

*This is a free translation of Adocia's reference document issued in the French language, for informational purposes only.*

Reference  
document  
2018

# INNOVATIVE MEDICINE FOR EVERYONE EVERYWHERE

Photo Lotte Meijer

ADOCIA





# ADOCIA

innovative medicine  
for everyone, everywhere



*This is a free translation of Adocia's reference document issued in the French language, for informational purposes only.*

A French société anonyme (corporation) with €693,124.40 in share capital

Registered office: 115 avenue Lacassagne

69003 Lyon, France

Lyon Trade and Companies Registry No. 487 647 737



This registration document was filed with the Autorité des Marchés Financiers (the "AMF") on April 12<sup>th</sup>, 2019 in accordance with Article 212-13 of its General Regulation. It may be used to support a financial transaction if supplemented by a securities note approved by the AMF. This document was prepared by the issuer and is the responsibility of its signatories.

Copies of this registration document are available free of charge from the Company at 115, Avenue Lacassagne, 69003 Lyon. In addition, an electronic version is available on the Company's website ([www.adocia.com](http://www.adocia.com)) and on the AMF website ([www.amf-france.org](http://www.amf-france.org)).

## NOTICE

In this registration document, the terms "Adocia" or the "Company" refer to Adocia, a French société anonyme (corporation) whose registered office is located at 115, Avenue Lacassagne, 69003 Lyon, France, and which is registered with the Lyon Trade and Companies Registry under number 487 647 737 and, when appropriate, its subsidiary, Adocia Inc., a company incorporated in the state of Delaware, whose head office is located at 2090 Dipinto Avenue, Henderson, NV 89052, U.S.A.

The consolidated financial statements prepared under IFRS for the fiscal year ended December 31, 2018 are presented on pages 126 to 158 of this registration document. The statutory auditors' report on the consolidated financial statements prepared under IFRS for the fiscal year ended December 31, 2018 is presented on pages 159 to 165 of this registration document.

The corporate financial statements prepared under French GAAP for the fiscal year ended December 31, 2018 are presented on pages 166 to 179 of this registration document. The statutory auditor's report on the corporate financial statements prepared under French GAAP for the fiscal year ended December 31, 2018 is presented on pages 180 to 185.

Pursuant to Article 28 of Commission Regulation (EC) No. 809/2004 of April 29, 2004,

- The consolidated consolidated financial statements ended December 31, 2017 and the related statutory auditors' reports presented respectively in paragraph 4.1 and 4.2 of the 2017 registration document filed with the AMF on April 19<sup>th</sup>, 2018 with reference D.18-0347.
- The consolidated consolidated financial statements ended December 31, 2016 and the related statutory auditors' reports presented respectively in paragraph 20.A of the 2016 registration document filed with the AMF on April 11<sup>th</sup>, 2017 with reference D.17-0363

Are incorparetd by reference in this registration document.

The non-included parts of this(ese) document(s) are either irrelevant for the investor or covered elsewhere in the registration document.

A glossary containing the definitions of certain technical terms used in this registration document, as well as an index of abbreviations used, can be found in paragraph 6.6. Terms indicated by an asterisk (\*) are defined in the glossary.

## DISCLAIMER

### Market and competition information

This registration document contains, in particular in section 1.3 "*Description of Activities*", information about the Company's markets and competitive position. This information is taken, in particular, from studies conducted by external sources. Publicly available information that the Company deems reliable has not been verified by independent experts, and the Company cannot guarantee that a third party using different methods to collect, analyze or calculate data on these markets would obtain the same results.

### Forward-looking information

This registration document contains information on the Company's outlook and development priorities. At times, this information is identified by the use of the future or conditional tense or forward-looking words such as "consider", "plan", "think", "have as an objective", "expect", "intend", "should", "aspire to", "estimate", "believe", "wish", "could" or, where applicable, the negative form of these terms, or any variation thereof or similar terminology. This information is not historical data and should not be viewed as a guarantee that the facts and events described will occur. This information is based on data, assumptions and estimates that the Company deems reasonable. It may change or be modified due to uncertainties associated with, in particular, the economic, financial, competitive and regulatory environment. This information is provided in the various sections of this registration document and includes data related to the Company's intentions, estimates and objectives with respect to, among other things, the market in which it operates and its strategy, growth, results, financial position, cash position and forecasts. The forward-looking information in this registration document is provided only as of the date of this registration document. The Company operates in a constantly changing competitive environment. Therefore, it cannot anticipate all risks, uncertainties and other factors that may affect its business, the potential impact thereof on its business, or the extent to which the occurrence of a risk or combination of risks could have significantly different results from those mentioned in any forward-looking information. It should be noted that none of this forward-looking information is a guarantee of actual results.

### Risk factors

Investors are advised to carefully review the risk factors described in paragraph 1.5 "*Risk Factors*" of this registration document before making any investment decision. The occurrence of any or all of these risks may have a material adverse impact on the Company's business, financial position, results or outlook. Furthermore, other risks not yet identified or not deemed significant by the Company as of the date of this registration document may also have a material adverse impact.





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**1**  
**PRESENTATION**  
**OF ADOCIA**  
**AND ITS**  
**ACTIVITIES**





# Chapter 1

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# 1 PRESENTATION OF ADOCIA AND ITS ACTIVITIES

## 1.1 Selected financial information

### Condensed income statement

<i>In (€) thousands, Consolidated financial statements, IAS/IFRS</i>	<b>FY 2018 (12 months)</b>	<b>FY 2017 (12 months)</b>
Operating revenue	53 930	27 177
Of which revenue	47 389	19 469
<b>PROFIT (LOSS) FROM ORDINARY OPERATING ACTIVITIES</b>	<b>9 707</b>	<b>(8 180)</b>
Financial income (loss)	2 050,7	(335,4)
Profit (loss) before tax	11 758	(8 516)
Tax	(4 144)	(35)
Net income (loss)	7 615	(8 550)
<b>TOTAL NET PROFIT (LOSS)</b>	<b>7 458</b>	<b>(8 741)</b>

### Condensed balance sheet

<i>In (€) thousands, Consolidated financial statements, IAS/IFRS</i>	<b>FY 2018 (12 months)</b>	<b>FY 2017 (12 months)</b>
<b>Non-current assets</b>	<b>9 058</b>	<b>9 069</b>
of which: land, building, fixtures and facilities	7 399	7 327
of which: laboratory equipment	942	1 253
<b>Current assets</b>	<b>60 984</b>	<b>44 692</b>
of which: cash and cash equivalents	39 841	34 778
<b>TOTAL ASSETS</b>	<b>70 043</b>	<b>53 761</b>
<b>Equity</b>	<b>45 848</b>	<b>36 857</b>
<b>Non current liabilities</b>	<b>9 340</b>	<b>8 022</b>
of which: long-term financial debts	4 892	5 781
<b>Current liabilities</b>	<b>14 854</b>	<b>8 882</b>
<b>TOTAL LIABILITIES</b>	<b>70 043</b>	<b>53 761</b>

### Condensed cash flow statement

<i>In (€) thousands, Consolidated financial statements, IAS/IFRS</i>	<b>FY 2018 (12 months)</b>	<b>FY 2017 (12 months)</b>
Net cash flow generated by operating activities	6 313	(22 227)
Net cash flow in connection with investment transactions	(1 034)	(1 685)
Net cash flow in connection with financing transactions	(216)	653
<b>Changes in net cash</b>	<b>5 063</b>	<b>(23 259)</b>
Cash and cash equivalents at the start of the year	34 778	58 037
Cash and cash equivalents at year-end	39 841	34 778

## 1.2 About Adocia and its evolution

### 1.2.1 Legal presentation of the company

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The company's legal name is Adocia.

It is registered with the Lyon Trade and Companies Registry under number 487 647 737.

It was incorporated on December 16, 2005 as a French *société à responsabilité limitée* (limited liability company) for a term of 50 years from the date of its registration with the Trade and Companies Registry on December 22, 2005, i.e., until December 22, 2055, unless such term is extended, or the Company is dissolved before its term expires.

It was converted into a *société par actions simplifiée* (simplified joint stock company) by a decision of the sole shareholder adopted on July 31, 2006, and then into a *société anonyme* (corporation) with a board of directors by decision of the general shareholders' meeting on October 24, 2011.

The company is a *société anonyme* governed by French law and, with respect to its operations, is primarily subject to Article L. 225-1 et seq. of the French Commercial Code (*Code de Commerce*).

The closing date for its fiscal year is December 31.

The company's registered headquarters is located at 115 Avenue Lacassagne, 69003 Lyon, France.

The company's contact information is shown below:

Phone: +33 (0) 4 72 61 06 10

Fax: +33 (0) 4 72 36 39 67

Email: [contactinvestisseurs@adocia.com](mailto:contactinvestisseurs@adocia.com)

### 1.2.2 General presentation of the company

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#### 1.2.2.1 Mission

Adocia's goal is to deliver "Innovative medicines for everyone, everywhere."

Adocia is a clinical biotechnology company specializing in the development of innovative formulations of pre-approved therapeutic proteins and peptides. In the diabetes field, Adocia's portfolio of injectable products for treatment of diabetes, is among the largest and most differentiated of the industry, featuring six clinical-stage products and one in preclinical stage. Additionally, Adocia expanded its portfolio to include the development of treatments of obesity and short bowel syndrome.

The BioChaperone<sup>®</sup> patented technological platform aims to improve the efficacy and/or safety of therapeutic proteins, while also making them easier for patients to use. Adocia adapts BioChaperone for each protein for a given application.

Adocia's clinical pipeline contains five innovative insulin formulations for the treatment of diabetes: two ultra-rapid insulin lispro analogs (BioChaperone<sup>®</sup> Lispro U100 and U200), a rapid-acting human insulin (HinsBet<sup>®</sup> U100) and a combination of long-acting insulin glargine and rapid-acting insulin lispro (BioChaperone<sup>®</sup> Combo) and a prandial combination of human insulin with amylin pramlintide (BioChaperone<sup>®</sup> PramInsulin). It also includes an aqueous formulation of human glucagon (BioChaperone<sup>®</sup> Glucagon) for the treatment of hypoglycemia. Adocia's preclinical pipeline includes combinations of insulin glargine with GLP-1 receptor agonists (BioChaperone<sup>®</sup> Glargine GLP-1) for the treatment of diabetes, a ready-to-use combination of glucagon and a GLP-1 receptor agonist BioChaperone<sup>®</sup>

## Presentation of Adocia and its activities

Glucagon GLP1) for the treatment of obesity and a ready-to-use aqueous formulation of teduglutide (BioChaperone® Teduglutide) for the treatment of short bowel syndrome.

Adocia and Chinese insulin leader Tonghua Dongbao Pharmaceuticals Co. Ltd entered into a strategic alliance. In April 2018, Adocia granted Tonghua Dongbao Pharmaceuticals Co. Ltd licenses to develop and commercialize BioChaperone Lispro and BioChaperone Combo in China and other Asian and Middle-Eastern territories. The licensing included 50 million dollars upfront and up to 85 million dollars development milestones, plus double-digit royalties on sales. In June 2018, Tonghua Dongbao agreed to manufacture and supply active pharmaceutical ingredients insulin lispro and insulin glargine to Adocia globally, excluding China, to support Adocia's portfolio development in these territories. Detailed information on this partnership and on Tonghua Dongbao Pharmaceuticals Co. Ltd are available under section 1.3.7 of this registration document.

### 1.2.2.2 Significant events in the development of the company's business

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As the results of these research efforts and their commercial development take many years, for the first ten years the company's annual financial statements have mainly reflected research and development costs which, for the most part, have been financed by capital increases, Bpifrance repayable advances and grants and the research tax credit.

Since its inception on December 16, 2005, and before its IPO, the company raised over €27 million through capital increases subscribed, in particular, by the its founders, Messrs. Gérard, Olivier and Rémi Soula, and institutional investors (IdInvest, Amundi, Viveris, BioAm, SHAM and InnoBio). In 2012, the Company was listed on the Euronext Paris regulated market and raised more than €27.4 million (excluding transaction costs). In March 2015, it completed a private placement of nearly €32 million by issuing new shares to investors specialized in the healthcare sector, particularly in the United States.

In 2009, the Company recorded its first revenue when it concluded research and collaboration agreements. At the end of 2011, a major license agreement was signed with the Eli Lilly group, from which it received an up-front payment of €7.6 million in early 2012. In July 2013, the Company announced the end of this collaboration agreement, thereby recovering its rights to develop an ultra-rapid analog insulin and enabling it to conduct its own clinical studies to establish proof of concept.

Following the clinical results obtained in late 2013 and throughout 2014, Adocia convinced Eli Lilly to renew their collaboration. On December 19, 2014, the two companies signed a licensing agreement for the development of an ultra-rapid insulin called BioChaperone® Lispro. At the time the agreement was signed, the Company received a non-repayable up-front payment of \$50 million (€41 million).

The years 2015 and 2016 were marked by intense activity under this partnership with the completion of six clinical studies on the BioChaperone Lispro formulation and the receipt of a \$10 million milestone payment following the positive results of the bioequivalence study of the concentrated formulation of BioChaperone Lispro.

Throughout 2016, the Company focused its efforts entirely on diabetes by discontinuing its monoclonal antibodies and Driveln programs and launching new BioChaperone Combo projects, combinations of long-acting insulin glargine with GLP-1 and, recently, combinations of prandial insulins.

On January 26, 2017, the Company announced that Eli Lilly was ending the collaboration on BioChaperone Lispro. Adocia has recovered all its rights to this product and is looking for a new partner to continue phase 3 development.

In 2017 Adocia achieved key milestones in the development of its products, by demonstrating a better fast-off profile for BioChaperone Lispro than for the Novo Nordisk ultra-rapid insulin Fiasp®, successfully completing the first clinical trial for the BioChaperone Glucagon project and demonstrating the dose linearity of BioChaperone Combo. The company also announced the expansion of its portfolio to new therapeutic fields other than diabetes, with the launch of two new projects for the treatment of obesity and short bowel system.

