resolution)	€68,827.61		26 months 8/23/2017	None	€68,827.61



6/23/2015	Increase in share capital through the issuance of common shares or securities giving access to common shares while maintaining the preferential subscription right (10 <sup>th</sup> resolution)	€1,000,000 €80,000,000 (debt securities)		26 months 8/23/2017	None	€1,000,000 €80,000,000 (debt securities)
6/23/2015	Capital increase through the issue of shares and/or securities giving immediate or future access to common shares, with elimination of the preferential subscription right of shareholders to the benefit of categories of investors* (11 <sup>th</sup> resolution)	€500,000 €80,000,000 (debt securities)		18 months 12/23/2016	None	€500,000 €80,000,000 (debt securities)
6/23/2015	Capital increase through the issue of shares and/or securities giving immediate or future access to common shares, with elimination of the preferential subscription right of shareholders to the benefit of categories of investors* (12 <sup>th</sup> resolution)	€100,000 €80,000,000 (debt securities)		18 months 12/23/2016	None	€100,000 €80,000,000 (debt securities)
6/23/2015	Capital increase through the issue of shares and/or securities giving immediate or future access to common shares, with elimination of the preferential subscription right of shareholders to the benefit of categories of investors** (13 <sup>th</sup> resolution)	5% of the Company's share capital		18 months 12/23/2016	None	5% of the Company's share capital
6/23/2015	Capital increase through the issue of shares and/or securities giving immediate or future access to common shares, with elimination of the preferential subscription right, by way of public offering (14 <sup>th</sup> resolution)	€500,000 up to a limit of €1,000,000*** €80,000,000 (debt securities)		26 months 8/23/2017	None	€500,000
6/23/2015	Capital increase through the issue of shares and/or securities giving immediate or future access to common shares, with elimination of the preferential subscription right of shareholders to the benefit of categories of investors through an offering described in Article L.411-2(II) the French Monetary and Financial Code (15 <sup>th</sup> resolution)	20% of share capital (per 12-month period) up to a limit of €1,000,000*** €80,000,000 (debt securities)	€1,000,000	26 months 8/23/2017	12/3/2015 in the amount of €94,000	€906,000 up to a limit of 20% of the share capital

6/23/2015	Increase in the number of shares to be issued in the event of a capital increase with or without elimination of the preferential subscription right (17 <sup>th</sup> resolution)	Limited to 15% of the initial issue pursuant to the 11 <sup>th</sup> , 12 <sup>th</sup> and 13 <sup>th</sup> resolutions of the General Meeting of June 23, 2015	18 months 12/23/2016	None	
6/23/2015		Limited to 15% of the initial issue pursuant to the 10 <sup>th</sup> , 14 <sup>th</sup> and 15 <sup>th</sup> resolutions of the General Meeting of June 23, 2015	26 months 8/23/2017	None	
6/23/2015	Increase in the number through the issue of common shares and securities giving access to common shares in the event of a public exchange offer initiated by the Company (18 <sup>th</sup> resolution)	€1,000,000 (allotted to the ceiling fixed by the 14 <sup>th</sup> and 15 <sup>th</sup> Resolutions of the General Meeting of June 23, 2015)	26 months 8/23/2017	None	€906,000
6/23/2015	Capital increase by incorporation of reserves, profits or premiums (20 <sup>th</sup> resolution)	€1,000,000	26 months 8/23/2017	None	€1,000,000
6/23/2015	Authorization to grant stock options to the benefit of employees and/or corporate officers of the Company and ERYTECH Pharma Group companies (21 <sup>st</sup> resolution)	5% of share capital	38 months 8/23/2018	None	5% of share capital
6/23/2015	Authorization to award existing or new bonus shares (22 <sup>nd</sup> resolution)	5% of share capital	38 months 8/23/2018	None	5% of share capital

\* Individuals or legal entities under French or foreign law habitually investing in health-related securities.

\*\* Corporate officers and employees of the Company and persons bound by a service or consultant agreement to the Company.

\*\*\* Within the limit of a total nominal ceiling of €1,000,000 for the maximum nominal amount of capital increases and €80 million for the maximum nominal amount of debt securities.

#### Use of these delegations:

The Combined General Meeting of June 23, 2015, in its 15<sup>th</sup> resolution, delegated to the Board of Directors its power to issue, on one or more occasions, ordinary shares as part of so-called private placement offers to qualified investors or a restricted circle of investors, as described in Article L.411-2-II of the French Monetary and Financial Code, which may be subscribed either in cash or by offsetting receivables for a number 1,381,906 new ordinary shares, representing up to 20% of the existing share capital of the Company.

The Board of Directors made use of this authorization at its meeting on December 2, 2015, by approving the principle of a capital increase under certain conditions and gave full powers to the Chairman and Chief Executive Officer, who made use of this delegation on December 3, 2015, and decided to carry

out a capital increase in cash with suppression of the preferential subscription rights for a nominal amount of €94,000 through the issue of 940,000 new ordinary shares with a nominal value of €0.10 at a fixed price at €27 per share (€0.10 par value and an issue premium of €26.90), for a capital increase of €94,000 and, issue premium included, of €25,380,000. The Chairman and Chief Executive Officer noted the final completion of the increase on December 7, 2015.

The Board of Directors noted the use of these delegations by the Chairman and Chief Executive Officer on January 10, 2016 and amended the bylaws of the Company accordingly.

#### **21.1.6 Company capital forming the object of an option or a conditional or unconditional agreement stipulating its placement under option**

To the Company's knowledge, no call or put options or other commitments exist to the benefit of the Company shareholders or granted by the latter and pertaining to the Company shares.

#### **21.1.7 Evolution of the share capital**

The table below outlines the evolution of the Company's share capital during the last three financial years, it being specified that in 2015 the Company undertook the following:

- On June 23, 2015, a capital increase resulting from the exercise of warrants in the amount of €653 by the issue of 6,530 new ordinary shares at a par value of €0.10.
- On December 2, 2015,
  - o , a capital increase resulting from the exercise of warrants as of October 31, 2015 in the amount of €1,375 by the issue of 13,750 new ordinary shares at a par value of €0.10.
  - o , a capital increase resulting from the exercise of warrants as of November 30, 2015 in the amount of €649 by the issue of 6,490 new ordinary shares at a par value of €0.10.
- On December 11, 2015, a capital increase by the issue, with the removal of shareholders' preferential subscription rights and via a private placement, of 940,000 new ordinary shares with a par value of €0.10 each, making an increase of €94,000.

SHAREHOLDERS	12/31/2013			12/31/2014			12/31/2015		
	SHARES	% of capital	% of the total voting rights <sup>1</sup>	SHARES	% of capital	% of the total voting rights <sup>1</sup>	SHARES	% of capital	% of the total voting rights <sup>1</sup>
<b>MANAGEMENT</b>	<b>558,350</b>	<b>10.04%</b>	<b>13.16%</b>	<b>599,230</b>	<b>8.71%</b>	<b>13.94%</b>	<b>225,670</b>	<b>2.85%</b>	<b>3.80%</b>
Gil Beyen				34,000	0.49%	0.41%	0	0.00%	0.00%
Pierre-Olivier Goineau	263,490	4.74%	6.20%	263,490	3.83%	6.36%	<i>No longer part of management<sup>2</sup></i>		
Yann Godfrin <sup>3</sup>	292,990	5.27%	6.90%	292,990	4.26%	7.07%	218,070	2.75%	3.72%
Jérôme Bailly				3,500	0.05%	0.04%	2,040	0.03%	0.02%
Other management	1,870	0.03%	0.06%	5,250	0.08%	0.06%	5,560	0.07%	0.06%
<b>FINANCIAL INVESTORS/PE FUNDS</b>	<b>2,827,284</b>	<b>10.04%</b>	<b>60.51%</b>	<b>1,069,742</b>	<b>15.54%</b>	<b>22.70%</b>	<b>1,069,742</b>	<b>13.50%</b>	<b>22.23%</b>
AMORCAGE RHONE ALPES	109,200	1.96%	2.59%	0	0.00%	0.00%	0	0.00%	0.00%
IDINVEST Partners <sup>4</sup>	1,221,392	21.97%	25.72%	51,530	0.75%	1.24%	51,530	0.65%	1.06%
AURIGA Partners <sup>5</sup>	1,018,212	18.32%	20.94%	1,018,212	14.79%	21.46%	1,018,212	12.85%	20.98%
AXA	478,480	8.61%	11.26%	0	0.00%	0.00%	0	0.00%	0.00%
<b>RECORDATI ORPHAN DRUGS</b>	<b>431,034</b>	<b>7.75%</b>	<b>5.07%</b>	<b>431,034</b>	<b>6.26%</b>	<b>5.20%</b>	<b>431,034</b>	<b>5.44%</b>	<b>8.88%</b>
<b>MEMBERS OF THE BOARD OF DIRECTORS</b>	<b>0</b>	<b>0.00%</b>	<b>0.00%</b>	<b>10,500</b>	<b>0.15%</b>	<b>0.13%</b>	<b>12,500</b>	<b>0.16%</b>	<b>0.13%</b>
<b>OTHER SHAREHOLDERS</b>	<b>67,502</b>	<b>1.21%</b>	<b>1.54%</b>	<b>61,263</b>	<b>0.89%</b>	<b>1.21%</b>	<b>163,534</b>	<b>2.06%</b>	<b>3.11%</b>
<b>SUB-TOTAL REGISTERED SHAREHOLDERS</b>	<b>3,884,170</b>	<b>69.87%</b>	<b>80.29%</b>	<b>2,171,769</b>	<b>31.55%</b>	<b>43.17%</b>	<b>1,902,480</b>	<b>24.01%</b>	<b>37.96%</b>
<b>SUB-TOTAL BEARER SHAREHOLDERS</b>	<b>1,674,782</b>	<b>29.18%</b>	<b>19.71%</b>	<b>4,710,992</b>	<b>68.45%</b>	<b>56.83%</b>	<b>6,022,131</b>	<b>75.99%</b>	<b>62.04%</b>
<b>TOTAL</b>	<b>5,558,952</b>	<b>100.00%</b>	<b>100.00%</b>	<b>6,882,761<sup>3</sup></b>	<b>100.00%</b>	<b>100.00%</b>	<b>7,924,611<sup>6</sup></b>	<b>100.00%</b>	<b>100.00%</b>

1 See also Section 18.3 of this Reference Document.

2 Pierre-Olivier Goineau resigned from his positions of Deputy Chairman, Deputy Chief Executive Officer, and Director at the end of the Board of Directors' meeting of January 11, 2015. Consequently, the number of shares held by Mr. Goineau (see Chap. 18.1) have been placed in the "Other shareholders" account.

3 Effective December 31, 2015, Yann Godfrin resigned as Deputy Chief Executive Officer and Director at the end of the Board of Directors meeting of January 10, 2016.

4 Based on the information available, the funds held by IDINVEST Partners hold a total of 332,366 shares representing 4.19% of share capital and 2.39% of voting rights.