In April 2018, Adocia signed with the Chinese company, Tonghua Dongbao Pharmaceuticals Co. Ltd, a strategic alliance for the development and commercialization of BioChaperone® Combo and BioChaperone® Lispro in China and in certain other countries. These licensing agreements have a total potential value of \$ 135 million (Adocia is

expected to receive double-digit royalties on the future sales of both products) including \$50 million when the partnership was signed. In June 2018, the companies also signed two global supply agreements for Insulin Lispro and Insulin Glargine. Thus, Adocia will be able to carry out its BioChaperone Lispro et BioChaperone Combo projects in Europe, in the US and in Japan.

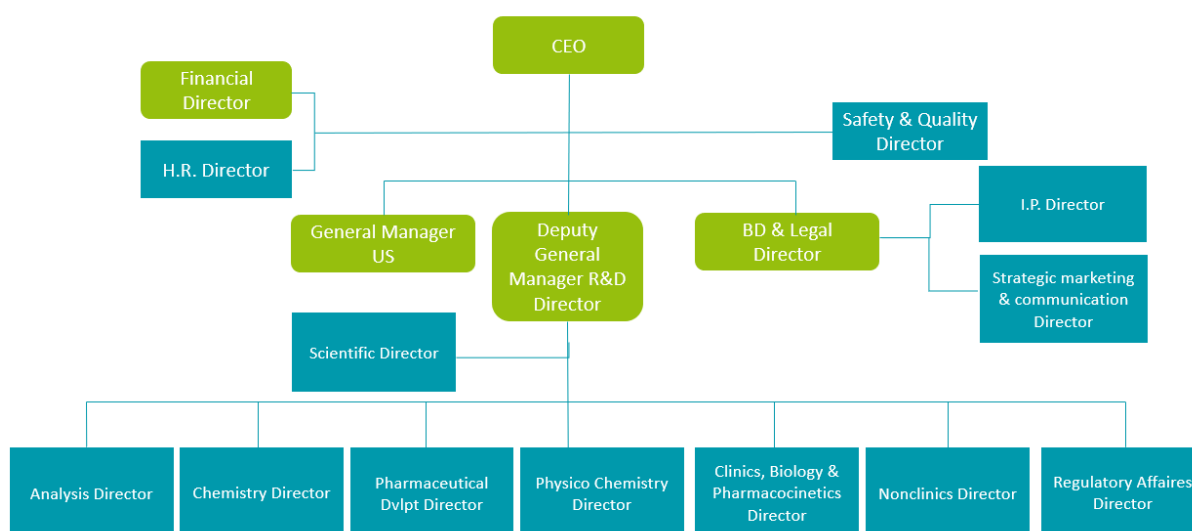
In 2018, Adocia carried on with the development of both products in this new partnership. The company also further developed its portfolio and successfully lead the first clinical trial on BioChaperone Pramlintide Insuline in people with type 1 diabetes.

In legal affairs, 2018 was also marked by the two-parts arbitration procedure launched against Eli Lilly & Co., which are detailed in paragraph 1.3.7.3.

## 1.2.3 Organizational chart

### 1.2.3.1 Organization of the Company

At the date of issue of this registration document, the organizational chart for the Company is as follows:



### 1.2.3.2 Subsidiaries, branches and secondary establishments

In February 2015, the company founded Adocia Inc., a subsidiary in the United States, a company incorporated in the state of Delaware, whose head office is located at 2090 Dipinto Avenue, Henderson, NV 89052, U.S.A. Adocia wholly owns its subsidiary Adocia Inc., which at the date of the present registration document had two employees: a marketing director and a business development director. The objective is for the subsidiary to facilitate interaction with the US market and to locate the Company's advocacy activities in the United States. M. Stephen Daly is US General Manager.

Stephen Daly has more than 30 years of experience in commercialization and business development for pharmaceutical and biotech products across multiple therapeutic categories. Before Adocia, he served as the Vice President of Commercial at Halozyme Therapeutics for their ultra-rapid insulin program. Stephen Daly's experience in the diabetes field also includes several years at Amylin Pharmaceuticals in marketing and brand leadership for Byetta® and Symlin®.

## Presentation of Adocia and its activities

At the date of this registration Document, the Company does not have a branch or a secondary establishment.

### 1.2.3.3 Management

ADOCIA is managed by an executive committee made up of four members: Gérard Soula, CEO, Valérie Danaguezian, CFO, Olivier Soula, Deputy General Manager – R&D Director, Rémi Soula, Business Development and Legal.

They have significant experience in managing technological innovation and partnerships with major biopharmaceutical groups, as well as in drug delivery of therapeutic proteins and in the development of medical devices.

Their experience is summarized below,

**Dr. Gérard Soula, PhD, MBA – President and CEO:** cf. paragraph 3.1.4 of the current reference document.

**Dr. Olivier Soula, PhD, MBA – Deputy General Manager – R&D Director:** cf. paragraph 3.1.4 of the current reference document.

**Dr. Rémi Soula: Director of Business Development and Legal**

Rémi Soula holds a doctorate in polymer chemistry from CPE Lyon. He did a post-doctorate at Max Planck Institute in Berlin. He also holds an MBA at HEC Paris. He began his career with Flamel Technologies as a Senior researcher in the synthesis of new polymers. After 3 years at Flamel, he co-founded Adocia with Gérard and Olivier Soula.

Today he is Director of Business development and Legal. He is the co-author of 30 patents and 6 scientific publications

**Mrs. Valérie Danaguezian: Administrative and Financial Director**

Valérie Danaguezian is a graduate of ISC and began her career in corporate auditing and financial consulting with Calan Ramonilo et Associés, a member of Deloitte & Touche, where she stayed for four years. In 1991, she joined Sanofi Pasteur where she was in charge of the group's financial consolidation, eventually being promoted as Director of the group's research and development expenditures management control. In 2003 she joined Flamel Technologies and held the position of administration and financial officer for 3 years. In 2006 Valérie Danaguezian joined Adocia as CFO and member of the Executive team. She is specialized in the financial management of innovative research and development projects, and has acquired extensive experience in management control systems, international standards and internal controls.

## 1.2.4 Investments and real estate

The company outsources a significant portion of its research and development activities. Its investments in fixed assets are therefore relatively low in value compared with its research and development expenditures, with the exception of the real estate investments presented in the section below.

<i>In (€) thousands</i>	<b>FY 2018 (12 months)</b>	<b>FY 2017 (12 months)</b>
Intangible assets	70	77
Property, plant and equipment	5	861
Other tangible assets	764	709
Non-current financial assets	250	0
<b>TOTAL</b>	<b>1 089</b>	<b>1 648</b>

### 1.2.4.1 Major investments

#### ▪ Description of real estate

The Company is headquartered in Lyon, 115 avenue Lacassagne in the 3rd *arrondissement* (district) of the city of Lyon.

The Company has been located at these premises since it was founded, initially as a tenant of the city of Lyon (Métropole de Lyon), and then as owner. In February 2016, to make its presence at this site permanent, the Company acquired the building with a total area of 7,120 m<sup>2</sup>, the land on which the building is located and parking spaces. The acquisition of this property for a total of €5.5 million was financed by a bank loan. In 2017, the company added to its installation on the site by acquiring a hangar adjacent to the main building for €0.5 million and developing a green space in the interior courtyard for €0.3 million.

In 2018, after the signature of the partnership with the Chinese company Tonghua Dongbao Pharmaceuticals Co. Ltd, the Company initiated refurbishing on two floors of 450 sqm each, mainly dedicated to the Analytical Department.

#### ▪ Other property, plant and equipment

The principal property, plant and equipment that the company holds is described in note 2 to the notes to the corporate financial statements prepared in accordance with IFRS, in chapter 4 of this reference document.

### 1.2.4.2 Major current and future investments

Over the course of 2019, the Company plans to finalize the design of the additional 900 sqm floorspace for new labs and offices of the Analytical Department.

Adocia also plans to purchase the scientific material needed for the research and development activities of its current and future projects.

Further refurbishment of the building would require new financial income.

## 1.3 Description of activities

Adocia is a French biotechnology company founded in December 2005 by Gérard, Olivier and Remi Soula. It focuses on the treatment of diabetes and other metabolic diseases with innovative formulations of approved proteins and peptides, using its BioChaperone<sup>®</sup> technology. Adocia's portfolio of injectable treatments for diabetes, featuring five clinical-stage products and two preclinical products, is among the largest and most differentiated of the industry.

Adocia's mission is to 'Deliver more physiologic treatments to people with diabetes and other metabolic diseases in a simple and affordable way to help them avoid the long-term consequences of their disease.'

Diabetes is a global pandemic, affecting in 2017 more than 425 million people worldwide<sup>1</sup>. Despite significant progress made in the treatment of diabetes over the last 30 years, there is still a significant medical need, with it estimated that nearly 79% of people with diabetes experience severe complications<sup>2</sup>. The complexity of treatments and their costs place additional constraints on the lives of those who live with diabetes and may be responsible for a decline in their compliance, as well as a deterioration in the long term in quality of care (for example, linked to treatment abandonment).

1 International Diabetes Federation, 2017

2 Hazel-Fernandez & al; American Journal of Managed Care. 2015

## Presentation of Adocia and its activities

For the same reasons, the capacity of healthcare systems to cope with the enormous costs of this disease is in question, in the context of an overall increase in pressure on healthcare costs. In 2012, in the United States, the costs associated with diabetes amounted to \$245 billion, including \$29 billion for drugs and medical devices<sup>3</sup>. In its annual results presentation for 2017, Novo Nordisk estimated that medicine and devices global costs for the treatment of diabetes were above \$80 billion.

Adocia therefore believes that any new diabetes treatment must meet a threefold challenge:

- **Offer better performance**, through more 'physiologic' treatment approaches to address the disease in its complexity;
- **Facilitate the use of treatments**, to maximize the chances of patient compliance without placing further daily constraints on the patient;
- **Guarantee affordable prices**, to ensure the greatest number of patients can access the best treatment and to guarantee the sustainability of our healthcare systems.

1

To meet this threefold challenge, Adocia is adopting an original strategy which consists of improving the efficacy and/or safety of already-approved therapeutic proteins and peptides while facilitating their use by patients. To do this, Adocia has developed its proprietary formulation technology, BioChaperone<sup>®</sup>. The formulation approach is simple to implement and provides the opportunity to improve and combine in an original way already-approved protein. It also takes advantage of the track record of already-used therapeutic proteins in terms of safety, efficacy and production infrastructure. Thus, it enables Adocia to develop innovations by decreasing risk margins, accelerating clinical development and reducing the amount of investment required (at the clinical and production stages) compared to a strategy to develop novel proteins. Its relatively low cost-intensive business model enables Adocia to develop innovative treatments with improved performance while enabling attractive drug pricing in an extremely competitive environment.

By adapting BioChaperone to each protein to meet the technical challenges posed, Adocia has developed a portfolio of innovative formulations of metabolic hormones for the treatment of diabetes among the most differentiated on the market. Each product aims to meet the specific needs of people living with diabetes. Adocia's goal is to develop its products until their entry into phase 3 clinical studies in order to maximize the value of its projects prior to licensing out to potential partners in the field of diabetes and other metabolic diseases, whether this be one of the established leaders of the field, or new entrants wishing to immediately take position in the market with differentiated bio-betters rather than standard biosimilars.

Since April 2018, Adocia entered a partnership with Chinese company Tonghua Dongbao Pharmaceuticals Co. Ltd, which acquired the rights to develop and commercialize the BioChaperone Lispro et BioChaperone Combo insulin programs in China and other Asian and Middle-East territories.

### 1.3.1 The BioChaperone<sup>®</sup> technological platform

Adocia has designed and developed a technological platform based on novel polymers, oligomers, and innovative small molecules, called BioChaperone<sup>®</sup>. These compounds have the property of spontaneously combining with certain therapeutic proteins. This non-covalent combining helps increase the solubility and efficacy of the therapeutic protein and protects it from enzymatic breakdown.

BioChaperone technology is derived from the functional mechanism of heparin. This natural polysaccharide forms molecular complexes with growth factors, increasing their solubility, protecting them from enzymatic breakdown and thereby extending their time of action. The goal of the first generation of BioChaperone molecules developed by Adocia was to mimic the interaction properties of heparin with growth factors whilst avoiding its anticoagulant effect. Its was also aimed at increasing reaction versatility in order to diversify the proteins with which BioChaperone could react.

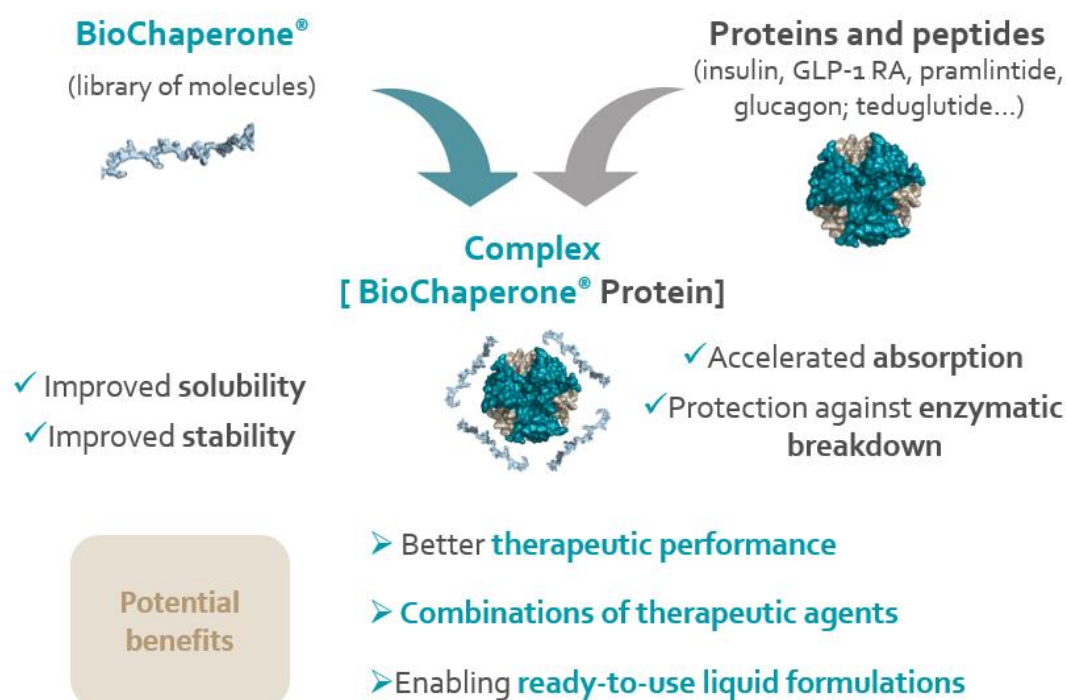
<sup>3</sup> American Diabetes Association, 'Economic Costs of Diabetes in the US in 2012,' 2013.



The first innovative BioChaperone polymers were composed of a sugar backbone (e.g., dextran or pullulan) modified by both anionic groups\* (carboxylates with a negative electric charge for instance) and by hydrophobic amino acids. Adocia then extended its BioChaperone family to include other shorter compounds (oligomers and small molecules) presenting the same properties. BioChaperone compounds have no intrinsic biological activity and should therefore be registered with regulatory authorities as new excipients.

BioChaperone compounds form complexes with proteins by binding non-covalently to their surface (adsorption). The complex forms spontaneously and is based on hydrophobic and electrostatic interactions and on the formation of hydrogen bonds. These BioChaperone polymers interact reversibly and non-degradatively with the proteins. The complex forms spontaneously when the two constituents are simply mixed in aqueous solution. This process occurs immediately and does not require heating or the use of an organic solvent.

The formulation-based approach presents the advantage of being easily industrializable as it relies on the addition of BioChaperone in the formulation process to the other excipients (preservatives, salt, etc.), and does not require adaptation of the industrial tools. Furthermore, the BioChaperone chemical synthesis processes are simple and low in cost compared to the therapeutic proteins themselves. These two aspects make it possible to envisage manufacturing costs for the BioChaperone formulations in par with those of the original formulations.



Four key properties of the BioChaperone technology, via the formation of the complex with the protein or peptide, have been demonstrated:

- increased solubility of proteins or peptides that are relatively insoluble at physiological pH;
- increased stability of proteins or peptides during storage;
- protection of proteins or peptides against enzymatic breakdown; and
- stabilization of the activity of proteins or peptides in the presence of cells.

Pharmaceutical products developed using BioChaperone technology are therefore designed to be more effective, easier to use and sometimes offer new uses at prices comparable to existing treatments.

At present, Adocia research teams have developed more than 500 BioChaperone compounds, an impressive collection that grows in size over time. The main distinctions among these compounds are their size, nature, and the number of anionic and hydrophobic grafts. This collection of molecules was rapidly extended to enable

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interactions with several classes of therapeutic proteins, notably the insulins and other metabolic hormones used in the treatment of diabetes.

BioChaperone technology is at present protected by 39 patent families for BioChaperone molecules and formulations. The first of the patents protecting formulations tested in clinical studies will expire in 2033.

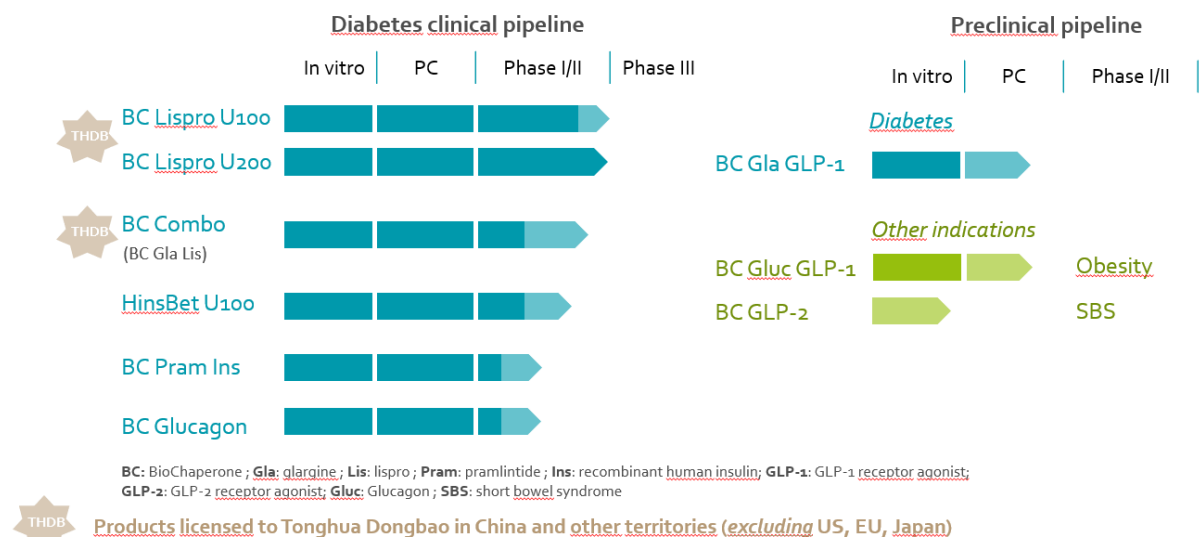
### 1.3.2 Pipeline presentation

Since its creation, Adocia has developed a broad portfolio of injectable treatments for type 1 and 2 diabetes patients based on its BioChaperone technology. In January 2018, Adocia sought to extend its portfolio to include new therapeutic indications that could benefit from BioChaperone technology and the knowledge accumulated by the Company over the previous twelve years.

At present, Adocia's **clinical portfolio** features five innovative insulin formulations for the treatment of diabetes: two ultra-rapid insulin analogs (BioChaperone Lispro U100 and U200), a rapid-acting human insulin (HinsBet U100), a combination of long-acting insulin glargine and rapid-acting insulin lispro (BioChaperone Combo), a combination of human insulin with pramlintide, an amylin analog, amylin being a synergetic hormone to prandial insulin (BioChaperone Pramlintide Insulin) and a ready-to-use aqueous formulation of human glucagon (BioChaperone Glucagon).

In 2018, Adocia granted the Chinese company Tonghua Dongbao Pharmaceuticals Co. Ltd, two licenses for the development and commercialization of BioChaperone Lispro et BioChaperone Combo insulin programs. These two agreements cover China, and some Asian and Middle-East territories. Adocia retains the rights to develop and license these two insulin programs in worldwide markets outside of the territories covered by these agreements, including the United States, Europe, Latin America and Japan.

Adocia also has in **preclinical development** two combinations of insulin glargine with GLP-1s (BioChaperone Glargine Dulaglutide and BioChaperone Glargine Liraglutide), a ready-to-use aqueous formulation of teduglutide, a GLP-2 analog for the treatment of short bowel syndrome (BioChaperone Teduglutide), and a combination of glucagon and a GLP-1 receptor agonist for the treatment of obesity (BioChaperone Glucagon GLP-1).



## 1.3.3 BioChaperone portfolio for the treatment of diabetes

### 1.3.3.1 Diabetes

Using its proprietary BioChaperone technological platform, Adocia is developing innovative formulations of therapeutic proteins for the treatment of diabetes.

Adocia develops new, more effective, easier to use, and more affordable injectable treatment options to improve the long-term quality of life for people living with diabetes.

#### ▪ Epidemiology

Diabetes represents a group of global chronic diseases with a high rate of expansion, in particular in emerging countries. The International Diabetes Federation<sup>4</sup> forecasts an increase by 48% of the number of people with diabetes worldwide between 2017 and 2045. (among people aged between 20 and 79 years), that is an increase from 425 million people with diabetes to 629 million. Although Europe (+15%) and North America (+36%) should experience growth rates inferior to the global average, emerging countries should face an acute raise of the number of people with diabetes.

By 2045 the proportion of people with diabetes should be over 8% in most regions of the world, except for Africa.

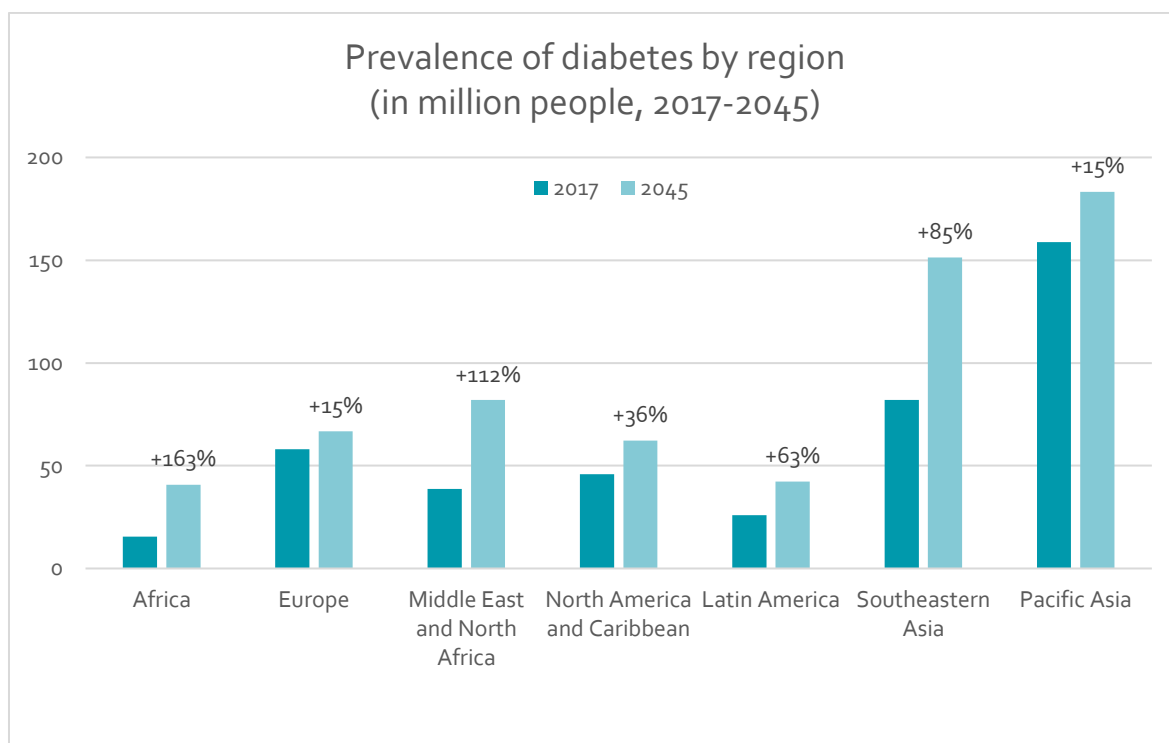


Figure 1 : Estimates of the number of people with diabetes (in millions) among people aged between 20 and 79 years worldwide in 2017 and forecasts for 2045. The percentages show growth rates from 2017 to 2045 per region. Source: International Diabetes Federation, 2017

#### ▪ Disease and complications

Diabetes is a chronic disease where the patient experiences high levels of sugar in the blood (hyperglycemia) due to a deficiency or total lack of insulin, a pancreatic hormone.

<sup>4</sup> Diabetes Atlas 8th edition (2017), Fédération Internationale du Diabète

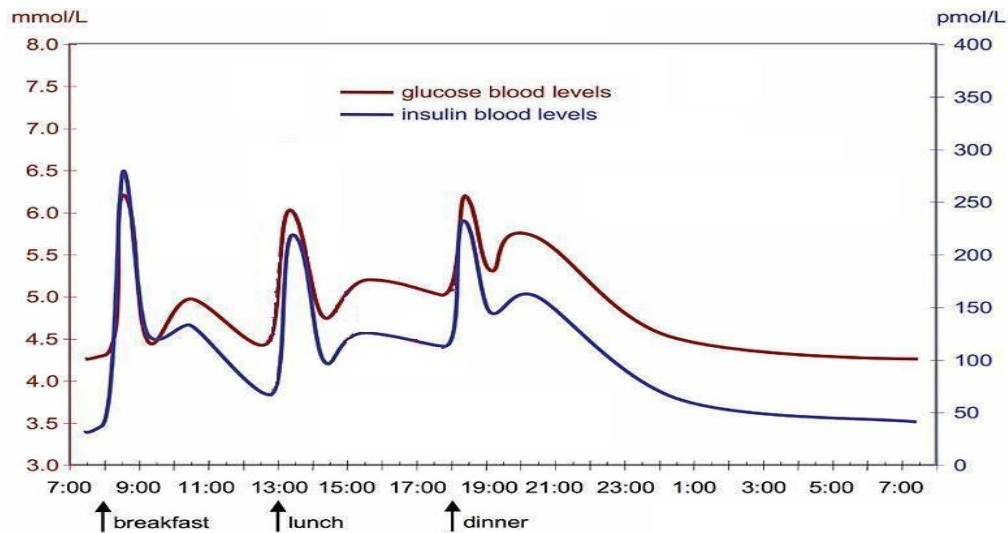


Figure 2 : Schematic representation of daily glycemic (red line) and insulin secretion (blue line) patterns in a person without diabetes

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Insulin plays a major role in the control of glycemia, by enabling the capture of circulating glucose by cells. In a subject without diabetes, the surge of glycemia following the ingestion of a meal is immediately associated with a rapid increase of endogenous insulin concentration in the blood, which enables the capture of the glucose by the cells and consequently maintains the glycemia level in the blood in a range comprised between 4.4 mmol/L (0.80 g/L) and 7 mmol/L (1.4 g/L). The control of glycemia is considered as ideal when blood glucose stays within this range.

However, if the blood glucose concentration dips under 0.80 g/L, the subject enters into an hypoglycemic state (which is hazardous, and could potentially be lethal) and when this concentration goes over 1.4g/L, she enters into an hyperglycemic state (which can lead to ketoacidosis in the short term and to numerous complications in the long term). In a person with diabetes, the regulation of blood glucose is deficient, which results in chronic exposure to hyperglycemic states. With time chronic hyperglycemia is responsible for micro- and macrovascular complications.