5 Based on the information available, the funds held by AURIGA Partners hold a total of 1,147,522 shares representing 14.489% of share capital and 22.31% of voting rights.

6 Increase in the number of shares resulting from exercise of the BSPCE<sub>2012</sub> and BSA<sub>2012</sub>. The capital increase will be recognized in a future Board of Directors' meeting, in conformity with Article L.225-149 of the Code of Commerce.

To its knowledge, the company has no pledges on its capital.

Since December 31, 2015, the Company confirmed, on January 10, 2016, that the capital increase resulting from the exercise of warrants on December 23, 2015 in the amount of €7,508 by the issue of 75,080 new ordinary shares with a par value of €0.10 each.

The table below summarizes the operations occurring on the share capital during the last three financial years:

Date	Operation	Securities issued/exercised	Amount of capital increase (excluding issue premium)	Number of shares/securities issued	Nominal value	Issue premium per share	Number of shares after operation	Price per share (issue premium included)	Capital post-operation
4/30/13	Capital increase	Remuneration for bond interest	€8,375	83,750	€0.10	€11.50	3,237,300	€11.60	€323,730
4/30/13	Capital increase	New Shares	€144,058.40	1,440,584	€0.10	€11.50	4,677,884	€11.60	€467,788.40
4/30/13	Capital increase	Convertible bonds	€86,206.80	862,068	€0.10	€11.50	5,539,952	€11.60	€553,995.20
7/18/13	Capital increase	BSA <sub>2012</sub>	€60,073.92	8,160	€0.10	€7.262	5,548,112	€7.362	€554,811.20
12/3/13	Capital increase	BSA <sub>2012</sub>	€79,804.08	10,840	€0.10	€7.262	5,558,952	€7.362	€555,895.20
5/5/2014	Capital increase	BSA <sub>2012</sub> BSPCE <sub>2012</sub>	€762.00	7,620	€0.10	€7.262	5,566,572	€7.362	€556,657.20
12/4/2014	Capital increase	BSA <sub>2012</sub> BSPCE <sub>2012</sub>	€9,170	91,700	€0.10	€7.262	5,658,272	€7.362	€565,827.20
12/4/2014	Capital increase	Issue of new shares	€122,448.90	1,224,489	€0.10	€24.40	6,882,761	€24.50	€688,276.1
6/23/15	Capital increase	BSA <sub>2012</sub> BSPCE <sub>2012</sub>	€653	6,530	€0.10	€7.262	6,889,291	€7.362	€688,929.10
12/2/15	Capital increase	BSA <sub>2012</sub> BSPCE <sub>2012</sub> BSPCE <sub>2014</sub>	€1,375	13,750	€0.10	€7.262 BSPCE <sub>2012</sub> €12.15 BSPCE <sub>2014</sub>	6,903,041	€7.362 BSPCE <sub>2012</sub> €12.25 BSPCE <sub>2014</sub>	€690,304.10
12/2/15	Capital increase	BSPCE <sub>2012</sub>	€649	6,490	€0.10	€7.262	6,909,531	€7.362	€690,953.10
12/3/15	Capital increase	Issue of new shares	€94,000	940,000	0.10	€26.90	7,849,531	€27	784,953.10
1/10/16*	Capital increase	BSPCE <sub>2012</sub>	€7,508	75,080	0.10	€7.262	7,924,611	€7.362	792,461.10

\* Date of the confirmation of capital increase by the Board of Directors following the exercise on December 23, 2015, of 7,508 BSPCE<sub>2012</sub>.

### 21.1.8 Stock trends

Since the first listing of the Company's shares for trading on the regulated market of NYSE Euronext in Paris on May 7, 2013 and up to December 31, 2015, 21,802,894 shares were traded.

The share, which traded at €11.60 at the first listing of the Company's shares, traded at €25.62 on December 31, 2015.

The low recorded in 2015 was €23.04 on December 11, 2015, and the high was €40.20 on August 4, 2015.

Market capitalization at December 31, 2015 was €203,028,534.

From December 31, 2015 until January 31, 2016, 736,862 shares were traded.

The share, which traded at €11.60 on the first day of trading of the Company's shares, traded at €22.38 on January 31, 2016.

Market capitalization at January 31, 2016, was €177,352,794.

## 21.2 Main provisions of the articles of incorporation

### 21.2.1 Corporate purpose (Article 3 of the articles of incorporation)

The Company has the purpose, in France and in any country, of:

- the research, manufacture, import, distribution, and commercialization of experimental drugs, medications, devices, and 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.

### 21.2.2 Administration and Senior Management (Articles 17 to 24 of the articles of incorporation)

#### 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 are appointed, renewed, or removed in Ordinary General Meetings. They can 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 sixty-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 surpassed, 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 position.

##### *II. Directors as legal persons*

Directors can 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 several liabilities 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.

Where the legal person revokes the term of office of its permanent representative, he/she is required to provide the Company, without delay and by registered letter, this revocation as well as the identity 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.

## **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 sixty-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 term of office. He/she can 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.

With the Board of Directors, the observers shall perform a general mission of consultation and supervision.

## **BOARD DELIBERATIONS**

The Board of Directors shall meet as often as the Company's interests so require, upon summons by its Chairman or the Chief Executive Officer. 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, summon 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.



## **POWERS OF THE BOARD OF DIRECTORS**

The Board of Directors determines the orientation 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 to which the Board of Directors or its Chairman submits.

## **SENIOR MANAGEMENT**

### *1 - Operating methods*

Senior Management is provided under its responsibility, by a natural person appointed by the Board of Directors and holding the title of Chief Executive Officer. This natural person can be the Chairman of the Board of Directors.

The Board of Directors chooses between two operating methods for the Senior Management.

The Board resolution pertaining to the choice of operating method for the Senior Management 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 by 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 Chief Executive Officer's duties is determined by the board at the time of his/her appointment. However, where the Chief Executive Officer is a director, the duration of his/her duties cannot exceed that of the director term of office.

Any person older than seventy years of age cannot be appointed as Chief Executive Officer. When the Chief Executive Officer reaches this age limit, he/she shall be deemed as having duly resigned.

The Chief Executive Officer can 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, except where the Chief Executive Officer holds the position of Chairman of the Board of Directors.

The Chief Executive Officer 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 purpose and without prejudice to those that the law expressly assigns to the shareholders and to the Board of Directors.

He shall represent the Company in its relations with third parties. The Company is committed by the actions of the Chief Executive Officer 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 may limit the powers of the Chief Executive Officer, but these limitations are not binding against third parties.

### *3 – Deputy Chief Executive Officers*

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 Chief Executive Officer.



The Board of Directors may choose the Chief Operating Officers from among the directors or elsewhere, and cannot appoint more than five (5) persons.

The age limit is set at seventy (70) years. When a Chief Operating Officer reaches this age limit, he/she shall be deemed as having duly resigned.

The Chief Operating Officer can be removed at any time by the Board of Directors, upon such proposal by the Chief Executive Officer. 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 Chief Operating Officers 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 Chief Executive Officer, the Board of Directors shall determine the extent and duration of powers granted to the Chief Operating Officers. The Chief Operating Officers shall have, in relation to third parties, the same powers as the Chief Executive Officer.

## **REMUNERATION OF DIRECTORS**

1 - The 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 is 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 Chief Executive Officer, and the Deputy Chief Executive Officer. This remuneration can be fixed and/or proportional.

## **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.

## **REGULATED AGREEMENTS**

All agreements taking place between the Company and a member of its Board of Directors, a shareholder holding more than a 10% share of the voting rights, or, for a shareholder that is a company, the company controlling it as pursuant to Article L. 233-3 of the Commercial Code, 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 referred to in the previous paragraph has an indirect interest or in which the person has dealings with the Company through a third party. Agreements taking place between the Company and another company must likewise be submitted for prior authorization where a member of the Company's Board of Directors is the owner, shareholder with unlimited liability, manager, director, member of the Board of Supervisors, or generally any executive officer of this company.

Prior authorization by the Board of Directors is based on considerations of the benefit of the agreement to the Company, particularly in respect to the financial conditions associated with it.

Agreements concluded and authorized in previous years and in force the preceding year are reviewed each year by the Board of Directors and communicated to the Statutory Auditor as required by law.

The provisions of the foregoing paragraphs are not applicable to agreements involving current transactions and concluded under normal conditions, or to agreements concluded between two companies, one of which directly or indirectly holds the entire capital of the other, after deducting the minimum number of shares required to satisfy the requirements of Article 1832 of the French Civil Code or Articles L.225-1 and L.226-1 of the French Commercial Code.

The report specified in Article L.225-102 of the French Commercial Code mentions, except where there are agreements involving current transactions and concluded under normal conditions, agreements entered into directly or through another person, between, on the one hand the chief executive officer, a deputy chief executive officer, a director, or a shareholder owning more than 10% of the voting rights in the Company, and on the other hand another company in which the Company directly or indirectly owns more than half its capital.”

### **21.2.3 Rights, privileges, and restrictions attached to shares (Articles 9 to 16 of the articles of incorporation)**

#### **SHAREHOLDING DISCLOSURES**

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.

#### **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 can 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.

#### **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 acknowledgment of receipt sent at least fifteen days prior to the date established for each payment. Payments shall be paid either at the headquarters 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.

## **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 amortized in accordance with legal provisions. Amortization of the capital may be decided in an Extraordinary General Meeting and must be performed, through sums distributable in accordance with Article L. 232-11 of the Commercial Code, 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 amortized shall lose the right to reimbursement at their nominal value, up to the amount of this amortization. They shall retain all their other rights.

## **SHARE TYPES**

The shares are nominal, up to their full payment. Where they are fully paid up, they can 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 authorized by the French Minister of the Economy and Finance.

## **INDIVISIBILITY OF THE SHARES – BARE OWNERSHIP – USUFRUCT**

The 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 headquarters, 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.

## **ASSIGNMENT AND TRANSFER OF SHARES**

Shares can be freely traded, without prejudice to legal and regulatory provisions.

The ownership of shares issued in nominal form shall result from their registration in the name of the owners on the registers held to this end. Shares that are registered as necessarily being nominal 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.

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 of 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.

## **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.

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 the shareholders in General Meetings and to these articles of incorporation. Assignments shall include all dividends matured and not paid or maturing in future, as well as any share in the reserve funds, except where provisions to the contrary are reported 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.

### **21.2.4 Actions required to modify shareholders' rights**

The rights of shareholders may be modified in accordance with legal conditions, by way of a modification of the Company's articles of incorporation, an operation that only the Extraordinary General Meeting is authorized to perform.

### **21.2.5 General Meetings (Articles 26 to 30 of the articles of incorporation)**

#### **NATURE OF 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.

#### **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 (the “BALO”), French Bulletin of compulsory legal notices, 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 departement where the headquarters is located, and a notice, furthermore, in the 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. The Board of Directors has the right to accept voting forms and proxies arriving at the Company after the deadline 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 accordance with legal provisions. Shareholders who are legal persons shall participate in meetings through their legal representatives or through any representative designated to this end.