There are two main types of diabetes, known as type 1 and type 2 diabetes.

### Different types of diabetes

**Type 1 diabetes** is an autoimmune disease, most commonly diagnosed in young people. Type 1 diabetes has been estimated to affect 10% of people with diabetes<sup>5</sup>. A person with type 1 diabetes makes antibodies which attack the beta cells of the pancreas, responsible for producing insulin in the islets of Langerhans. When a large majority of beta cells are destroyed (about 90%), treatment with insulin becomes unavoidable. Type 1 diabetes cannot be considered a 'genetic disease'; in 90% of new cases there is no parental history at all of type 1 diabetes and the risk of developing type 1 diabetes if one of the two parents has it is lower than 2–3%<sup>6</sup>.

**Type 2 diabetes** is characterized primarily by resistance of cells to insulin, i.e., insulin resistance. Type 2 diabetes has been estimated to affect 90% of people with diabetes<sup>7</sup>. Type 2 diabetes is a progressive disease: insulin resistance leads firstly to excess insulin production, which degrades the islets of Langerhans. Once this degradation is initiated, the amount of insulin produced decreases. Type 2 diabetes is considered asymptomatic and is only discovered when measuring blood glucose levels (glycemia). It is estimated that the majority of patients to be diagnosed have already lost half of their beta cells. Genetic predisposition is a predominant factor and being overweight is an aggravating cause of type 2 diabetes.

5 Business Insights - The Diabetes Market Outlook to 2016–May 2011

6 Diabetology Department, Prof. Altman, Georges Pompidou European Hospital (<http://www.hegp.fr/diabeto/causetype1.html>)

7 Business Insights - The Diabetes Market Outlook to 2016–May 2011

Other forms of diabetes called secondary forms (owing to the fact they are a consequence of other disorders or pathologies) do exist although their prevalence is marginal: genetic insulin secretion defects, genetic insulin sensitivity defects, diabetes due to pancreatitis or pancreatic cancer, drug-induced diabetes, etc. Pregnancy can also cause diabetes which, even if it disappears after childbirth, can nonetheless be a precursor to type 2 diabetes.

### A complex hormonal disorder

Although insulin is a life-saving treatment for people with type 1 diabetes, as insulin triggers the metabolism of ingested glucose, the reality of hormonal deregulations due to diabetes is more complex than a simple lack of insulin.

Indeed, in a person who does not have diabetes, glycemia is regulated by a multitude of metabolic hormones, including insulin, acting in synergy to keep glycemia levels within a very precise range.

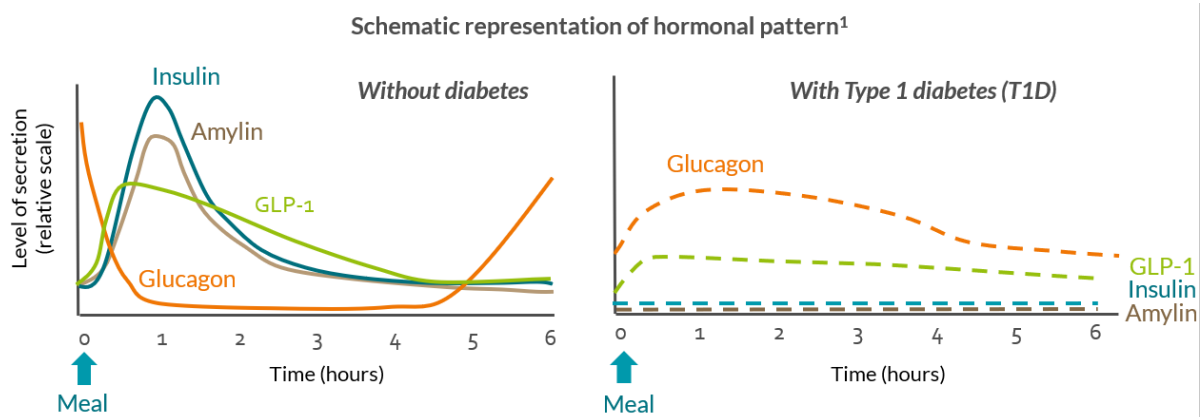


Figure 3: Schematic representation of the secretion pattern of 4 key metabolic hormones around mealtimes: insulin, amylin, GLP-1 and glucagon. Source: Adocia, adapted from Toff-Neilsen et al., *J. Clin Endocrinol Metab* 2001;86:3717-3723; Cummings DE et al., *Diabetes* 2001;50:1714-1719; Aronoff SL et al., *Diabetes Spectrum* 2004; 17(3): 183-190

In particular, four hormones play a key role in controlling glycemia levels: Insulin, amylin and GLP-1 are hypoglycemic agents, while glucagon is a hyperglycemic agent (Cf. figure 3)

- **Insulin and amylin** act in synergy. Insulin and amylin are co-secreted by the beta cells of the pancreas, at the 'basal' rate between meals, and at a higher level each time food is consumed, the so-called 'prandial' rate. Insulin acts on the liver, the muscles and the adipose tissues to promote uptake by these organs of sugar in the blood stream. Amylin works by suppressing the secretion of glucagon in the pancreas, promoting a sensation of satiety in the brain and slowing gastric emptying.
- **GLP-1** also has an action that works in synergy with those of insulin and amylin. It is mainly produced in the intestines following a meal. GLP-1 has several effects which all contribute to slowing the rate at which glucose enters the bloodstream. Firstly, via receptors in the pancreas, GLP-1 stimulates the secretion of insulin and suppresses the secretion of glucagon. Secondly, by affecting the central and peripheral nervous system, GLP-1 slows gastric emptying and induces a feeling of satiety.
- **Glucagon**, produced by alpha cells in the pancreas, is a hyperglycemic agent; that is, it promotes the release of glucose from the muscles and liver into the bloodstream. This is particularly useful between meals and during periods of exertion (physical or mental).

Combined, these four hormones keep glycemia levels within a very precise range, avoiding both hypoglycemia, which can be immediately debilitating or even fatal if severe, and hyperglycemia, responsible in the long-term for severe complications<sup>8</sup>.

<sup>8</sup> D.Nathan et al, *Diabetes Care* 2014 Jan; 37(1): 9-16 (overview of the Diabetes Control and Complications Trial)

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In each of these four classes, at least one compound has been approved by the FDA. We shall only mention here those with a short action, for postprandial use. These compounds are:

- Prandial insulins: recombinant human insulin (named also « rHI », several brands worldwide) or analogs (insulin lispro, Humalog<sup>®</sup>, Eli Lilly; or Admelog<sup>®</sup>, Sanofi), insulin aspart (Novolog/NovoRapid<sup>®</sup>, Novo Nordisk); insulin glulisine (Apidra<sup>®</sup>, Sanofi)
- Pramlintide (Symlin<sup>®</sup>, AstraZeneca), an amylin analog;
- GLP-1 receptor agonists: exenatide (Byetta<sup>®</sup>, AstraZeneca), lixisenatide (Lyxumia<sup>®</sup>, Sanofi)<sup>9</sup>.
- Human glucagon (Glucagon<sup>®</sup>, Eli Lilly, and Glucagen<sup>®</sup>, Novo Nordisk)

In people with type 1 diabetes, this precise hormonal regulation is severely impaired (see figure 1): not only does the destruction of beta cells in the pancreas lead to the absence of insulin and amylin secretion, GLP-1 secretion by intestinal cells is also reduced. In the absence of glucagon suppressants i.e., GLP-1 and amylin, glucose is abnormally secreted at mealtimes.

Prandial hyperglycemia therefore has at least three causes: glucagon secretion, which leads to the release of sugars even before the person starts eating, faster gastric emptying resulting in a massive surge of glucose, and the absence of insulin, which prevents the uptake of these endogenous and exogenous sugars. This might explain in part why prandialinsulin injection alone is not enough to completely control post-prandial hyperglycemia in a person with diabetes.

### Complications of diabetes

Cardiovascular complications are the main cause of mortality in patients with type 2 diabetes: cardiovascular morbidity and mortality are multiplied by a factor of 2–3 in men and 4–5 in women. About 20% of cerebrovascular accidents (stroke) occur in people with diabetes. In the long term, diabetes can damage the heart, blood vessels, eyes, kidneys and nerves<sup>10,11</sup>.

- Heart disease and strokes are responsible for the death of 50% of people with diabetes;
- Kidney failure is responsible for the death of 10–20% of people with diabetes;
- Diabetic retinopathy is a significant cause of blindness resulting from accumulating damage to the small vessels in the retina; after approximately 15 years, 2% of people with diabetes are losing their sight and about 10% have a serious visual impairment;
- Diabetic neuropathy is nerve damage caused by diabetes; up to 50% of people with diabetes experience it. Common symptoms are tingling, pain, numbness or weakness in the feet and hands. Neuropathy, associated with poor blood circulation, increases the risk of venous ulcers and foot ulcers, which may lead to amputation;
- The overall risk of death is at least twice as high in people with diabetes.

### 1.3.3.2 Diabetes treatment - Insulinotherapy

Diabetes is a global pandemic affecting hundreds of millions of people which continues to grow at a significant rate, mainly due to changing lifestyles (more urban, more sedentary, with diets higher in fat and sugars) for many populations throughout the world. Historically, the injectable diabetes treatment market has been dominated by

<sup>9</sup> Among the GLP-1 receptor analogs, there are also long-acting products, whose action is pharmacologic but not physiological, in particular Ozempic<sup>®</sup> (Semaglutide, Novo Nordisk, weekly injection) Victoza<sup>®</sup> (liraglutide, Novo Nordisk, daily injection), Trulicity<sup>®</sup> (dulaglutide, Eli Lilly, weekly injection), Bydureon<sup>®</sup> (long-acting exenatide formulation, AstraZeneca, weekly injection), and Tanzeum<sup>®</sup> (abliglutide, GlaxoSmithKline, weekly injection).

<sup>10</sup> Diabetology Department, Prof. Altman, Georges Pompidou European Hospital (<http://www.hegp.fr/diabeto/causetype1.html>)

<sup>11</sup> DTTC study, NEJM, 1993, 329(14); EDIC study NEJM, 2005, 353(25)

three major players: Eli Lilly, Novo Nordisk and Sanofi, with all three initially focusing on insulin and, more recently, on GLP-1s. However, the dominance of these three players may well come to change under the influence of several major trends, including treatment personalization and commoditization.

According to Novo Nordisk, the global market for diabetes treatment with injectable products (insulins, GLP-1 analogs, glucagon) grew by 18.1% per year between 2008 and 2018, accounting for \$29 billion<sup>12</sup>, i.e., more than 50% of the total market for antidiabetic medications. (cf. figure 4).

This domination of injectable medicinal products, particularly insulin, compared to other drug classes, is explained simply by the fact that insulin is absolutely needed to control glycemia in patients with type 1 diabetes, and that the use of insulin is also ultimately unavoidable for patients with type 2 diabetes.

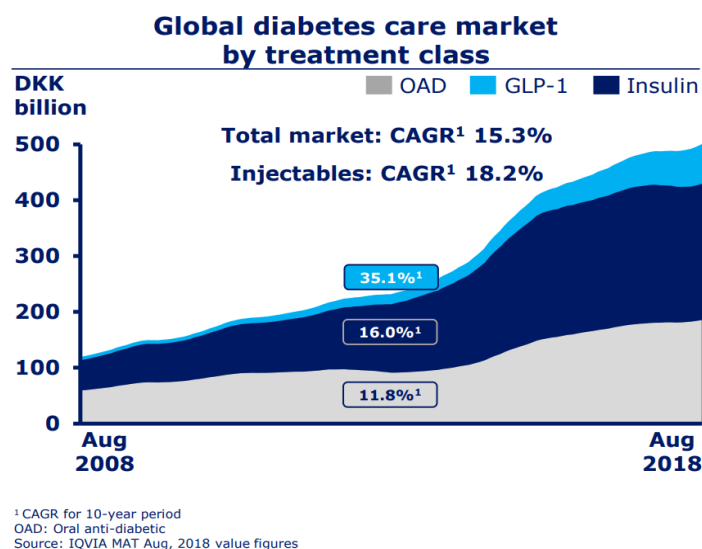


Figure 4: Global diabetes market per therapeutic class and changes between 2008 and 2018 OADs: Oral antidiabetic drugs; GLP-1: GLP-1 receptor agonists; insulin: insulin; CAGR: compound annual growth rate, over 10 years. The DKK-USD exchange rate on August 31, 2008, was DKK1 to \$0.198. On August 31, 2018, the exchange rate was DKK1 to \$0.156. (Source: Novo Nordisk, Investors Presentation First Nine Months of 2018, November 2018).

It is important to remember that treatments differ for type 1 and type 2 diabetes. In type 1 diabetes, treatment with insulin is unavoidable, as pancreatic beta cells are destroyed and there is no more production of insulin. The treatment should cover both the regulation of continuous glycemia due to hepatic glycogenesis between meals (basal glucose) and the regulation of post-prandial glycemia. This is achieved by two types of products: the so-called 'basal' or 'long-acting' insulins, injected once or twice per day, and the so-called 'rapid-acting' or 'prandial' insulins, injected with every meal. A third type of product, called 'premix,' injected twice per day, maintains both basal and prandial regulation. Premixes are based on prandial insulin, a part of which is rendered less rapid by coacervation with protamine. However, premixes are a suboptimal solution compared to individually using basal insulin (which lasts longer) and prandial insulin (which acts more rapidly).

Historically, purified animal insulin was used as the first insulinotherapy (early 20<sup>th</sup> century), followed in the 1980's by human recombinant insulin (Humulin<sup>®</sup>, Lilly; Novolin<sup>®</sup>, Novo Nordisk; Insuman<sup>®</sup>, Sanofi) and, more recently, since the end of 1990's by modified insulin analogs to either accelerate their prandial action (insulin lispro: Humalog<sup>®</sup>, Lilly; Admelog<sup>®</sup>, Sanofi insulin aspart: Novolog<sup>®</sup>/NovoRapid<sup>®</sup> Novo Nordisk; insulin glulisine: Apidra<sup>®</sup>, Sanofi), or to lengthen their basal action (insulin glargine: Lantus<sup>®</sup> and Toujeo<sup>®</sup>, Sanofi and Abasaglar<sup>®</sup>, Lilly; insulin detemir: Levemir<sup>®</sup>, Novo Nordisk; insulin degludec: Tresiba<sup>®</sup>, Novo Nordisk). Premixed insulins made from human recombinant insulin and insulin analogs (Humalog<sup>®</sup> Mix, Eli Lilly and Novomix<sup>®</sup>, Novo Nordisk) have also been developed.

<sup>12</sup>Estimations from annual reports. On the diagram below, this market is valued at \$49 billion dollars according to IMS data, reported by Novo Nordisk, a figure that does not take into account discounts granted to payers.

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In people with type 2 diabetes, disease progression is accompanied by treatment intensification: patients at first receive oral antidiabetic drugs and then move onto GLP-1 receptor analogs (that promote the secretion of insulin) and insulins (basal at first, then basal and prandial or premix).

### 1.3.3.3 The injectable diabetes treatment market: challenges and trends.

Despite insulin treatment for people with type 1 diabetes, and the large range of treatments for those with type 2 diabetes, there is still a significant medical need in these two indications.

#### Trend #1: improve the quality of life and extend the lifespan of patients by focusing on more specific criteria

It has been demonstrated that improving glycemic control can help limit the disease's short- and long-term consequences<sup>13</sup>. Generally, there is a strong trend in the endocrinologist community to start evaluating new treatments on more diverse aspects than glycated hemoglobin (HbA1c) alone, which reflects only an average of glycemia over 3 months.

For instance, it has been proposed<sup>14</sup> to pay closer attention to:

- Time-in-target-range: "time-in-range", the glycaemic range being typically set between 70-140mg/mL): the notion of time in range permits a more precise representation of the glycemic variations that patients endure and their impact on their quality of life;
- Risk of hypoglycemia (the definition of which was recently reviewed by several scientific societies):
- hypoglycemia is a major risk for patients treated for diabetes and presents related risks;
- Long-term benefits of certain drugs: for instance, cardiovascular benefits observed with new classes such as GLP-1 receptor agonists and SGLT-2 inhibitors.

More generally there is also a need to actively promote and support patient involvement to avoid treatment misuse or discontinuation.

#### Trend #2: Integrate technologies and drug therapies

Interest given to finer indicators of glycemic variability has, amongst others, been made possible with the rapid evolution of technology: development of increasingly accurate continuous blood glucose monitoring (CGM) devices, ability to use Big Data data to address patient behavior, development of decision support algorithms (eg IBG Star Sanofi) or control pumps (eg BetaBionics), etc. For a short while, companies such as Eli or BigFoot in collaboration with other companies (like Dexcom) have been developing complete solutions (also known as "artificial pancreas" or "closed-loop systems") including a continuous blood glucose monitoring (CGM) system, an insulin pump and an algorithm that automatically takes into account blood glucose measurements and injects the right dose of insulin.

Similar systems using "smart" pens rather than pumps are also under development. More generally, the various major players in insulin have recently partnered with big data companies to develop new diabetes monitoring and management solutions (Sanofi-Google partnerships, Medtronic-IBM Watson, Novo Nordisk-Glooko ...). The development of these new solutions could have a significant impact on the market in the years to come.

#### Trend # 3: Market commoditization

At the same time, the diabetes market is becoming more commoditized given the combined effect of the approval of the first biosimilars and the pressure on healthcare systems to constrain rapidly increasing costs. Within the field of insulin, the first biosimilar of glargine, a basal insulin (Basaglar®, Eli Lilly) has recently been introduced to the European (2015) and American (2016) markets, a few years after similar products were introduced to the Chinese

<sup>13</sup> DTTC, NEJM study, 1993, 329(14); EDIC NEJM study, 2005, 353(25)

<sup>14</sup> Travaux de consensus de l'ADA (American Diabetes Association) et de l'EASD (European Association for the study of diabetes), Travaux de l'EMA (European Medical Agency), interventions d'associations comme le JDRF (Juvenile Diabetes Research Foundation) ou DiaTribe...



(Basalin<sup>®</sup>, Gan & Lee) and Indian (Basalog<sup>®</sup>, Biocon) markets. As of the third quarter of 2018, Basaglar had acquired an 11% market share of the global basal insulin market. That market actually lost 4% of its global value over a year following the introduction of Basaglar in the US and EU.

In April 2018, Sanofi also launched on the US market the first FDA-approved insulin lispro biosimilar, Admelog<sup>®</sup>. Several new entrants and historical players in insulin are positioning themselves globally in the biosimilars field, such as Mylan and Biocon (Semglee<sup>®</sup>, insulin glargine, approved in Europe in 2018 and launched in the UK in November 2018 and in Japan in 2017, in registration in the US), or Sandoz and Gan & Lee who signed in 2018 a partnership to develop and commercialize biosimilars of insulins glargine, aspart and lispro in multiple markets, including the US and Europe.

At a regional level, one should also mention TUL, Fosun WangBang or Tonghua Dongbao Pharmaceuticals Co. Ltd in China, or Biocon and Wockhardt in India. In the GLP-1 field, Teva announced in January 2017 its intention to market a biosimilar of liraglutide (Victoza<sup>®</sup>, Novo Nordisk).

The commoditization of these markets has begun to have a downward impact on historical product revenues, particularly for basal insulins, but is also pushing for innovation, in order to develop products "immune" from the competition of biosimilars. For example, Novo Nordisk and Eli Lilly, world leaders in prandial insulins with Novolog and Humalog products, developed two high-speed insulins, Fiasp<sup>®</sup> (approved in 2018) and LY900014 (in Phase 3). Similarly, Novo Nordisk and Sanofi have developed a new generation of basal insulins, Degludec<sup>®</sup> and Toujeo<sup>®</sup>, which outperform the historic products Lantus<sup>®</sup> and Detemir<sup>®</sup>.

By developing innovation using already-approved products, Adocia is responding to these two trends in the diabetes market, which should lead to offering better treatments to patients while making them affordable for as many people as possible.

### 1.3.3.4 BioChaperone Lispro U100 and U200

- **Ultra-rapid insulins for a more physiologic action**

Ultra-rapid insulin is an insulin that has a more rapid absorption profile than rapid-acting insulin analogs currently on the market. Currently marketed insulin analogs must be injected 5–15 minutes before meals, whilst human recombinant insulin must be injected 30 minutes before. This is in contrast to what happens in a non-diabetic person, for whom insulin secretion is immediate and proportionate to the meal, which limits glycemic excursion and its long-term effects. To mimic this 'physiologic' action profile, injected prandial insulins should ideally start acting very rapidly and for a duration limited to a few hours (to avoid any mismatch between insulin concentration in the blood and glycemia) .

A mealtime injection, or right-after-mealtime injection, would enable patients to better determine the appropriate insulin dose because the exact contents of the meal would be known, and also to avoid overdosing or delayed dosing, which can lead to hypo- or hyperglycemia respectively, which both have severe short and long-term consequences. This would also give patients some flexibility in terms of the time of injection, which is important in day-to-day life.

To respond to this need, **Adocia has developed two ultra-rapid insulin lispro formulations: BioChaperone Lispro U100 (standard insulin concentration: 100 IU/mL) and BioChaperone Lispro U200 (twice as concentrated solution, i.e., 200 IU/mL).** These two products could offer a significant medical benefit to all users of prandial insulin. They may, however, be of particular importance for specific populations of people with diabetes:

- **Children:** it is particularly difficult to predict exactly when a child will eat and in what quantities. To avoid the risk of severe hypoglycemia, parents tend to inject insulin to their children with diabetes at mealtimes or after meals, which, together with prandial insulins currently on the market, can result in hyperglycemia. In the long-term, chronic hyperglycemia is correlated to serious complications of diabetes.
- **Insulin pump users:** the development of ultra-rapid insulin is a key element to facilitate the development of fully-automated insulin pumps (also called an 'artificial pancreas' 'closed-loop systems' or 'automated insulin delivery systems') that deliver insulin automatically, in real time, depending on the patient's blood

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glucose levels. Concentrated ultra-rapid insulin may also facilitate the miniaturization of devices and/or increase autonomy between refills.

- **People with type 2 diabetes:** BC Lispro U200, an ultra-rapid insulin concentrate, may also improve glycemic control for these people whilst also limiting the volume required for each injection.
- **Results obtained with BC Lispro U100 & U200**

To date, BioChaperone Lispro has been successfully tested in 9 clinical studies, in more than 250 people with type 1 or type 2 diabetes. BioChaperone Lispro has been repeatedly shown to display an ultra-rapid profile compared to reference analog insulins aspart and lispro, whereas it was injected via syringes or insulin pumps and also showed superiority on some pharmacodynamic and pharmacokinetic parameters over Fiasp<sup>®</sup>, the only commercialized ultra-rapid insulin.

### Phase 2a clinical results – Pharmacokinetic and pharmacodynamic study in people with type 1 diabetes (n=36)

The objective of this study was to compare the pharmacokinetic and pharmacodynamic profiles of the BioChaperone Lispro U100 complex to those of Humalog<sup>®</sup> U100. In April 2014, Adocia announced the results of this study, which showed the **30% faster onset of action and 69% better early metabolic effect of BioChaperone Lispro compared to Humalog** in 36 patients with type 1 diabetes. These results are consistent with the pharmacokinetics of BioChaperone Lispro, which reaches its concentration peak 35% faster than Humalog; the amount of insulin present in the blood for the first 30 minutes is also 170% greater when it is formulated with BioChaperone.

### Phase 2a clinical results – Second pharmacokinetic and pharmacodynamic dose-response study in people with type 1 diabetes (n=37)

In May 2014, Adocia initiated a second Phase 2a clinical study that aimed to evaluate the linearity of the effect of BioChaperone Lispro U100 for various doses in a range covering the needs of the majority of patients (0.1, 0.2 and 0.4 IU/kg). Positive results from this study were announced in September 2014. In this usual dose range, BioChaperone demonstrated the ultra-rapid linearity of its pharmacokinetic profile with respect to the dose (normalization test). The ultra-rapid effect was also observed in all pharmacodynamic profiles, whatever the dose tested.

The results of these two studies convinced Eli Lilly to enter into a new collaboration with Adocia. On December 19, 2014, Adocia and Eli Lilly announced they had signed a global licensing agreement for the development of an ultra-rapid insulin, BioChaperone Lispro. The agreement covered the development of two formulations: BioChaperone Lispro U100 and U200. Since signing the agreement, Eli Lilly and Adocia have successfully completed six clinical studies of BioChaperone Lispro U100 and U200. Lilly announced its decision to withdraw from this agreement on January 26, 2017<sup>15</sup>.

### Phase 2a clinical results – Study of the response to a standardized meal in people with type 1 diabetes (n=38)

Adocia and Lilly jointly announced in January 2015 that Adocia would initiate the first clinical study under this partnership. This Phase 1b/2a study aimed to evaluate the improvement in postprandial glycemic control obtained with BioChaperone Lispro compared to Humalog in 38 patients with type 1 diabetes after a standardized meal. The results of this study were jointly announced by both companies in June 2015. They showed a 61% reduction in postprandial glycemic excursions compared to Humalog. This study also confirmed the ultra-rapid pharmacokinetic profile of BioChaperone Lispro by demonstrating that insulin lispro's speed of absorption was significantly faster. Early exposure also increased by 168% at the same dose for BioChaperone Lispro compared to Humalog.

The results of this study were the subject of an oral presentation given by Dr. Tim Heise (Profil Neuss) at the American Diabetes Association's 76th Scientific Sessions (June 2016, New Orleans, USA) and a further oral presentation by Dr.

<sup>15</sup> For more information on legal procedures opposing Adocia and Lilly following the termination of this contract, please see section « Litigation » 1.3.7.3 of the present reference document

Heise at the European Association for the Study of Diabetes 52nd Annual Conference (September 2016, Munich, Germany).

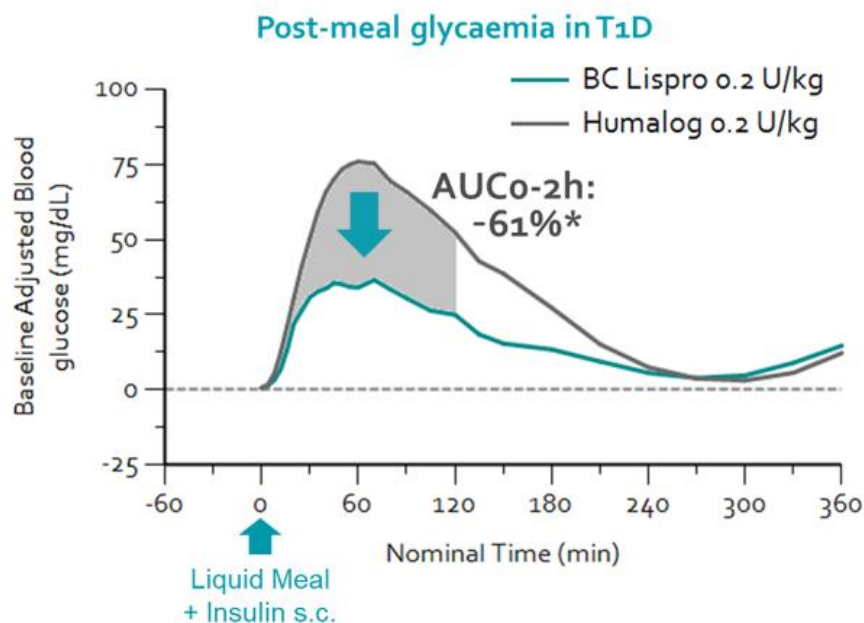


Figure 5: Comparison of the effect on postprandial glycaemia of BioChaperone Lispro U100 vs. Humalog U100 in 38 people with type 1 diabetes. Glycemia is measured for six hours after injecting the treatment at the time of consuming a standardized liquid meal.