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 videoconference 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 BALO.

Shareholders who use, to this end and within the required timelines, the electronic voting form offered on the website arranged by the coordinator of the shareholders' meeting shall be considered equal 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, as well as the acknowledgment of receipt that is given in such case, shall be considered a fully irrevocable and enforceable submission, 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 at 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.

## **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 meeting may nevertheless, in all circumstances, remove one or more members of the Board of Directors and proceed with their replacement.

#### **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 delegated to this end by the Board. Failing this, the shareholders' meeting shall itself designate its 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.

#### **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.

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 granted, in accordance with legal conditions, to all shares fully paid up for which evidence is provided, at the latest on the second day prior to the date of the shareholders' meeting, 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 the shareholder's 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, profit, or issue premiums, the double voting right is granted, upon issue, to registered bonus shares awarded to replace existing shares already carrying double voting rights.

The double voting right shall be automatically 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.

#### **21.2.6 Clauses of the articles of incorporation such as may have an effect on the occurrence of a change of control**

No clauses of the articles of incorporation are such as may have the effect of delaying, deferring, or impeding a change of control in the Company.

### **21.2.7 Crossing of thresholds set by the articles of incorporation**

The Company's articles of incorporation do not stipulate obligations other than those established by the law and regulations (Article 9 of the Company's articles of incorporation).

### **21.2.8 Special provisions governing modifications to the share capital**

All modifications to the share capital are subject to legal requirements, the articles of incorporation not stipulating any specific provisions.



## 22 MAJOR CONTRACTS

The major contracts for the Company during the last two years, other than those stipulated in the normal course of business, are the following:

### 22.1 Partnership and cooperation agreements

#### 22.1.1 Financed agreements

##### 22.1.1.1 Erytech/Inserm/Aphp/Diaxonhit

The parties have stipulated a cooperation agreement within the scope of the TEDAC project: “Therapeutic Enzymes to Deplete Amino acids to treat Cancers resistant to radio/chemotherapy.”

This agreement entered into effect retroactively as of January 1, 2012, for a duration of 8 years.

Within the scope of this project, BPI France (formerly Oséo) will finance the Company in the amount of €7 million, which shall be paid in multiple tranches, €4.9 million of which is in repayable advances and €2.1 million in non-repayable grants.

The BPI France assistance is composed of a grant, as well as repayable assistance, in accordance with the following structure:

Beneficiary	Amount of the project (in euros)	Cost of eligible activities included (in €)			Maximum assistance provided (in €)		
		Industrial research	Experimental development	Total	Grants	Repayable advances	Total assistance
ERYTECH Pharma	14,363,850	4,573,760	9,790,090	14,363,850	2,058,194	4,895,052	6,953,246*

\*That being 48% of the project amount

The project is monitored through a series of key milestones defined with a view to enabling BPI France to evaluate the progress of the project and determine the assistance to be paid. The key milestones are as follows (t0 having been established as July 1, 2012):

Key Milestone	Stopwatch	Date	ERYTECH Condition
Key Milestone 1	t0 + 12 months	Jul-13	Provision of contract between ERYTECH and the enzyme supplier
Key Milestone 2	t0 + 24 months	Jul-14	Enzyme encapsulation capacity
Key Milestone 3	t0 + 36 months	Jul-15	Results of toxicology study, selection of therapeutic indication for Phase I/II
Key Milestone 4	t0 + 48 months	Jul-16	Design of study I/II, approval of regulatory authorities for Phase I/II
Key Milestone 5	t0 + 60 months	Jul-17	Intermediate results Phase I/II
Key Milestone 6	t0 + 72 months	Jul-18	Design of study II/III, approval of regulatory authorities II/III, results of I/II
Key Milestone 7	t0 + 84 months	Jul-19	Intermediate results Phase II/III
Key Milestone 8	t0 + 96 months	Jul-20	Final report

The estimated amount of payments is established in the following tables:

#### Payments of non-repayable grants by key milestone (in €)



	First payment of non-repayable grants	Key Milestone 1	Key Milestone 2	Key Milestone 3	Key Milestone 4	Key Milestone 5	Key Milestone 6	Key Milestone 7	Key Milestone 8	Total grant payments (in €)
ERYTEC H Pharma	992,257	463,054	294,153	0	0	0	0	0	308,730	2,058,194

	First payment of repayable advances	Payments of repayable advances by key milestone (in €)								Total payments of repayable advances (in €)
		Key Milestone 1	Key Milestone 2	Key Milestone 3	Key Milestone 4	Key Milestone 5	Key Milestone 6	Key Milestone 7	Key Milestone 8	
ERYTEC H Pharma	62,607	0	0	217,121	901,807	1,018,028	1,454,167	507,064	734,258	4,895,052

The first payment was made after signature of the Framework Agreement with BPI France. In May 2012, the Company therefore received the above-mentioned amounts, i.e., €992,257 in non-repayable grants and €62,607 in repayable advances.

These amounts were therefore received as an advance, and therefore correspond to the amount of expenses estimated for Key Milestone 1 to which the assistance rate is applied.

At the end of Key Milestone 3, as of June 30, 2015, the Company had incurred expenses amounting to €981,765, not reaching the volume for which it had received the advance of €992,257. Consequently, the Company was unable to request payment of the advance for the next Key Milestone. The Company had, furthermore, already recorded deferred revenues amounting to €368,436 as of December 2014.

The following payments are made after each review of a Key Milestone. The amount effectively paid has a ceiling at the amount of the Key Milestone in question, decreased by any overpayments at previous Key Milestones. The total amount of payments made prior to the final Key Milestone shall not exceed 85% of the anticipated amount of the assistance.

The final payment of an estimated amount of 15% of the total amount of assistance shall be made after the Key Milestone and the final review of the project R&D identifying the end of the project and acceptance by BPI France.

Within the context of closing its books on December 31, 2015, the Company achieved all of the forecast expenses in Key Milestone 4, the milestone to be completed in June 2016. As subsidies are booked on a pro rated basis for costs incurred (corporate financial statements and IFRS), at the end of 2015 the Company did not report deferred income given the uncertainty over obtaining the grant to be received on June 30, 2016 (amount not specified in Key Milestone 4 in the schedule of grant payments).

The Financial Repayments shall be made in specific payment amounts, in function of the anticipated sales revenue generated by the direct or indirect development of products or services resulting from the Project, as listed below:

- Therapeutic products, simple or combined, used in the treatment of a solid tumor and composed of enzymes intended to break down a specific amino acid, encapsulated in the red blood cells.

The Financial Repayments include repayment of the Repayable Advance and the Additional Payments explained below. We specify that the amounts of the repayment maturities on the Repayable Advance take into account an annual discount rate of 3.05% (three point zero five percent), calculated according to the methods below.

The amounts  $M(m)$  of the advance payments and repayment payments arising in month (m) are thus based on the economic conditions of the month ( $m_0$ ) of signature of the agreement, according to the following calculation:

$$M(m_0) = M(m) (1.0305)^{-(n/12)}$$

Where  $n$  represents the number of months elapsed between  $(m_0)$  and  $(m)$ ,  
And the dates to be taken into consideration are:

- for a payment of the Repayable Advance, the date of disbursement by BPI France;
- for a repayment, the collection date identified by BPI.

The Company undertakes to repay BPI an amount of €5,281,000 (five million, two hundred eighty-one thousand euros) upon achieving a cumulative amount of before-tax sales revenue equal to or greater than €10,000,000 (ten million euros), known as “trigger sales revenue,” according to the following estimated lump-sum payment schedule:

Year 1 at the latest on June 30	€500,000 (five hundred thousand euros)
Year 2 at the latest on June 30	€750,000 (seven hundred fifty thousand euros)
Year 3 at the latest on June 30	€1,500,000 (one million, five hundred thousand euros)
Year 4 at the latest on June 30	€2,531,000 (two million, five hundred thirty-one thousand euros)

In the event of sale of the intellectual property rights resulting from the project, as well as the assignment of prototypes, test series, and models created within the scope of the project, an annuity equal to 50% (fifty percent) of the income generated shall be owed to BPI France.

Where repayment of the Repayable Advance has been made in accordance with the above provisions, the Company shall pay BPI, for a duration of five consecutive years after the termination date of said repayment and insofar as it has achieved a cumulative amount of before-tax sales revenue equal to or greater than €60,000,000 (sixty million euros), 2.5% of the annual sales revenue generated by the use of products resulting from the Project.

In any case:

- the amount of the Additional Payments shall have a ceiling of €15,000,000,
- the total period for the lump-sum repayments and the profit-sharing payments is limited to 15 years.

Early repayment of the Repayable Advance may be required by BPI, particularly in the event of a change of control in the Company.

The Company must notify BPI of any change of control. Within two months, BPI will ascertain either:

- The possibility of continuing the project, or
- The impossibility of continuing the project.

If BPI finds it impossible to continue the project, BPI will announce the immediate repetition of the assistance to the Company. The amount to be paid to BPI will thus be equal to the assistance amounts paid and not reimbursed plus any late penalties at 0.7% per calendar month overdue.

## 22.1.2 Partnership agreements

### 22.1.2.1 Erytech/Teva Group

On March 28, 2011, ERYTECH signed a licensing and exclusive distribution agreement with Abic Marketing Limited (Teva Group), a global player in the pharmaceutical industry based in Israel, to distribute GRASPA® in that country for the treatment of ALL. Additionally, if other marketing authorizations are issued in Europe for GRASPA® in indications other than ALL, Teva may choose to extend its marketing exclusivity to such other indications in Israel. Teva Group is a diversified pharmaceutical group with a strong strategy in innovative specialized products and particularly in therapeutic fields such as the central nervous and respiratory systems, women’s health, oncology, and pain.

In accordance with the terms of the agreement, Teva Group will submit an application for approval of the drug in Israel and will provide for its marketing and long-term distribution in that country. ERYTECH is responsible for the manufacturing and transportation of the product directly to the consumer. Teva Group is responsible for all regulatory and marketing processes and has agreed to reimburse ERYTECH for part of its transportation expenses. ERYTECH does not expect that Teva

Group will seek regulatory approval in Israel until a marketing approval has been issued for GRASPA® in the European Union.

Under the terms of this agreement, ERYTECH received an advance payment of €40,000 upon signing the contract and may receive up to €45,000 in milestone payments in the event of the completion of specific regulatory steps, and a part of Teva Group's profits if Teva Group extends its distribution rights to other indications. ERYTECH will receive half of the profits of all sales of GRASPA® in Israel, calculated according to the terms provided in the agreement. The agreement is concluded for an initial term of ten years and will be automatically renewed for five successive years unless the parties give notice of non-renewal within six months. Early termination of the agreement may be requested by a party in the event of a transfer of control of the other party.

#### **22.1.2.2 ERYTECH/Orphan Europe (Recordati Group)**

On November 23, 2012, ERYTECH signed an exclusive licensing and marketing agreement with Orphan Europe, a company specialized in the development, production, and marketing of drugs for orphan diseases. Orphan Europe is a subsidiary of Recordati, a major pharmaceutical group in Europe.