**Phase 1b clinical results – Study evaluating the potential for bioequivalence of the BioChaperone Lispro U200 formulation compared to BioChaperone Lispro U100, based on their pharmacokinetic and pharmacodynamics profiles in healthy volunteers (n= 26)**

In June 2014, Adocia announced it was developing BioChaperone<sup>®</sup> Lispro U300, a concentrated insulin lispro formulation at 300 IU/mL of insulin lispro with BioChaperone. Preclinical data demonstrated that BioChaperone Lispro U300 had an ultra-rapid action compared to Humalog 100 IU/mL. This ultra-rapid action was equivalent to that obtained with BioChaperone Lispro U100 in the same model.

As part of the partnership with Lilly, a 200 IU/mL formulation, BioChaperone<sup>®</sup> Lispro U200, was developed, with Eli Lilly marketing a Humalog formulation at this concentration, Humalog U200. Further to positive preclinical results, BioChaperone Lispro U200 was clinically tested in a pilot bioequivalence study comparing it to BioChaperone Lispro U100, the positive results of which were announced in December 2015.

This pilot study aimed to demonstrate the potential for bioequivalence between the two products.

BioChaperone Lispro U200 fulfilled all the study's predefined endpoints (two standard bioequivalence parameters, C<sub>max</sub> and AUCLispro<sub>(0-infinity)</sub>, and two parameters characterizing the ultra-rapid action (AUCLispro<sub>(0-1 h)</sub> and early t<sub>50%</sub>C<sub>max Lispro</sub>). These positive feasibility results support the development of BioChaperone Lispro U200, based on the demonstration of bioequivalence.

These positive results led to a \$10 million milestone payment from Eli Lilly in December 2015.

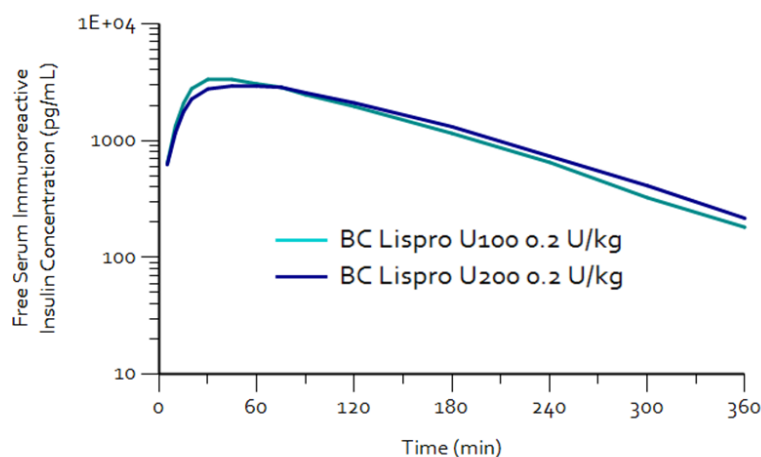


Figure 6: Mean pharmacokinetic profiles (variation in insulin level in the blood) of BioChaperone Lispro U100 (light blue curve) and BioChaperone Lispro U200 (dark blue curve) obtained from 26 healthy volunteers.

1

The results of this study were the subject of an abstract published in the Diabetes Care scientific journal at the American Diabetes Association's 76th Scientific Sessions (June 2016, New Orleans, USA).

### Positive topline results for the Phase 1b clinical study: repeated administration of BioChaperone Lispro U100 in people with type 1 diabetes (n= 36)

In March 2016, Adocia and Lilly jointly announced the positive results of a Phase 1b clinical study comparing the effects of BioChaperone Lispro and Humalog injected daily, at each meal, either at the time of the meal, or 15 minutes before, or 15 minutes after, on postprandial glycemic control in people with type 1 diabetes over a period of two weeks. This study showed: (i) at the beginning of the 14-day treatment period, BioChaperone Lispro U100 showed a 31% reduction in glycemic excursions over the first two hours compared to Humalog, when the treatments were injected when a solid meal was consumed and; (ii) after 14 days of treatment, a reduction of 42% in glycemic excursions during the first two hours compared to Humalog, when the treatments were injected at the mealtimes. This study was presented during multiple scientific conferences, and was also published in a peer-reviewed journal<sup>16</sup>.

### Positive topline results for the Phase 1b clinical study: repeated administration of BioChaperone Lispro U100 in people with type 2 diabetes (n=51)

In April 2016, Adocia and Lilly jointly announced the positive results of a Phase 1b study comparing the effects on postprandial glycemic control of BioChaperone Lispro and Humalog injected daily at mealtimes for 14 days in people with type 2 diabetes. BioChaperone Lispro demonstrated an ultra-rapid pharmacokinetic profile with a statistically significant increase of 83% in exposure to insulin lispro during the first 30 minutes post injection, compared to Humalog. On the basis of a post-hoc analysis including four meal tests per patient for each treatment (days 1, 2, 13 and 14), BioChaperone Lispro also showed a statistically significant decrease of 22% in glycemic excursions for the first two hours, compared to Humalog.

Main results from this study were published in Diabetes Care following the 77th Scientific Sessions of the American Diabetes Association (June 2017, San Diego, USA).

### Positive topline results for a Phase 1 clinical study: evaluation of BioChaperone Lispro U100 in healthy Japanese subjects (n=15)

In May 2016, Adocia and Lilly jointly announced the positive results of a Phase 1 study evaluating BioChaperone Lispro U100 ultra-rapid insulin in Japanese subjects. This study aimed to compare the pharmacokinetic and pharmacodynamic profiles of BioChaperone Lispro to those of Humalog in 15 healthy Japanese subjects under

<sup>16</sup> Andersen G, Meiffren G, Lamers D, DeVries JH, Ranson A, Seroussi C, Alluis B, Gaudier M, Soula O, Heise T. Ultra-rapid BioChaperone Lispro improves postprandial blood glucose excursions vs insulin lispro in a 14-day crossover treatment study in people with type 1 diabetes. Diabetes Obes Metab. 2018 Nov;20(11):2627-2632

euglycemic clamp conditions. Although the study was not designed to perform statistical analysis, the results show an acceleration in the pharmacokinetic and pharmacodynamic profiles of BioChaperone Lispro compared to Humalog, as well as the linearity of insulin exposure as a function of the dose administered. The results of the study should allow for the inclusion of Japanese diabetes patients into the Phase 3 program in compliance with the global registration plan planned for this product.

### Positive topline results for Phase 1b clinical study: evaluation of BioChaperone Lispro U100 in people with type 1 diabetes using an insulin pump vs. Humalog® (n=44)

In December 2016, Adocia and Lilly jointly announced the success of a Phase 1b clinical study comparing the effects of BioChaperone Lispro and Humalog on postprandial glycemic control in people with type 1 diabetes using an insulin pump. During this study, BioChaperone Lispro U100 demonstrated a statistically significant increase in insulin exposure over the first 30 minutes after a mealtime bolus compared to Humalog. The accelerated absorption of BioChaperone Lispro U100 was also observed in the three insulin delivery devices tested (Roche Accu-Chek® Spirit, Medtronic Paradigm® Veo™ and a syringe with insulin).

### Positive topline results for the Phase 1b clinical study: evaluation of BioChaperone Lispro U100 in people with type 1 diabetes using an insulin pump vs. Fiasp® and Novolog® (n=42)

In December 2017, Adocia announced the success of a Phase 1b clinical study comparing BioChaperone Lispro both to the rapid-acting insulin Novolog® (Novo Nordisk) and to the recently approved ultra-rapid insulin aspart formulation Fiasp® (Novo Nordisk) in patients with type 1 diabetes. This study was the first direct comparison of two ultra-rapid insulin formulations. Forty-two participants received, under euglycemic clamp conditions, single doses of these three products via an insulin pump during three separate visits. The objectives of the study included comparing the glucodynamic effects and pharmacokinetic profiles obtained with the three treatments.

BioChaperone Lispro satisfied the primary endpoint, showing a statistically significant increase of 63% in metabolic effect during the first hour compared to Novolog®. This result confirms the ultra-rapid profile observed in previous studies when compared to Humalog®. Furthermore, BioChaperone Lispro showed a statistically significant 'faster-off' metabolic profile compared to the other two products, reaching the late half-T<sub>max</sub> 18 minutes before Fiasp® and 22 minutes before Novolog®. BioChaperone Lispro also showed an early metabolic effect similar to that of Fiasp® during the first hour.

Thus, BioChaperone Lispro has demonstrated a reproducible absorption profile through several studies, several populations and several modes of administration.

Results from this study were made public in an abstract in the scientific journal *Diabetes Care* following the 78<sup>th</sup> Scientific Sessions of the American Diabetes Association (June 2018, Orlando, USA), an oral presentation during the 54<sup>th</sup> Annual Conference of the European Association for the Study of Diabetes (October 2018, Berlin, Germany) and in a peer-reviewed publication<sup>17</sup>.

- **Ongoing study using iLet™ bionic pancreas (n=30)**

In January 2019, Adocia announced the initiation of a first home-use trial testing the ultra-rapid insulin BioChaperone Lispro with BetaBionics automated insulin delivery system, the iLet™.

The iLet is a so called "Hybrid Closed-Loop" system, that consist of an autonomous, infusion pump that use clinically tested mathematical dosing algorithms driven by machine learning, to calculate and dose insulin as needed, based on data from a continuous glucose monitor. The iLet to be used in this trial will be set in an insulin-only configuration (another version allows the co-infusion of glucagon)

<sup>17</sup> Heise T, Meiffren G, Alluis B, Seroussi C, Ranson A, Arrubla J, Correia J, Gaudier M, Soula O, Soula R, DeVries JH, Klein O, Bode BW. Pharmacodynamic and pharmacokinetic properties of BioChaperone Lispro vs faster aspart and insulin aspart in patients with type 1 diabetes on continuous subcutaneous insulin infusion. A randomized euglycemic clamp study. *Diabetes Obes Metab.* 2018 Dec 18. [Epub ahead of print]

## Presentation of Adocia and its activities

The use of an ultra-rapid insulin in a hybrid closed-loop system should improve the reactivity and so the efficiency of this system to control glycemia.

This, multi-arm, cross-over, USA-only clinical trial, will recruit up to 30 people with type 1 diabetes to participate in three 7-day study arms comparing the pharmacokinetic and pharmacodynamic profiles of insulin lispro, insulin aspart, and BioChaperone Lispro in the bionic pancreas between and within subjects. The co-primary outcomes will be mean continuous glucose monitoring glucose (CGMG) and fraction of time spent with CGMG <54 mg/dl.

Results are expected in 2019.

### ▪ Partnership with Tonghua Dongbao Pharmaceuticals Co. Ltd

Adocia and the Chinese insulin leader Tonghua Dongbao Pharmaceuticals Co. Ltd announced in April 2018 a strategic partnership whereby Adocia granted exclusive development and commercialization rights to Tonghua Dongbao for BioChaperone® Combo and BioChaperone® Lispro in China and other Asian and Middle East countries.

Adocia received an upfront payment of \$10 million for BioChaperone Lispro. Additionally, Adocia is entitled to receive development milestone payments up to \$35 millions and to receive double-digit royalties on the sale of this product in the designated territories. Tonghua Dongbao will also reimburse some of Adocia's expenses for research and development activities performed during the terms of the agreements.

Adocia retains the rights to develop and license BioChaperone Lispro in worldwide markets outside of the territories covered by these agreements, including the United States, Europe and Japan. Adocia remains responsible for the development and the manufacturing of BioChaperone® pharmaceutical excipients.

In June 2018, Tonghua Dongbao Pharmaceuticals Co. Ltd also agreed to manufacture and supply insulin glargine and insulin lispro to Adocia worldwide, excluding China, to support the development of Adocia programs in these regions. This agreement gives us full control, over the further development of BioChaperone Lispro. This also opens additional collaboration opportunities with biopharmaceutical companies focused in diabetes with no existing insulin manufacturing facilities and, also, device companies integrating synergies between innovative medicines, devices and care management systems.

Additional information about these contracts and the company Tonghua Dongbao Pharmaceuticals Co. Ltd are available in the section 1.3.7. of this document.

### Achieved partnership with Eli Lilly:

BioChaperone Lispro program was previously licensed to the American company Eli Lilly: first between December 2011 and January 2013 (partnership terminated by common agreement) and then between December 2014 and January 2017 (partnership terminated by Eli Lilly, that gave priority to an internal project, LY90014). Some legal procedures are ongoing facing Adocia to Eli Lilly: they are detailed in the section "Litigations" 1.3.7.3 of this document.

Following the termination of the second partnership, Adocia took back the full ownership of the rights that were licensed and continued the development of this product.

### ▪ Next steps

Based on BioChaperone Lispro's strong clinical dossier, Adocia is seeking a new partner for entry into phase 3 and commercialization of the product in territories excluded from the licensing agreement with Tonghua Dongbao Pharmaceuticals Co. Ltd. (THDB), which is to say mainly the US, EU, Latin America and Japan.

Adocia intends to launch in 2019 a so-called "bridging study" enabling to demonstrate the comparability of THDB's insulin lispro API with the one used in former formulations of BioChaperone Lispro (insulin lispro used in Humalog, Lilly). This will allow the use of all previous clinical data gathered for BioChaperone Lispro in its Phase 3 registration process.

## ▪ Competition

Several companies have sought to develop an ultra-rapid insulin with an action profile close to the physiologic activity of insulin.

**Novo Nordisk** has developed a high-speed formulation of insulin aspart called Fiasp®. In 2016, Fiasp received the approval of the European Medicines Agency for its launch on the European market for the treatment of type 1 and type 2 diabetes. Following a request for additional information from FDA (Complete Response Letter), Novo Nordisk resubmitted its file early in 2017 and Fiasp was approved by the FDA in September 2017. Fiasp has been available in the United States since January 2018 at a price similar to that of Novolog. In the third quarter of 2018, Fiasp recorded \$ 26 million in sales in Europe and the United States.

A Phase 1b study of Fiasp in 52 patients with type 1 diabetes showed that the product had early pharmacokinetic and pharmacodynamic profiles significantly faster than insulin aspart. On the other hand, this does not translate into a fast-out / fast-off effect (faster insulin release / shorter duration activity), as has been shown for BioChaperone Lispro U100 in several Phase Studies. 1b. This latter effect is desirable as it may reduce the risk of hypoglycaemia. In Phase 3 studies, Fiasp confirmed its high-speed absorption profile, but did not show superiority in terms of hypoglycaemia compared to insulin aspart.

In 2017, at the same time as the collaboration with Adocia ended, **Eli Lilly** announced that it had developed a competing high-speed insulin project LY900014 (insulin lispro formulated with treprostinil and citrate, among other excipients). The first results were presented at the ADA annual conference in June 2017. LY900014 has faster pharmacokinetic and pharmacodynamic profiles than Humalog (insulin lispro) in the first few minutes after injection. Nevertheless, Lilly has not demonstrated a more significant fast-out / fast-off effect than insulin lispro, unlike BioChaperone Lispro. Lilly announced in 2018 that it had achieved the primary objectives of the two Phase three trials in people with type 1 or type 2 diabetes. Thus, compared to Humalog, LY900014 met the non-inferiority criterion for the reduction of glycated hemoglobin (HbA1c) and demonstrated better glucose control after a meal. Lilly announced that the detailed results will be presented at a future conference and that the regulatory file will be submitted to the FDA in 2019.

**Mannkind**, founded in 1991, developed Afrezza, an inhalable human insulin with a high-speed profile, whose peak concentration is observed 12 to 15 minutes after inhalation. On June 27, 2014, the FDA approved the use of Afrezza to improve glycemic control in adults with diabetes. This approval, however, was accompanied by restrictions on patient populations (not recommended for smokers and patients with ketoacidosis) that could use Afrezza and a "black box warning" (warning about the potential risk of a drug, which should be included in the list). explicitly on the packaging), regarding the risk of bronchospasm associated with treatment. In addition, the FDA requested that Mannkind carry out four postmarketing clinical trials. An Afrezza marketing agreement with Sanofi in 2014 was terminated on April 4, 2016. Since then, Mannkind has continued to market Afrezza by its own means. Afrezza's sales for the years 2016 to 2018 remained very weak, although slightly increasing.

Finally, in January 2019, the company **Arecor** announced the initiation of its first human study of its high-speed insulin (AT-247).

Other competing projects have been abandoned, in particular the association between human insulin and hyaluronidase developed by Halozyme (which refocused its activities on the applications of hyaluronidase in oncology at the end of 2014) and the high-speed formulations BIOD-250 and BIOD-238 developed by Bidel (which was the subject in 2016 of a "reverse-merger" operation by Albireo, which resulted in the deprioritization of Bidel's historical activities).

### 1.3.3.5 BioChaperone Combo: a safer alternative to premixed insulin for treatment intensification in people with type 2 diabetes.

Type 2 diabetes is a progressive disease requiring progressive treatment intensification. At present, 50% of patients on basal insulin do not meet their glycemic control targets<sup>18</sup>.

<sup>18</sup> Sanofi communication – Q3 2015 presentation

## Presentation of Adocia and its activities

To improve glycemic control, the patient may be recommended to add a prandial component to his/her treatment regimen. This can be achieved via the addition of prandial insulin to the basal insulin, or by replacing basal insulin with premixed insulin. Premixed insulin is a fixed combination of a soluble fraction and a precipitated fraction of the rapid-acting prandial insulin analog. It is usually injected twice per day. It is thus an easier regimen than multiple insulin injections: one product only, twice per day at a fixed ratio (rather than two products, four times per day at variable doses).

Premixed insulins are therefore particularly recommended for elderly patients. They are also widely used in emerging countries. However, they do not offer ideal medical performance owing to a delayed and prolonged prandial action, a basal action profile of less than 24 hours and an elevated risk of hypoglycemia.

To meet the medical need for a regimen as simple as that of premixed insulin but as effective as a multiple-injection regimen, Adocia has developed BioChaperone Combo, a combination of insulin glargine (basal, Lantus, Sanofi) and insulin lispro (prandial, Humalog, Eli Lilly) at neutral pH. For a longtime, it was technically impossible to actually combine the gold-standard basal acting insulin, insulin glargine, and a rapid acting insulin into the same product, as they could not be formulated in the same pH range. BioChaperone technology makes it possible to solubilize insulin glargine at neutral pH and thus make it compatible with any prandial insulin.

By truly combining a basal insulin and a prandial insulin without changing their individual pharmacodynamic profiles, BioChaperone Combo could advantageously replace premix insulins in populations using them.

- **Clinical results obtained with BioChaperone Combo**

To date, BioChaperone Combo has been successfully tested in 5 clinical studies in 143 people with type 1 or type 2 diabetes, and repeatedly showed a faster prandial profile and longer basal profile compared to an analog insulin premix (HumalogMix 75/25).

### Phase 1b clinical results – First pharmacodynamic and pharmacokinetic study in people with type 1 diabetes (n=20)

In the first quarter of 2014, Adocia announced positive results for a study that had aimed to compare the pharmacodynamic and pharmacokinetic profiles of BioChaperone Combo to those of HumalogMix (insulin lispro premix 75/25, Eli Lilly) in people with type 1 diabetes under euglycemic clamp conditions. The following positive results were obtained: onset of action of BioChaperone was at least 30% faster than that of HumalogMix; the duration of action observed for BioChaperone Combo was longer than 30 hours in the majority of patients but only 18 hours with HumalogMix; and BioChaperone Combo was well tolerated.

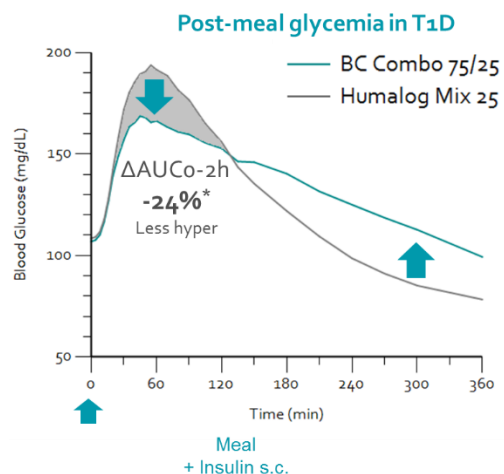
### Phase 1b clinical results – Evaluation of the effects of BioChaperone Combo on postprandial glycemic control in people with type 1 diabetes (n=28)

In early November 2015, Adocia announced positive results for a Phase 1b clinical study evaluating postprandial effects of BioChaperone Combo in 28 patients with type 1 diabetes. This randomized double-blind crossover study compared the effect on postprandial glycemia of individualized doses of BioChaperone Combo and HumalogMix™75/25 (Eli Lilly), injected at the start of a standardized meal. The study fulfilled its primary endpoint, demonstrating that BioChaperone Combo decreased postprandial glycemia significantly more than Humalog Mix™75/25 during the first two hours ( $\Delta AUC_{BG(0-2h)}$ ). The minimal blood glucose level observed during the period was also significantly better controlled with BioChaperone Combo vs. Humalog® Mix™ 75/25. Although this study was not designed to measure differences in the incidence of hypoglycemic episodes between the two treatment groups, a reduced number of hypoglycemic events was observed with BioChaperone Combo vs. Humalog® Mix™ 75/25



Figure 7: Pharmacodynamic profiles for BioChaperone Combo 75/25 and HumalogMix 25 after a liquid meal obtained from 28 people with type 1 diabetes (NCT#02514954). 1 p=3.10-3.2 p=8.10-3.

The results of this study were the subject of an oral presentation given by Dr. Steve Edelman (University of California, San Diego) at the American Diabetes Association's 76th Scientific Sessions (June 2016, New Orleans, USA) and a poster at the European Association for the Study of Diabetes 52nd Annual Conference (September 2016, Munich, Germany).



### Phase 1b clinical results – Pharmacokinetic and pharmacodynamic study of people with type 2 diabetes comparing BioChaperone Combo to HumalogMix 75/25™ and to the dual injection of Lantus and Humalog. (n=24)

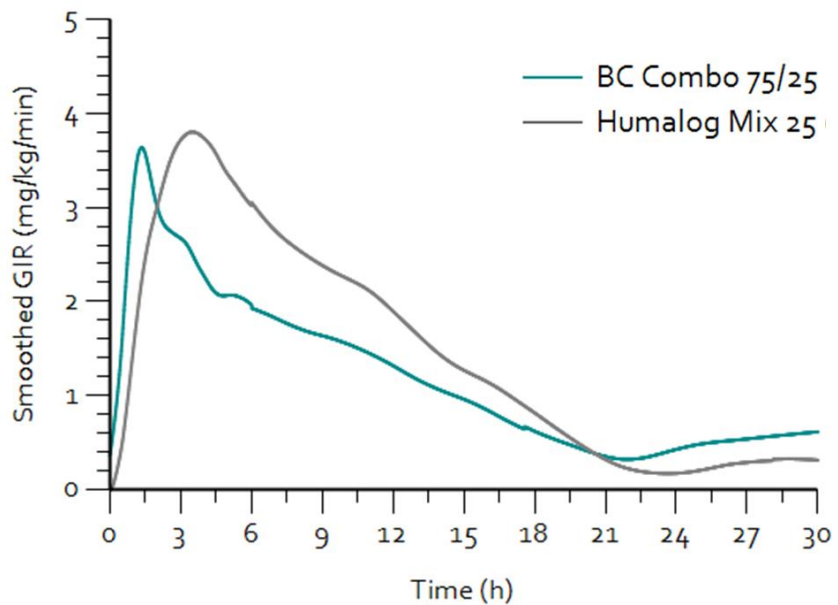
In late November 2015, Adocia announced positive topline results for a Phase 1b study comparing the pharmacokinetic and pharmacodynamic profiles of BioChaperone Combo to those of HumalogMix 75/25™ and to the dual injection of Lantus and Humalog in patients with type 2 diabetes.

This randomized, double-blind, crossover phase 1b clinical study evaluated BioChaperone Combo in 24 patients with type 2 diabetes under euglycemic clamp conditions. The topline results consisted of comparing the pharmacodynamic profile of BioChaperone Combo to that of Humalog Mix75/25™ (Eli Lilly) and to separate, simultaneous injections of Lantus (insulin glargine, Sanofi) and Humalog (insulin lispro, Eli Lilly). The two key parameters in this comparison were the early prandial effect ( $AUC_{GIR(0-2\ h)}$ ) and the delayed basal effect ( $AUC_{GIR(24-30\ h)}$ ) of these three treatments.

In this study, BioChaperone Combo demonstrated a significantly superior early prandial action and a longer metabolic effect compared to Humalog Mix75/25™, which confirms results previously obtained during the first pharmacokinetic and pharmacodynamics study conducted in patients with type 1 diabetes.

## Presentation of Adocia and its activities

Figure 8: Pharmacodynamic profile (glucose infusion rate) of BioChaperone Combo 75/25 and Humalog Mix 25 for 30 h after injection in 24 subjects with type 2 diabetes under euglycemic clamp conditions (NCT#02514850).



Furthermore, this study also established the proof-of-concept that BioChaperone Combo has a similar effect to that of the dual injection of Lantus and Humalog on these two parameters in people with type 2 diabetes.

The results of this study were presented in a poster discussed by Dr. Eda Cengiz (Yale School of Medicine) at the American Diabetes Association's 76th Scientific Sessions (June 2016, New Orleans, USA) and an oral presentation by Dr. Simon Bruce, Medical Director at Adocia, at the 52nd annual conference of the European Association for the Study of Diabetes (September 2016, Munich, Germany).

### Phase 1b clinical results – Evaluation of the effects of BioChaperone Combo on postprandial glycaemic control in people with type 2 diabetes. (n= 39)

In June 2017, Adocia announced the positive topline results for a study intended to measure the effect of BioChaperone Combo injected at mealtimes on postprandial glycaemic control in patients presenting type 2 diabetes compared to that obtained with Humalog Mix25™ premixed insulin (Eli Lilly), and with separate injections of Lantus (Sanofi) and Humalog (Eli Lilly).

Firstly, BioChaperone Combo showed a statistically significant decrease of 18% in glycaemic excursions for the first two hours after the meal compared to Humalog Mix25™. The number of hypoglycaemic episodes per patient was also significantly lower with BioChaperone Combo than with Humalog Mix25™. Moreover, BioChaperone Combo led to at least as good postprandial glycaemic control as that achieved with simultaneous and separate injections of Lantus and Humalog, and a similar number of hypoglycaemic episodes per patient.

### Phase 1b clinical results – BioChaperone Combo dose-proportionality study in people with type 2 diabetes. (n= 32)

In January 2018, Adocia announced positive topline results for a Phase 1b study evaluating the relationship between insulin exposure and hypoglycaemic response to the BioChaperone Combo 75/25 dose for three different doses in people with type 2 diabetes. During his study, 32 participants were randomly allocated a sequence of four treatments: one of the three doses of BioChaperone Combo 75/25 (0.6 IU/kg; 0.8 IU/kg or 1.0 IU/kg) or a single dose of Humalog Mix25™ at 0.8 IU/kg. BioChaperone Combo exhibited dose-proportional exposure and a linear relationship of hypoglycaemic response to the dose when tested at 0.6; 0.8 and 1.0 IU/kg in people with type 2 diabetes. These results are essential to complete the regulatory dossier. The study also confirmed previous results showing that BioChaperone Combo acts significantly faster (prandial effect) and lasts significantly longer (basal effect) than HumalogMix.

## ▪ Partnership with Tonghua Dongbao Pharmaceuticals Co. Ltd

In 2018, Adocia and the Chinese leader of insulin Tonghua Dongbao Pharmaceuticals Co. Ltd entered strategic alliance. In April 2018, Adocia granted Tonghua Dongbao Pharmaceuticals Co. Ltd two licensed for the development and commercialization rights of BioChaperone Lispro and BioChaperone Combo in China and in other Asian and Middle East territories.