Orphan Europe holds a portfolio of orphan drugs already on the market in different areas, such as neonatology, pediatrics, and metabolic disorders. Orphan Europe is a leading player in the field of orphan diseases and has the medical, clinical, regulatory and commercial expertise to market and effectively sell GRASPA® in Europe. Orphan Europe is a strategic business for Recordati, which acquired the company in 2007 for €135 million and built it up further with the acquisition of a portfolio of rare and orphan disease drugs in the United States for \$100 million.

Orphan Europe will market GRASPA® in 38 European countries, including all the countries in the European Union for the treatment of ALL and AML. The parties have the opportunity to discuss the extension of this agreement to other areas in Europe's periphery and to other indications.

Under the terms of the agreement, ERYTECH is responsible for obtaining regulatory approval for GRASPA® for the treatment of ALL in the European Union and Orphan Europe is responsible for the regulatory processes for the 11 countries that are not EU Member States. Furthermore, Orphan Europe will seek marketing approval for GRASPA® for the treatment of AML in the 38 countries of Europe. If GRASPA® obtains this marketing approval, Orphan Europe will be tasked with assisting the Company in obtaining regulatory approvals for pricing and reimbursement. Orphan Europe has agreed, at its expense, to make reasonable commercial efforts to market and promote GRASPA® after it has been approved. ERYTECH has agreed to use reasonable commercial efforts to manufacture and deliver GRASPA® in the quantities requested by Orphan Europe, on the basis of forecasts that Orphan Europe will transmit to ERYTECH. ERYTECH is responsible for the delivery of GRASPA® directly to consumers.

Under the agreement, Orphan Europe contributed €5 million upon signing. Orphan Europe will pay ERYTECH up to €37.5 million on future milestones depending on various clinical, regulatory, and commercial events. Orphan Europe will participate in the costs of the clinical development of GRASPA® in AML and ERYTECH will receive a price for product delivered, and royalties on the sales performed by Orphan Europe with GRASPA®, for a total of up to 45% of the net sale price.

The Company has granted Orphan Europe a right of first negotiation for the marketing of GRASPA® in additional indications, in addition to LAL and AML in Europe, and for marketing GRASPA® for all indications in other territories such as Turkey, Russia, specific states of the Middle East and throughout Africa. Orphan Europe has agreed not to be involved in the development and marketing of any competitor product containing L-asparaginase for the treatment of ALL and AML.

The term of the agreement varies by country. For EU Member States, the period is ten years from the marketing approval date for GRASPA® for the treatment of ALL and will be automatically extended

by 10 years from the date of the marketing approval for the treatment of AML if it occurs before the end of 2019. For countries that are not part of the European Union, the period is 10 years from the marketing approval date for GRASPA® for the treatment of either ALL or AML, but it can be extended to more than three years after the expiry of the term for the Member States of the European Union. At the end of the contract, Orphan Europe is entitled to request an additional 10-year renewal if it is in accordance with the terms of the agreement. If the Company refuses to renew the agreement under specific circumstances, the Company may be subject to financial penalties as provided in the agreement. In addition, the agreement stipulates that Orphan Europe can automatically terminate the contract, require the reimbursement of certain expenses and lower milestone payments in the event that the intellectual property for which the Company was granted a license is deemed invalid.

Separately, another Recordati Group company has purchased bonds that were converted into an investment in ERYTECH equity worth €5 million at the time of the initial public offering on the Euronext Paris regulated market (see also Section 18.1 of the 2014 Reference Document).

As part of this partnership, the Company invoiced to Orphan Europe the costs incurred for the Phase II clinical trial in AML as presented in Note 5.22 in the Notes to the consolidated financial statements.

### **22.1.3 License agreement**

### **22.1.4 Erytech/National Institutes of Health (NIH)**

The NIH has granted a license, pertaining to the intellectual property covering a diagnostic method to predict the efficacy of L-asparaginase in patients (see also Chapter 11.2 Intellectual Property). This license covers the United States and the development in leukemia and solid cancers. It is exclusive for five years after the FDA approval of the drug to be developed by ERYTECH. The license is granted in return for an annual fee. In the event of commercial use of this license, the Company will be required to pay an additional royalty proportionate to the net sale price.

## **22.2 Supply contracts**

### **22.2.1 Erytech/Établissement Français Du Sang (EFS)**

The parties have entered into multiple agreements for the sale of packed red blood cells for therapeutic use intended for the manufacture of ERY-ASP/GRASPA®, specifically:

- on September 1, 2009, as part of the GRASPALL 2009-06 clinical trial;
- on October 19, 2012, as part of a potential temporary authorization to use the product ERY-ASP/GRASPA®;
- on January 4, 2013, as part of the GRASPA-AML-2012-01 clinical trial.

To ensure long-term contractual relations with EFS, the Company also on October 21, 2015, signed a framework agreement to sell packed red blood cells for therapeutic use intended for the manufacture of ERY-ASP/GRASPA®.

### **22.2.2 Erytech/American Red Cross (ARC)**

The parties have stipulated a forward contract according to which the ARC undertakes to supply ERYTECH within the scope of its requirements for packed red blood cells in the United States.

This contract entered into effect on July 1, 2009, and will expire on December 4, 2016.

### 22.2.3 Erytech/medac

ERYTECH and Medac, a German company, have signed two exclusive supply contracts for asparaginase intended for the manufacture of ERY-ASP/GRASPA®.

- The first contract entered into effect on December 10, 2008 for a duration of 20 years, and concerns the native form of asparaginase currently used by ERY-ASP/GRASPA® for its European clinical trials in ALL and AML.
- The second contract covers any new formulations of asparaginase that Medac could develop and that ERYTECH may potentially use. In particular, medac develops a recombinant asparaginase (in Phase III in Europe) and a pegylated asparaginase (in Phase I in Europe) (see also Chapter 6 of this Reference Document). For supplies for clinical usage, this contract entered into effect on April 6, 2011 for a duration of 10 years; for supplies for commercial usage, it will enter into effect on the date of commercial approval, for a duration of 5 years.

This second contract contains some clauses providing that ERYTECH may have to refrain from any form of promotion of ERY-ASP/GRASPA® if such product was produced from a new formulation of asparaginase registered and marketed prior to ERY-ASP/GRASPA® as the first-line treatment. It is specified that any restriction against promotion will only be applicable for the country or countries in which the new formulation is approved first and only for the indication or indications that it obtains, and will not impede the prescription of ERY-ASP by a physician and its sale by ERYTECH.

It is reiterated that ERY-ASP/GRASPA® is currently manufactured in Europe using native asparaginase and therefore covered by the first supply contract, which contains no marketing-related restrictions. The Company may plan to manufacture ERY-ASP/GRASPA® in Europe using any new Medac formulation, in the event such new formulation is developed, but has no obligation to do so.

In any event, none of the provisions of contracts with medac are such as impede or restrict, in any country, a physician's ability to prescribe ERYTECH candidate drugs.

### 22.2.4 Other supply contracts

The Company has stipulated a supply contract for the provision of "Osmocell" devices, as well as the know-how associated therewith. This contract entered into effect on September 10, 2013 for a duration of one year, with tacit renewal for subsequent one-year periods.

The Company has entered into a supply contract for the provision of hemodialysis filters that the Company uses in its production system. The contract entered into effect on November 24, 2010, for a duration of 10 years.

## 22.3 Subcontracting agreements

### 22.3.1 Erytech/American Red Cross (ARC)

The parties have stipulated a subcontracting agreement for the production of batches of ERY-ASP for the Company's clinical trials in the United States.

The contract entered into effect on March 1, 2009, for an initial duration of three years, and is renewable in one-year periods or, where applicable, until the end of the clinical trial for which ARC produces the batches.

### 22.3.2 Other subcontracting agreements

The Company has stipulated a subcontracting agreement for the production of Lysis/resealing solutions that the Company uses within the scope of its activities involving molecule encapsulation in red blood

cells. The agreement entered into effect on March 8, 2011 for an initial duration of 2 years, and is renewable for one-year periods.

## **23 INFORMATION ORIGINATING FROM THIRD PARTIES, EXPERT DECLARATIONS, AND DECLARATIONS OF INTERESTS**

None



## **24 DOCUMENTS ACCESSIBLE TO THE PUBLIC**

Copies of this Reference Document are available free of charge at the Company's headquarters, 60 avenue Rockefeller, 69008 Lyon, France. This Reference Document can also be found on the Company's website ([www.erytech.com](http://www.erytech.com)) and on the AMF website ([www.amf-france.org](http://www.amf-france.org)).

The Articles of Incorporation, General Meeting minutes, and other Company documents, as well as the historical financial information and all assessments or declarations made by an expert upon the request of the Company and made available to the shareholders in accordance with applicable legislation can be found, free of charge, at the Company's registered office.

These documents are also available in paper format upon a simple request to the Company.

Further, pursuant to Article 221-3 of the General Regulation of the AMF, the information regulated under Article 221-1 of the same Regulations is available on the Company's website ([www.erytech.com](http://www.erytech.com)).

## **25 INFORMATION ON INVESTMENT STAKES**

At December 31, 2015, ERYTECH Pharma held 100% of the shares in ERYTECH Pharma Inc., an American company incorporated in April 2014 whose objective is to develop the Company's activities in the United States of America (see Chapter 20.1, Appendices 2.3 and 5.5, and the table of subsidiaries and investment stakes in the annexes to the corporate financial statements under Chapter 20.2).

## 26 GLOSSARY

- **AFSSAPS (now ANSM):** The French Agency for the Safety of Health Products (now the French National Security Agency of Medicines and Health Products), is a French public institution whose mission is to assess the health risks posed by drugs and issue drug marketing approvals (MA). It is the sole authority for regulating biomedical research.
- **American Red Cross (ARC):** Organization whose mission is the collection, storage, processing and distribution of blood. It provides almost 44% of blood donations in the United States. It distributes its products in more than 3,000 hospitals and transfusion centers in the United States.
- **MA:** Marketing Approval is the approval given to a holder of operating rights for a drug manufactured industrially so that said holder can sell it.
- **ANR:** (L'Agence Nationale de la Recherche [National Research Agency]) is a funding agency for public and private research projects, in the form of contract research.
- **Asparaginase:** Specific enzyme capable of suppressing circulating asparagine, thus depriving cancer cells of a key nutrient, causing them to die. Its introduction as the standard treatment for acute lymphoblastic leukemia (ALL) dates back to the 1970s, in particular thanks to a purified version of the enzyme from bacteria (*E. coli*). Asparaginase gradually established itself as a pillar of anti-leukemia chemotherapy.
- **GMP (Good Manufacturing Practice):** Set of mandatory standards governing the manufacture of industrial drugs that ensure the pharmaceutical quality of drugs and patient safety.
- **PRBCs (Packed Red Blood Cells):** Suspension of red blood cells aseptically obtained from a unit of whole blood after removing plasma.
- **Half Life:** Time required for the concentration of a drug present in tissue (e.g., blood) to decrease to half its initial value. In practice, a medicine is considered to no longer have a pharmacological effect after five to seven half-lives.
- **DSMB (Data Safety Monitoring Board):** A committee of independent experts responsible for monitoring the performance of clinical studies.
- **EMA (European Medicines Agency)** is a European Union agency based in London, which coordinates the evaluation and supervision of the development of new medicines in the European Union.
- **Erythrocytes:** Red blood cells
- **FDA (Food and Drug Administration)** is the US government agency responsible for the safety of food products as well as the control and regulation of drugs. Its responsibilities include assessing the safety and efficacy of drugs before issuing their marketing approval for the United States.
- **ERY-ASP/GRASPA® or ERY-ASP or GRASPA®** consists of an L-asparaginase encapsulated in a red blood cell. This medicine aims in particular to treat patients with acute leukemia. Encapsulation allows L-asparaginase to destroy asparagine, tumor growth factor, inside the red blood cell, while avoiding allergic reactions and reducing other side effects, thus providing prolonged therapeutic efficacy compared to other forms and a significantly improved safety profile, to treat fragile patients. The GRASPA® brand has been licensed to Orphan Europe (Recordati Group) to market the product in ALL and AML in Europe and to Teva Group for Israel.

- **IND (Investigational New Drug Application)** is an approval request to the FDA to administer an investigational drug or biological product to humans in the United States
- **Therapeutic Index:** Measurement of the relative safety of a drug, expressed as the ratio of toxic dose to therapeutically effective dose.
- **KOL (Key Opinion Leader):** An individual who, due to his/her reputation, expertise or intensive social activity, could influence the opinions or actions of a large number of individuals.
- **Orphan disease:** Orphan diseases refer to diseases for which there is no effective treatment; proposed treatments for these diseases are limited to reducing symptoms. Orphan diseases are often rare diseases, i.e., low-prevalence diseases, but there are highly prevalent diseases for which there is no treatment (such as Alzheimer disease, which is an orphan disease that is not rare).
- **ODD (Orphan Drug Designation):** Legislation enacted to promote the research and commercialization of products that treat rare diseases. Pharmaceutical companies eligible for this status benefit from market exclusivity for ten years as well as scientific, financial and administrative support incentives for product development in these indications.
- **Phase I:** Clinical trials in healthy volunteers. They have two objectives: to ensure that the toxicity in humans is similar to that tested in animals during the preclinical stage and to analyze what happens to the drug in the body (pharmacokinetics).
- **Phase II:** During this phase, the optimal dose of the drug in terms of efficacy is determined. These trials are performed on a small homogeneous group of one hundred patients.
- **Phase II/III:** A study combining a Phase II and a Phase III, studying efficacy and the overall risk/benefit ratio at the same time.
- **Phase III:** This phase involves a large group of patients and is to compare the drug under development to another drug with proven effect or a placebo (a medicine devoid of therapeutic activity). The objective is to demonstrate effectiveness and assess the efficacy/safety ratio.
- **Pegylation Process:** Non-toxic chemical processing of a molecule to increase its half-life in the body.
- **Hypotonic solutions:** A solution whose molecular concentration is lower than that of the reference environment (in particular, blood plasma). In a hypotonic solution, water tends to enter red blood cells through their semi-permeable membrane.
- **Reticuloendothelial system:** Set of cells scattered throughout the body with various functions including the production of blood components, the destruction of bodies considered foreign and immunity.
- **Companion Test:** Test specific to a drug making it possible to predict patient response to the treatment and suggest the most effective and appropriate treatment and/or drug dosage.
- **Enzymatic therapy:** therapeutic treatment based on the specific activity of an enzyme. Enzymes are specialized proteins that each have a specific action such as causing chemical reactions, rearranging molecules, adding or subtracting components. Enzymes are not destroyed or changed during their action.

## **APPENDIX 1 – Report by the statutory auditors on the chairman's report**

*(Free translation of a French language original)*

**Erytech Pharma S.A.**

**Headquarters: 60 avenue Rockefeller - Bâtiment Adénine - 69008 Lyon**

**Share capital: €792,461**

### **Report by the statutory auditor about the Chairman's report**

**Year ended December 31, 2015**

Dear Shareholders,

To the shareholders,  
In our capacity as Statutory Auditors of Erytech Pharma S.A., and in accordance with Article L.225-235 of the French Commercial Code (“Code de commerce”), we hereby report to you on the report prepared by the Chairman of your company in accordance with Article L.225-37 (limited liability company with a Board of Directors) of the French Commercial Code for the year ended December 31, 2015.

It is the Chairman's responsibility to prepare, and submit to the Board of Directors for approval, a report on the internal control and risk management procedures implemented by the company and containing the other disclosures required by Article L.225-37 particularly in terms of the corporate governance measures.

It is our responsibility:

- to report to you on the information contained in the Chairman's report in respect of the internal control and risk management procedures relating to the preparation and processing of the accounting and financial information, and
- to attest that this report contains the other disclosures required by Article L.225-37 of the French Commercial Code (“Code de commerce”), it being specified that we are not responsible for verifying the fairness of these disclosures.

We conducted our work in accordance with professional standards applicable in France.

#### **1. Information on the internal control and risk management procedures relating to the preparation and processing of accounting and financial information**

These standards require that we perform the necessary procedures to assess the fairness of the information provided in the Chairman's report in respect of the internal control and risk management procedures relating to the preparation and processing of the accounting and financial information. These procedures consisted mainly in:

- obtaining an understanding of the internal control and risk management procedures relating to the preparation and processing of the accounting and financial information on which the information presented in the Chairman's report is based and existing documentation;

- obtaining an understanding of the work involved in the preparation of this information and existing documentation;
- determining if any significant weaknesses in the internal control procedures relating to the preparation and processing of the accounting and financial information that we would have noted in the course of our engagement are properly disclosed in the Chairman's report.

On the basis of our work, we have nothing to report on the information in respect of the company's internal control and risk management procedures relating to the preparation and processing of accounting and financial information contained in the report prepared by the Chairman of the Board in accordance with Article L.225-37 of the French Commercial Code (“Code de Commerce”).

## 2. Other information

We hereby attest that the Chairman’s report includes the other disclosures required by Article L.225-37 of the French Commercial Code (“Code de commerce”).

The statutory auditors  
Lyon, February 23, 2016

For KPMG Audit Rhône Alpes Auvergne  
French original signed by

For RSM Rhône Alpes  
French original signed by

Sara Righenzi De Villers  
**Partner**

Gaël Dhalluin  
**Partner**

**APPENDIX 2 - POLICY WITH REGARD TO ENVIRONMENTAL, SOCIAL, AND SOCIETAL RESPONSIBILITY**

# 2015 SOCIAL AND ENVIRONMENTAL RESPONSIBILITY REPORT

erytech 



## I. ERYTECH PHARMA'S CONTRIBUTION TO SUSTAINABLE DEVELOPMENT

Our group, ERYTECH Pharma, is a biopharmaceutical company that strives to become an international leader in customized medicine in the field of cancer.

ERYTECH Pharma Company aspires to conduct each of its actions according to the principles of Corporate Social Responsibility (CSR).

Placing the patient at the heart of our priorities and demonstrating ethics and respect toward each person are shared values within ERYTECH Pharma, and they form the basis for its approach as a socially responsible enterprise.

Our employees promote these values and develop business on a day-to-day basis. The company has made a particular commitment to train them and offer them a healthy and safe work environment so that they can continue to form a team that is motivated by the company's success.

ERYTECH Pharma has made a sustained investment in R&D to meet the challenges of public health and to offer innovative and radical therapeutic responses, particularly in the field of cancer.

Our current activities are therefore concentrated in research and development and production for clinical trials. They are being developed in close cooperation with health professionals, particularly physicians and pharmacists, whose expectations guide our group.

The company holds regulated status as a Pharmaceutical Company.

The purpose of this report is to share with the company's stakeholders the company's contribution to Sustainable Development.

## THE ERYTECH PHARMA MANAGEMENT TEAM

### **Gil Beyen**



Chairman and Chief Executive Officer. Gil was the Co-founder and Chief Executive Officer (CEO) of TiGenix (NYSE Euronext: TIG BB) for 12 years. Before creating TiGenix, he led the Life Sciences division at Arthur D. Little in Brussels. He holds a master's degree in bioengineering from the University of Louvain (Belgium) and an MBA from the University of Chicago (USA).

### **Jérôme Bailly**



Chief Pharmacist and Director of Pharmaceutical Operations. Before joining the company in 2007, Jérôme was the Director of QA/Production at Skyepharma and Laboratoire Aguettant. Jérôme holds a doctorate in pharmacy and a degree in chemical engineering, specializing in biopharmaceutical engineering and cellular production from École Polytechnique de Montréal.

### **Iman El-Hariry**



Medical Director. Iman El-Hariry, MD, PhD, is an oncologist and has over 15 years of product development experience in the biopharmaceutical industry. She served as VP Clinical Research at Syntha Pharmaceuticals in Boston, Global Head Oncology at Astellas APGD in Chicago and Group Director at GSK Clinical Oncology in London. Iman is a graduate of the faculty of medicine in Alexandria, Egypt, and holds a doctorate from the Imperial College of Science and Medicine in London, United Kingdom. As medical director of ERYTECH Inc., based in Boston, Dr. El-Hariry is in charge of international clinical and medical development and regulatory affairs.

### **Eric Soyer**



Chief Financial and Operating Officer. Eric Soyer has over 20 years of experience in management positions in financial and operational departments of public and private companies, both new and established. Over the past eight years, he has served as Chief Financial Officer of EDAP-TMS, a Nasdaq company based in Lyon specializing in therapeutic ultrasound, where he was in charge of administration and finance, investor relations, legal affairs and human resources. During his last three years at EDAP-TMS, he was also Chief Executive Officer of the French subsidiary of the group, which was responsible for R&D, production and distribution for France, South America and EMEA. He previously served as Chief Financial Officer and Director of Information Systems for a leading French nursing home and care facility company, and Chief Financial Officer and Chief Legal Officer for a large French insurance company. He began his career as a financial controller within the Michelin Group. Mr. Soyer received his Executive MBA from HEC Paris and an MBA from the University of Kansas in the United States, and he is a graduate of ESC Clermont in France.

## Our Mission

Our mission is to help patients to feel better and live longer.

## Our Vision

Our goal is to become the leading biopharmaceutical company focused on innovative therapies thanks to our ERYCAPS platform to treat rare forms of cancer and other orphan diseases.

## Our Strategy

To finalize the development of our main product, GRASPA / ERY-ASP, to obtain its marketing authorization for the treatment of LAL in Europe and the United States, and to extend its clinical development to other indications in oncology and in other countries.

To consolidate our ERYCAPS platform to develop new innovative therapeutic solutions targeting rare forms of cancer and other orphan diseases.

## Our Values

In 2015, ERYTECH Pharma organized a themed meeting on the company's corporate values, at which every employee was invited to speak.

This cross-company exercise allowed us to develop the necessary action plans to deploy the company's five key values:

- Vision, innovation and entrepreneurship
- Excellence, engagement and responsibility
- Communication and open-mindedness
- Teamwork
- Personal development

## Vision, Innovation and Entrepreneurship

ERYTECH Pharma's desire to preserve its entrepreneurial and collaborative spirit is reflected in:

- The consolidation of its technological platform and the upholding of coherence within its pipeline of projects,
- The reinforcement of its visibility and the development of new partnerships or external collaborations.

## Excellence, Engagement and Responsibility

"No compromise on quality" is the motto of every employee at ERYTECH Pharma. In the field, this approach relies on the open and transparent sharing of information regarding the regulatory and normative requirements of our activities. Personal support permits everyone to quickly become an autonomous and responsible actor in the company's focus on quality.

## Communication and open- mindedness

The life of our company is based on active internal communication and participatory management. We regularly organize meetings within departments about the various projects.

For example, each quarter, a meeting is organized with HR during which a wide range of themes is discussed, such as training programs, end-of-year interviews, company insurance, incentives, etc.

Twice a year, ERYTECH Pharma offers "corporate days," which are essential for building cohesion among the teams. In 2015, these "corporate days" were held on January 22–23 and June 25–26.

Also in 2015, the company set up a monthly newsletter called *Erynews*, which is distributed to all employees and among other things offers timely information about how projects are progressing and HR news.

## Teamwork

ERYTECH Pharma's operational efficiency relies daily on cross-disciplinary teamwork. Employees are frequently involved and invested with responsibility through the implementation of internal action plans.

## Personal development

Our structure, based on project management, reinforces our employees' feeling of trust and satisfaction thanks to the regular communication of results.

Furthermore, constant dialog between managers and staff makes it possible to assess professional growth on an ongoing basis.

## **II. JOBS AND SOCIAL RESPONSIBILITY**

### **a) Jobs**

#### **The ERYTECH Pharma workforce**

ERYTECH Pharma's workforce is located:

- At the Bioparc, an HSE business park, developed in the heart of the Rockefeller Health Center in the 8th arrondissement of Lyon,
- In Cambridge, Massachusetts, in the heart of the biotechnology company cluster.

Staff are highly qualified: managers represented 47% of the personnel in 2015. At the end of the year, the personnel included 12 employees holding a doctorate in science, medicine or pharmacy, and 19 employees holding a degree in engineering or a master's degree, i.e., 22% and 35% respectively of the total staff.

#### **Hires and dismissals**

In 2015, 19 new employees joined the company under different contracts: 13 permanent contracts and 6 fixed-term contracts.

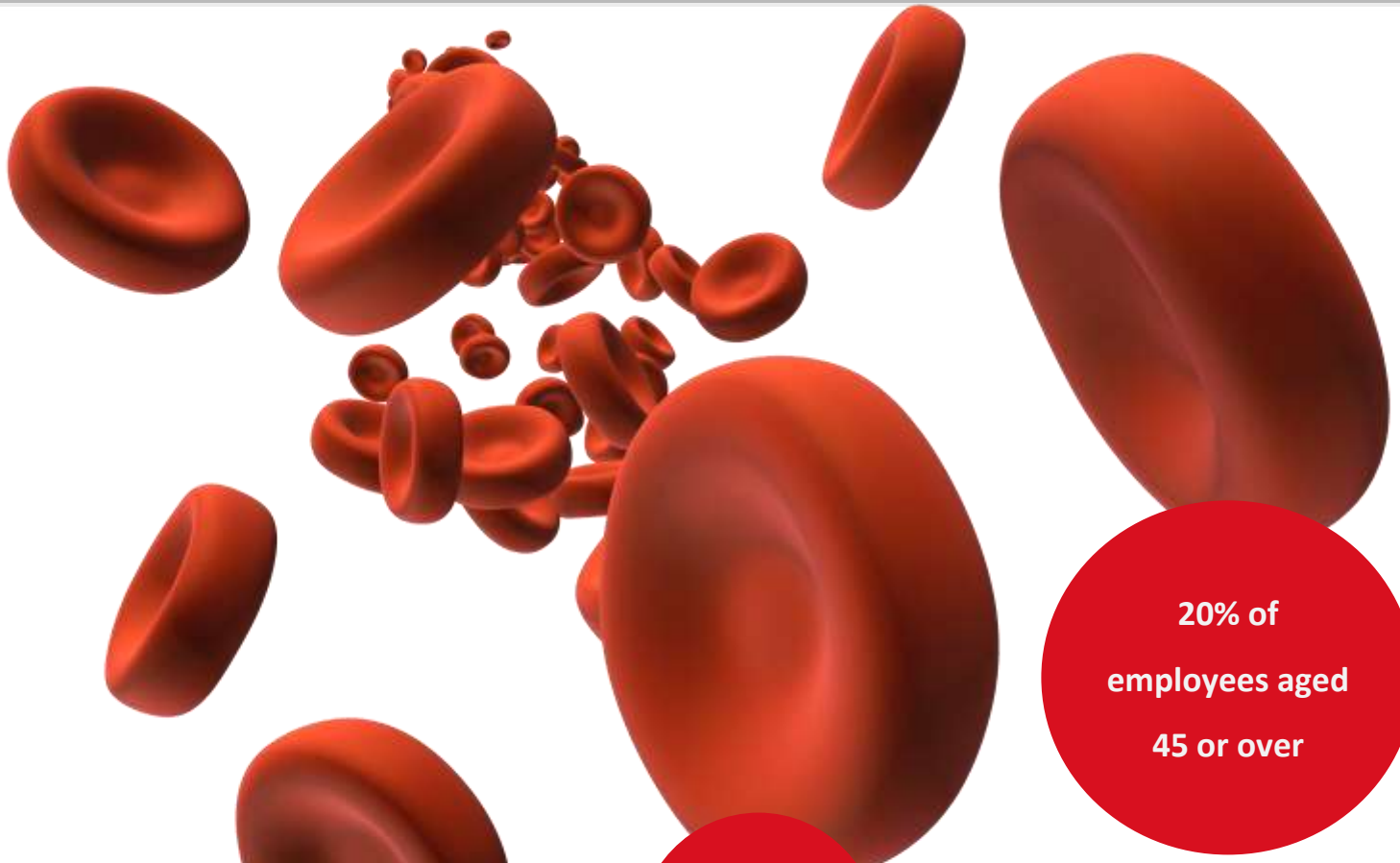
No layoffs were announced during the year. Five employees on permanent contracts resigned from the company as part of a dismissal process. One employee's fixed-term contract expired in 2015.

In 2015, ERYTECH Pharma hosted three interns coming from schools or universities. Interns received compensation that was above the legal minimum. As with any employee, they receive meal tickets, and their transportation costs are reimbursed at a rate of 50%. Internship periods are considered for purposes of seniority for those interns hired at the end of their internship.

ERYTECH Pharma also allows recent graduates to benefit from Volontariat International en Entreprise [International Volunteers in Business] (VIE). Additionally, the company sent one of its employees on an 18-month assignment to Philadelphia (USA).

#### **Remuneration and pay policy**

In addition to a fixed monthly salary, the company applies a variable pay component to every employee, that can vary from individual to individual. Bonuses take two factors into account: individual and collective performance based on achieving goals (quality, personnel, department, company).



20% of employees aged 45 or over

61% are women

Avg. age: 37

55 staff as of Dec. 31, 2015

89% are FTE

Avg. remuneration up 1% in 2015 (at comparable workforce)

46% of women are managers

10 jobs created

## **b) Organization of work**

ERYTECH Pharma complies with current law and has set the hours of the standard workweek to be 35 hours at the French site.

These terms apply on a prorated basis to part-time employees.

Employees working part-time do so at their request; this is due primarily, but not exclusively, to parental leave. In effect, in order to find an appropriate balance between professional activity and personal and family life for men and women, the company examines each request, with an aim to adapting the organization of duties.

The absenteeism rate (excluding maternity, paternity, or parental leave) is largely stable, with days of absence being due to illness and “sick child” days.

## **c) Labor relations**

Taking into account the size of its FTE workforce (fewer than 50 employees at the French site), the company has one employee representative and one alternate. Meetings with the employee representative are held regularly, in accordance with legal procedures and even beyond that, since all questions are considered, even those that do not lie within the purview of the powers awarded to the employee representative.

The agreements signed or commitment in the company are as follows:

- Incentive: an incentive agreement for the company’s staff was signed on November 29, 2013. This took effect on January 1, 2014. For 2014 and 2015, the company granted a supplementary profit-sharing and stipulated an amendment to contributions on employee savings plans such as PEE and PERCO (the management costs are borne 100% by the company).
- Remuneration for “sick child” days: unilateral commitment by the employer, who decides to pay for “sick child days.”
- Work on weekends/public holidays and annual leave: Personnel in the Quality Assurance, Research and Development, Quality Control, and Production departments may be required to work on weekends and/or public holidays. The memo of July 16, 2013, was modified on October 28, 2014, with a view to equalizing the remunerations established between departments and to propose remunerations equivalent to or greater than those that were previously established. The memo entered into effect on November 17, 2014.
- On-call weekends and public holidays: Personnel in the Quality Assurance, Quality Control, Production, and Research and Development departments may be required to work on weekends and/or public holidays through on-call duty. The memo of March 30, 2012 was modified on October 28, 2014 with a view to equalizing the remunerations established between departments and to propose remunerations equivalent to or greater than those that were previously established. The memo took effect on November 17, 2014.



**87% of staff  
are full-time**



**Absenteeism:  
1.9%**



#### **d) Health and safety**

In terms of Hygiene and Safety, ERYTECH Pharma complies with statutory and contractual requirements. As this provision is not mandatory, ERYTECH Pharma has not signed any collective agreement covering Workplace Health and Safety.

The company's activities are conducted in strict compliance with authorizations and approvals, and the safety of the personnel is a fundamental element for the company's sustainable development.

Additionally, from the beginning, the company has deployed a policy of management through quality with ISO 9001: 2008 certification covering all its processes. In this vein, ERYTECH has a general health and safety procedure governing the practices of personnel regarding biological and chemical risks.

As part of this, in 2015 ERYTECH Pharma appointed a Safety Officer in charge of protection and prevention of work-related risks (development, supervision and monitoring of a single document that identifies and evaluates work-related risks: DUERP).

No work-related accidents or illnesses were reported in 2015. However, a workplace accident in December 2014 resulted in 29 work days lost remaining in January 2015. This is why the severity rate was 0.4 in 2015.

Additionally, as part of assessing workplace strain and stress, in 2015 the company assessed the following four stress factors and concluded that they were not applicable to its employees:

- Work in a hyperbaric environment
- Nighttime travel
- Work in successive alternating shifts
- Repetitive work

Actually, no ERYTECH Pharma employee is exposed to these particular working conditions.

#### **e) Training**

The company continued its training policy within a long-term perspective, on the basis of actions intended to strengthen collective and individual skills and abilities.

ERYTECH Pharma has moreover defined the following areas of focus in relation to professional development for 2015:

- Excellence of experience and competencies;
- Better communication to work better together;
- Introduction of external professional practices;
- Communication in English.

These areas of focus have been defined based on economic outlook and changes in jobs, investments, and technologies within the business, and particularly for 2015:

- Internationalization;
- Improvement of the organization;
- The needs of a pharmaceutical company.

This is why 55% of employees aged 45 or over—or 6 out of 11 individuals—benefited from training activities.

**0  
workplace  
accidents**

**Frequency  
rate: 0.0**

**Severity  
rate:  
0.4**



**684.5 hrs  
training**

**14 hrs  
training  
per**

## **f) Equality of treatment**

### **Measures taken to promote gender equality**

In 2015, ERYTECH Pharma decided to continue the measures initiated in 2014 with a view to consolidating equality between men and women possessing equal qualifications and skills, and more particularly to give preference to the hiring of women at the “director” level and to give preference to the hiring of men at other levels. For example, Dr. Iman El-Hariry joined the company in June 2015 as Medical Director.

At December 31, 2015, in accordance with the interim provisions of Law no. 2011-103 of January 27, 2011, on the balanced representation of women and men on boards of directors and supervisory boards and on professional equality, more than 20% of directors were women.

### **Measures taken to promote employment and integration of disabled personnel and anti-discrimination measures**

ERYTECH Pharma’s hiring procedures:

- provide for the possible integration of disabled personnel,
- comply with the regulatory requirements regarding nondiscrimination when hiring,
- and illustrate these requirements through a list of “prohibited questions.”

In 2015, ERYTECH Pharma:

- published its job openings on the site Handi EM (specialized in hiring and retaining disabled persons in the pharmaceutical industry),
- or commissioned outside recruitment agencies, all committed to responsible hiring in terms of diversity.

Despite these measures, no applications were received from individuals with disabilities.

The company also decided to procure its office consumables from a regional disability-focused company, making it a regular supplier to the group.

## **g) Promotion and compliance with the stipulations of the fundamental conventions of the International Labor Organization as pertains to the respect for freedom of association and the right to collective bargaining, the elimination of discrimination in respect of employment and occupation, the elimination of forced or compulsory labor, and the effective abolition of child labor**

The group’s employees carry out their activities in France and the United States (Massachusetts).

It complies with the current regulations in these countries, particularly in terms of:

- Freedom of association: The company’s internal rules allow employees to participate in group activities. No restrictions or penalties are imposed where its employees are members of associations.
- Collective bargaining: Employee representatives may negotiate and stipulate one or more collective agreements pursuant to the conditions established under the Labor Code, where the purpose of such agreement is not covered by the collective agreement applicable to the company and/or is subject to collective bargaining in compliance with labor law.
- Elimination of forced or compulsory labor, and the effective abolition of child labor: The group does not operate in a country in which such practices exist.
- Elimination of job-related and professional discrimination.



### III. ENVIRONMENTAL INFORMATION

The activities implemented include contract industrial production. These activities therefore result neither in a massive use of raw materials, nor in significant energy consumption, nor any significant discharge of greenhouse gases into the environment, nor use of soil. Furthermore, the activities inherent to the company do not generate particular auditory nuisances for its employees or neighbors.

Activities are localized within the Bioparc, a health-, safety- and environment-focused business park developed as part of the Rockefeller Health Center in Lyon. The company possesses quantitative elements that allow it to monitor practically all of its water and electricity consumption (except for consumption in the common areas due to the ways the building is managed).

The company has not identified any significant environmental risks associated with its activity such as could lead to establishing a provision against these risks or specifically training its employees with regard to these issues.

To date, the company has not identified any opportunities for taking steps to protect biodiversity and adapting to the consequences of climate change.

In this setting, the following environmental indicators were chosen as being relevant:

- a) General environmental policy;
- b) Sustainable use of resources: energy consumption and water volume;
- c) Pollution and waste management: quantity of waste sent to a specific treatment center.

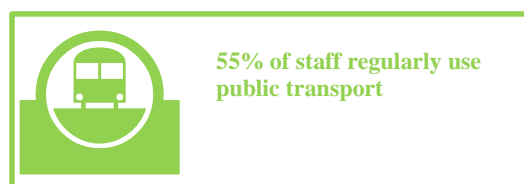
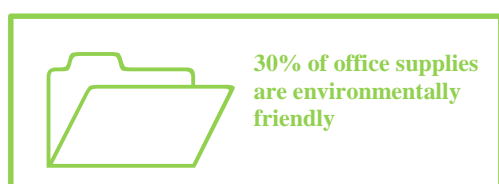
#### a) General environmental policy

Despite an environmental impact deemed to be low, the company and its employees are involved in the following actions related to sustainable development:

- The use of ecologically responsible practices in paper management:
  - ✓ Use of an electronic document management system.
  - ✓ Default configuration of all printers to print in black and white and double-sided.
  - ✓ Purchase of only “environmentally friendly” reams of paper (EU Ecolabel or PEFC).
  - ✓ Destruction and recycling of all unused internal and external documents (since the second half of 2013) by a specialized company.

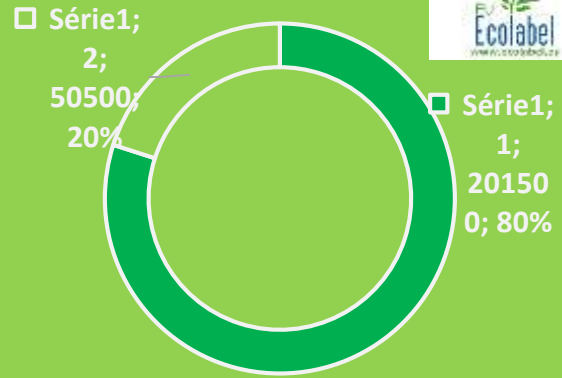
All these practices together constitute an ongoing virtuous cycle to minimize the number of trees that are cut down.

- The introduction of a responsible procurement policy for office consumables (buying “environmentally friendly” supplies whenever possible).
- Use of energy-saving devices: widespread use of timers for lights and air-conditioning.
- Use of teleconferencing instead of physically travelling to meetings.
- Encouraging employees to choose mass transit over personal vehicles. ERYTECH Pharma is based in the heart of Lyon’s health hub and is easily accessible by public transport, thus helping to limit car use.





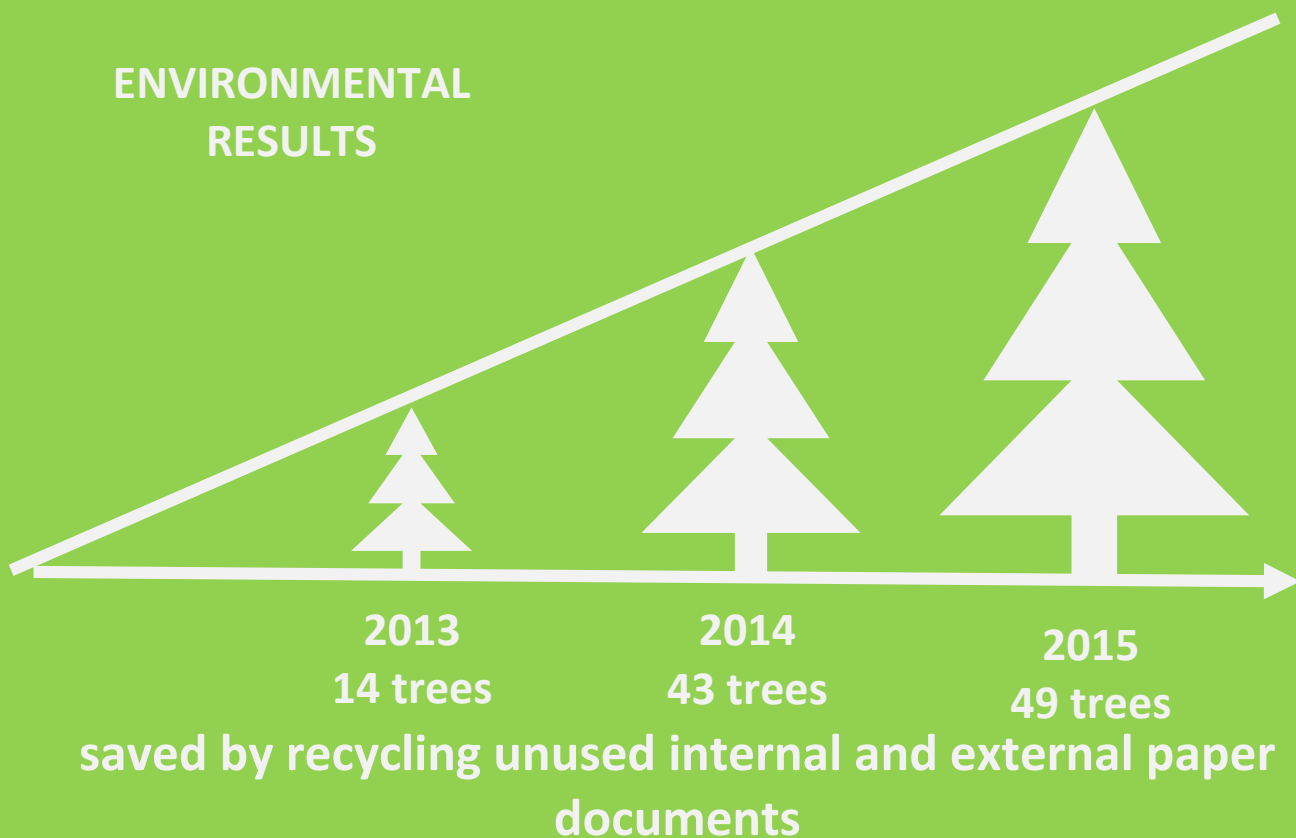
**RESPONSIBLE  
PURCHASING:**  
100% of paper reams  
used are  
environmentally  
friendly



**ELIMINATION BY  
SORTING AND  
RECYCLING WASTE**



**ENVIRONMENTAL  
RESULTS**



### b) Sustainable use of resources

- The only energy source used by the company is electric energy. Since November 1, 2015, the company has been powering its French premises with green energy (renewable wind, solar, and hydro power) sourced in France.

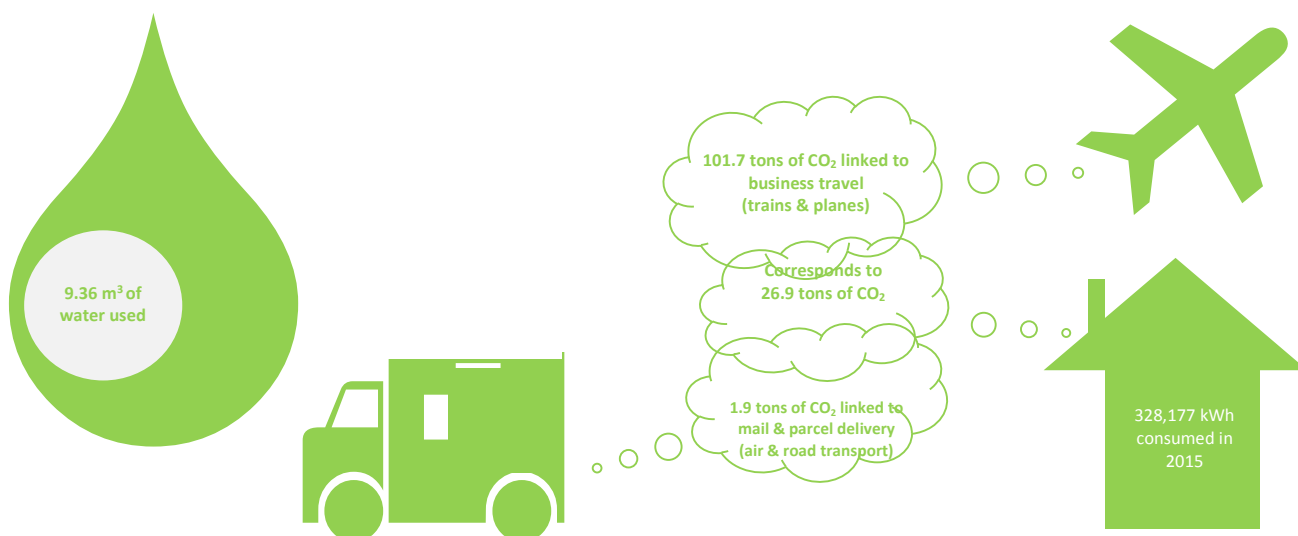
- Mains-water consumption corresponds to the pharmaceutical company's activities. Water discharged after use is water that comes from washing cycles (sinks, washing machines).

- The company outsources the logistics associated with its activities.

It does not have all the quantitative information enabling it to ensure the exhaustive monitoring of associated CO<sub>2</sub> emissions.

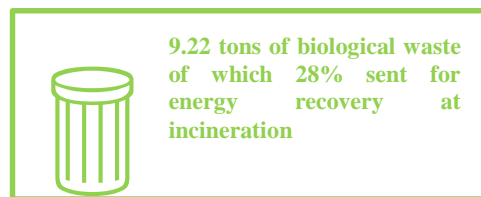
Intercontinental business trips are frequently necessary given that the company has been international since 2013.

Despite multiple attempts, information on CO<sub>2</sub> emissions associated with the shipment of drugs has not been successfully obtained.



### c) Pollution and waste management

Within the context of its CSR activities, ERYTECH Pharma works to make employees aware of how to methodically manage their consumables and waste. For example, as part of the objective to limit the environmental impact of its waste, the company arranges for a specialized company to systematically remove and treat its biological and chemical waste resulting from laboratory and production activities, with a view to ensuring full traceability through the treatment processes used.



## IV. SOCIETAL INFORMATION

### a) Territorial, economic and social impacts from the company's activity

The company's desire to align the development of its business with that of its region is a major characteristic of the group; in particular, it subcontracts certain preclinical studies to regional entities, and by creating partnerships with the Ecole Vétérinaire de Lyon [Veterinary School of Lyon] and Université Claude Bernard in Lyon. It also calls on numerous consulting firms in the region (patents, finance, etc.).

ERYTECH Pharma is also an active member:

Nationally: in three professional organizations in the field of health and/or biotechnology: Les Entreprises du Médicament (LEEM) [medicinal products companies], France Biotech and the Société Française des Sciences et Techniques Pharmaceutiques (SFSTP) [the French society for pharmaceutical sciences and technologies].

At the regional level: of the competition-focused Lyonbiopôle and Cancéropôle Lyon Auvergne Rhône Alpes, and it also renewed its membership of the Association des Fabricants de l'Industrie Pharmaceutique de la Région Rhône-Alpes (Association of Pharmaceutical Industry Manufacturers in the Rhône-Alpes Region - AFIPRAL) with the objective of growing the performance of member companies by mobilizing a regional network involving the sharing of industrial know-how.

Due to the nature of its activities and its geographical location, ERYTECH Pharma does not create a need for dialog with inclusion, environmental protection or consumer associations or with neighbors.

Nonetheless, ERYTECH Pharma seeks to create close relationships with training institutions and universities, and allows its employees to teach courses during their work time and within their field of expertise.

ERYTECH Pharma regularly participates in symposia, congresses and annual conferences, including, in 2015:

- BIO International Convention in Philadelphia;
- AACR (American Association for Cancer Research) Annual Meeting in Philadelphia;
- ASCO (American Society of Clinical Oncology) Annual Meeting in Chicago;
- ASH (American Society of Hematology) Annual Meeting in Orlando.

These meetings allow the company to meet healthcare professionals and key opinion leaders with a view to pursuing its areas of development in innovative products and to satisfying unmet medical needs.



## **b) Relationships with stakeholders**

### **Relationships with its shareholders and investors**

All shareholders have access to full, transparent and clear information, adapted to the needs of each person and useful for an objective assessment of the group's growth strategy and results. This financial communications policy is intended to ensure that all shareholders have information in compliance with the practices of the financial marketplace.

A wide variety of public documents, including those distributed as regulated information, covers the company's activity, strategy and financial information, and is accessible on the company's website under the Investors heading, in French and in English. It also has a dedicated e-mail address for investors ([investors@erytech.com](mailto:investors@erytech.com)).

In terms of regulated information, the company releases the annual information required of a listed company. The financial information is supplemented by periodic information and press releases intended for the financial community and more broadly the public, concerning subjects that are important for understanding the company's activities and strategy.

The success of the reserved capital increase in the form of a private placement in the amount of €25.4 million on December 3, 2015, attests to the company's influence not only on the European market, but also on the American market. This operation indirectly enhances the visibility of French biotechnology companies and regional know-how in France and abroad. Last, the funds raised during this capital increase will ensure:

- The continuation of the clinical development of its ERY-ASP/GRASPA product, particularly for the treatment of acute lymphoblastic leukemia (ALL) as a first-line therapy in Europe and the United States and of non-Hodgkins lymphoma;
- The development of new drugs, with the launch of a Phase I study for its candidate product ERY-MET and the incubation of the anti-tumoral ERY-VAX vaccination program;
- The development of the ERYCAPS technological platform and other preclinical development programs.

This biomedical research is performed with the goal of providing a tailored response to unmet medical needs in the indications studied.

On November 20–21, 2015, ERYTECH Pharma participated at the Actionaria Show in Paris in order to meet private investors.

### **Relationships with its partners**

At least once a year, steering committees are organized between the company and its primary partners, for the purpose of discussing strategy and progress in joint projects.

### **Partnership or sponsorship actions**

Through its sponsorship activities, ERYTECH Pharma supports associations and projects in the healthcare field, and particularly in the fight against cancer. Their areas of common interest are consistency with our values and our desire for building strong roots in the region.

Thus, in 2015, the company renewed its agreement with the Laurette Fugain Association. Under this agreement, its employees supported the national days devoted to fighting leukemia, organized for March 28 and 29, 2015, by distributing leaflets.

In addition, on October 4, 2015, 15 ERYTECH Pharma employees participated in the seventh Run in Lyon 10K race, wearing the association's logo on their race vests.

**ERYTECH** soutient  
les **JOURNÉES NATIONALES CONTRE LA LEUCÉMIE.**  
Rejoignez le mouvement,  
et faites un don pour soutenir la recherche médicale.  
**PARCE QU'ENSEMBLE, NOUS SOMMES PLUS FORTS.**  
Merci !

**JE  
DONNE  
TU  
CHERCHES  
ILS  
GUÉRISSENT**

*Si tu donnes  
t'es au top !*

*Enzo*

**28 et 29 mars 2015**  
**JOURNÉES NATIONALES  
CONTRE LA LEUCÉMIE**

*Enzo et Vanessa Demouy*



Pour vos dons RDV sur [www.contrelaleucemie.org](http://www.contrelaleucemie.org)

### **c) Subcontractors and suppliers**

Seeking to share its values with its suppliers and subcontractors, ERYTECH Pharma encourages regular collaborations, to the extent possible, with a view to building client-supplier and client-subcontractor relationships of trust. This aspect is strengthened by the strategic nature of certain suppliers. As such, the stakes surrounding strategic supplier relationships allow for a closer dialog. Each supplier contract is monitored internally by dedicated teams, and a single contact person is designated.

The company also has a supplier selection and monitoring procedure for its business relationships with suppliers for certain critical elements (clinical trials, nonclinical trials, pharmacovigilance and production unit suppliers). Given the regulatory aspects of the company's activities, most service providers and suppliers must also comply with the Best Laboratory and/or Clinical and/or Manufacturing Practices.

ERYTECH Pharma undertakes to apply CSR principles to its purchasing, selecting goods and services produced and provided in compliance with rigorous environmental, social and ethical principles. We pursue our involvement in the monitoring of CSR criteria compliance by suppliers, as specified in our internal procedures, giving preference to suppliers that have a CSR policy that complies with the requirements of Grenelle II during the preselection stage, all other factors being equal. ERYTECH Pharma assesses its suppliers based on an evaluation questionnaire, in order to learn about the CSR activities undertaken by its partners.

The company's procedures provide for supplier audits based on the type of purchases (pharmaceutical business supplier, new supplier, critical nature, etc.) as well as follow-up audits. However, supplier audits do not incorporate the CSR aspects given the structure of the upstream market.

### **e) Fair practices**

Various policies have been implemented to reinforce the approach to ethics:

- Procurement policy:
  - ✓ a limit of €20,000, excluding taxes, on authorizations to enter into contracts. Above that limit, authorization from the quality department is mandatory;
  - ✓ separation of duties for payments;
  - ✓ software barriers and traceability.
- Guide pertaining to the prevention of insider crimes and misconduct;
- Procedure for the management of health relations for the purpose of complying with the "Bertrand law";
- Management procedure for the handling of personal data and designation of a data protection contact person on August 29, 2014;
- Travel charter: indicating the rules governing business travel.

**e) Measures to promote patient health and safety**

At its current stage of development, none of the medicinal products being developed by the company today has been marketed or received marketing approval. The development of medicinal products is highly controlled by strict regulation. The various phases in the development of medicinal products require animal tests at the outset (preclinical development), and then tests with humans (clinical development). Each of the development phases requires prior authorization delivered by the oversight authorities and approval by the ethics committees.

As part of the research and development activities, the company implements preclinical studies within a strict framework. For these phases, the company may make use of service providers that conduct animal experiments. These experiments must follow a national procedure pertaining to the protection of animals used for scientific purposes, in accordance with Decree no. 2013-118 of February 1, 2013, which contains, in particular, an obligation to obtain approval prior to conducting any project involving the performance of one or more experimental procedures using animals.

**f) Other actions undertaken to promote human rights**

The company has not undertaken any additional action to promote human rights.