The BioChaperone Combo agreement includes an upfront payment of \$40 million, up to \$50 million development milestone payments and double-digit royalties on the sale of this product in the designated territories. Tonghua Dongbao Pharmaceuticals Co. Ltd will also reimburse some of Adocia's expenses for research and development activities performed during the terms of the agreement.

Adocia retains the rights to develop and license BioChaperone Combo in worldwide markets outside of the territories covered by these agreements, including the United States, Europe, Latin America and Japan. Adocia remains responsible for the development and the manufacturing of BioChaperone® pharmaceutical excipients.

In June 2018, Tonghua Dongbao Pharmaceuticals Co. Ltd agreed to manufacture and supply insulin lispro and insulin glargine APIs to Adocia worldwide, excluding China, to support the development of Adocia's portfolio in these territories.

This agreement gives us full control, outside China, over the further development of BioChaperone Combo. This also opens additional collaboration opportunities with biopharmaceutical companies focused in diabetes with no existing insulin manufacturing facilities.

Further details on these contracts and the company Tonghua Dongbao Pharmaceuticals Co. Ltd are available under the section 1.3.7 of the present reference document

## ▪ Next steps

Adocia is actively seeking a partner to further develop and market BioChaperone Combo, for territories non licensed to Tonghua Dongbao Pharmaceuticals Co. Ltd.

## ▪ Competition

**Premixed insulins**, which are prandial insulins of which some is precipitated with protamine, should be considered as direct competitors to BioChaperone Combo. These products include: HumalogMix® (**Eli Lilly**, made from insulin lispro) NovoMix®/NovologMix® (**Novo Nordisk**, made from insulin aspart), in addition to, in emerging countries, premixed insulins made from human insulin, which remain widely used (e.g., Humulin® 70/30 for Eli Lilly and Novolin® 70/30 for Novo Nordisk, as well as many locally-developed products). These products now represent an estimated combined turnover of **\$4 billion** for the three largest players, \$2.2 billion for analog premixes<sup>19</sup> and \$1.8 billion for human insulin premixes<sup>20</sup>. It should be noted that in China, 65% by volume of insulin sold consists of premixed insulin (according to estimates by IQVIA in 2017). Whilst the exact turnover of Chinese companies in the Chinese market is not known, it is acknowledged that the Chinese market is underestimated.

However, as previously explained, these products have several disadvantages, particularly in terms of:

<sup>19</sup> Overall turnover estimates for 2017, based on annual reports published by Eli Lilly and Novo Nordisk. NovoMix/NovologMix: Turnover in 2015 reported as 10 257 MDKK, estimated at \$1.552 billion (based on the \$/DKK average exchange rate per trimester). HumalogMix: Turnover in 2017 for Humalog (prandial and premix) reported as \$2.865 billion. After the survey of the ratios between Humalog and HumalogMix in volume based on IQVIA data from 2017 in Europe, in the US in Japon and in China. The estimated turnover of HumalogMix in 2017 was \$629 million. This equates to a total of \$2.181 billion. This figure is probably underestimated, as in emerging markets some players have already marketed analog insulin premixes, such as Gan & Lee in China (Iispromix).

<sup>20</sup> For premixed human insulin, we used the ratio between human prandial insulin and premixed human insulin reported in the same presentation by Novo Nordisk, i.e., 40% prandial and 60% premix. By applying this ratio to the total sales of Novo Nordisk's human insulin (Novolin DKK10,072million, i.e., \$1.526 billion), Lilly (Humulin, \$1.335 billion) and Sanofi (Insuman, \$121 million), we obtain a total of \$1.789 billion for premixed human insulin. This figure is probably underestimated, as in emergent markets, many other players are producing and marketing human insulin, in particular in premixed forms in the Asian and Latin American markets (e.g., Gan & Lee, DongBao, Fosun WangBang in China; Biocon in India; R-Pharm in Russia; Julpharm in the Middle East, etc.)

- **A delayed prandial action** compared to their benchmark insulin (human or analog). This delay leads to reduced postprandial glycemic control and an elevated risk of hypoglycemia linked to an overly slow transition between the prandial and basal effects. In clinical studies published to date, BioChaperone Combo and Ryzodeg present a similar onset of action to prandial insulin analogs.
- **An overly slow basal action**, always less than 24h, meaning two injections per day are required. With BioChaperone Combo, it is possible to gradually intensify treatment, switching from basal insulin to a single daily injection of BC Combo (at the time of the main meal of the day), then to two injections when disease progression requires it.

BioChaperone Combo may thus represent a superior solution to premixed insulin, at a similar price, to facilitate patient access to a better-performing and safer treatment, particularly in emergent countries wherein these products remain dominant.

**Novo Nordisk** has developed Ryzodeg<sup>®</sup>, the only other product truly combining a basal insulin (insulin degludec) and a prandial insulin (insulin aspart), Ryzodeg was tested in multiple clinical studies, either against a premixed insulin aspart, NovoMix<sup>®</sup>, against Lantus, or against the combination of Levemir and NovoLog. These results demonstrated the Ryzodeg is well tolerated in patients with type 1 and type 2 diabetes, and that this product can improve glycemic control vs. Lantus and reduce the incidence of hypoglycemic episodes vs. Novomix, confirming the expected benefits of a 'true' combo compared to premixed insulin. In 2013, Novo Nordisk obtained marketing authorizations for Tresiba and Ryzodeg in Europe and Japan. Ryzodeg is the first dual insulin combo product to enter the market. Tresiba and Ryzodeg were only approved in the United States in September 2015 after Novo Nordisk published positive interim results from the additional cardiovascular safety studies of Tresiba which the FDA had requested during the first submission of the regulatory dossier. Ryzodeg is now available in more than 25 countries. The pricing strategy of Novo Nordisk takes into account the investment consented in developing Tresiba and Ryzodeg is currently sold at a premium compared to Novomix.

BioChaperone Combo, the formulation developed by Adocia combining insulin glargine and lispro, benefits from the large amount of positive data on the safety of insulin glargine and lispro (Lantus<sup>®</sup> and Humalog<sup>®</sup>). BioChaperone Combo may also benefit from a competitive advantage in terms of cost, as the product is based on two insulins which fell in the public domain and benefit from large manufacturing infrastructure.

In 2018, Adocia secured its sourcing of lispro and glargine insulins from Tonghua Dongbao Pharmaceuticals Co. Ltd. of China.

### 1.3.3.6 HinsBet<sup>®</sup>

- **A rapid and cost-effective prandial insulin**

Seventy-seven percent of people with diabetes live in low- and middle-income countries where human insulin is the main type of insulin used. For these patients with diabetes, there is a real need for prandial insulin at an affordable price which acts as rapidly as insulin analogs.

HinsBet<sup>®</sup> U100 is a standard concentration human insulin formulation incorporating BioChaperone<sup>®</sup> to accelerate its action profile.

Some people with type 2 diabetes are severely resistant to insulin and their treatment may require daily doses of insulin two or three times higher than those normally administered to people with type 2 diabetes, i.e., more than 200 units per day.

It is difficult for these patients to use conventional insulin analogs or human insulin at 100 IU/mL, such as Humalog<sup>®</sup> or Humulin<sup>®</sup>, as the volumes involved for the administrations are too large.

The main option for insulin-based treatment for these highly insulin-resistant individuals in the United States is Humulin<sup>®</sup> U500 (Eli Lilly), a human insulin formulation at 500 IU/mL, that is, five times more concentrated than

standard products on the market. This product has rapidly growing revenues in the United States where estimates for 2014 amounted to more than \$300 million<sup>21</sup>.

### ▪ Clinical results obtained with HinsBet U100

Two formulations were developed for HinsBet: one conventional formulation, that enabled the clinical proof-of-concept to first be demonstrated, and an optimized formulation, which was tested in two clinical studies in people with type 1 diabetes.

#### Phase 1b clinical results – Pharmacokinetic and pharmacodynamic study of people with type 1 diabetes comparing HinsBet U100 (BioChaperone rHI) to Humalog (insulin lispro) and Humulin (rHI). (n=36)

In February 2015, Adocia announced positive topline results for this crossover double-blind study comparing the pharmacokinetic and pharmacodynamic characteristics of HinsBet with those of Humulin and Humalog. Thirty-six patients with type 1 diabetes received a single 0.2-U/kg dose of HinsBet, Humulin and Humalog under euglycemic clamp conditions. The results showed that HinsBet was significantly faster acting than human insulin in patients with type 1 diabetes: onset of action 70% sooner and double the early metabolic effect. The three formulations were well tolerated and did not induce any local reaction.

This rapid action of HinsBet is comparable to that of Humalog in the first hour, which is critical when it comes to prandial glycemic control.

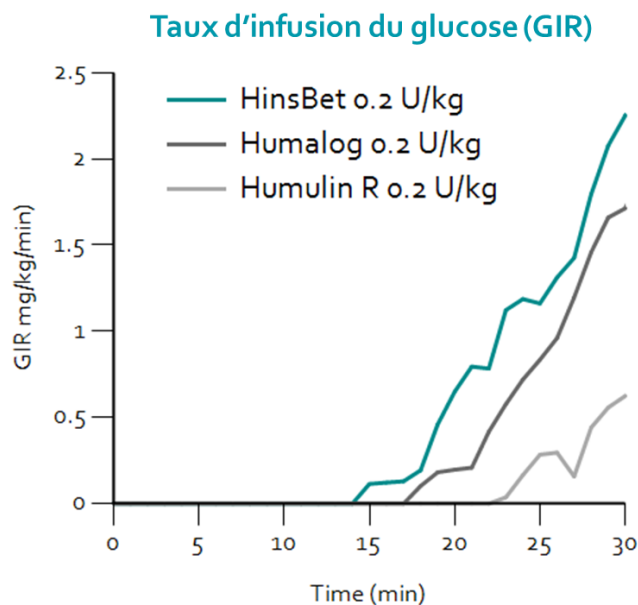


Figure 9: Pharmacodynamic profile (glucose infusion rate) of HinsBet U100 (0.2 U/kg), Humalog U100 and Humulin U100 for the first 30 minutes after injection in 36 subjects with type 1 diabetes under euglycemic clamp conditions (NCT#02213146).

#### Phase 1b clinical results – Evaluation of the effects of HinsBet U100 on postprandial glycemic control in people with type 1 diabetes. (n= 36)

On October 27, 2016, Adocia announced positive topline results for this study, which compared the postprandial effect of HinsBet U100 to those of Humalog and Humulin, injected at the same time as a mixed standardized meal. The clinical study achieved its principle objective of demonstrating the superiority of HinsBet over Humulin in terms of postprandial glycemic control one hour after the meal (glycemia level one hour after the meal:  $BG_{1h}$ =228 mg/dL with HinsBet vs. 253 mg/dL with Humulin, LSM ratio 0.9, 95% CI,  $p=0.0002$ ). HinsBet also showed a similar effect to that of Humalog in terms of postprandial glycemic control for the first hour after the meal. In addition, HinsBet significantly reduced postprandial glycemic excursions for the first hour compared to Humulin ( $AUC_{BG0-1h}$ =174  $h^*mg/dL$  avec HinsBet vs. 192  $h^*mg/dL$  with Humulin, LSM ratio 0.9, 95% CI,  $p=0.0002$ ). No significant differences

<sup>21</sup> RED BOOK 2013 - Truven Health Analytics - Thomson Reuters

were observed between HinsBet and Humalog for this last parameter ( $AUC_{BG0-1h}=174 \text{ h*mg/dL}$  with HinsBet vs.  $172 \text{ h*mg/dL}$  with Humalog, LSM ratio 1.0, 90% CI,  $p=0.5373$ ).

### ▪ Next steps

On the basis of these positive phase 1b results and given the particular potential of HinsBet in emergent countries with greater user demand for human insulin, Adocia intends to find one or several partners with which to continue HinsBet development in these markets.

### ▪ Competition

The global market for human prandial insulin for the three main players (**Novo Nordisk, Sanofi and Eli Lilly**) is currently estimated at \$1.238 billion<sup>22</sup>. Compared with conventional recombinant human insulin, HinsBet presents the advantage of an onset of action equally fast as that of an analog, for a cost similar to that of human insulin. HinsBet would therefore likely outperform human insulin in markets where it remains significant.

Ultimately, HinsBet will also compete with insulin analog biosimilars (aspart, lispro, glulisine). At present, an insulin lispro biosimilar developed by Sanofi (Admelog<sup>®</sup>) is approved in Europe and the United States, and some rapid-action insulin analog biosimilars have been approved (for instance a biosimilar of insulin lispro in China developed by Gan & Lee) or are in development (insulin lispro for Biocon in the preclinical stage in India) in emergent countries. Sanofi is also developing an insulin aspart biosimilar (phase 1). However, HinsBet should continue to enjoy a competitive advantage in terms of pricing, since human insulin production remains less expensive than that of insulin analogs.

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### 1.3.3.7 BioChaperone Glucagon

#### ▪ An aqueous formulation of human glucagon for the acute and chronic treatment of hypoglycemia

Glucagon is one of the main hormones regulating the metabolism. Its role is schematically the opposite to that of insulin. In a person without diabetes, glucagon is secreted in the event of hypoglycemia or during exertion in order to keep blood glucose at a normal level.

**Severe hypoglycemia** is defined by a blood glucose lower than 50-54 mg/dL. It is insulin's most feared short-term adverse event (due to overdosing). Its symptoms may include dizziness, transient cognitive impairment, convulsion and, in the most severe cases, coma and death. Due to those symptoms, treating severe hypoglycemia very often requires the help of a third party.

In the therapeutic field, human glucagon is the only approved treatment for severe hypoglycemia. Unfortunately, human glucagon is very unstable in aqueous solution and the only commercially-available products at present are the emergency (rescue) kits composed of lyophilized human glucagon that can be reconstituted just prior to injection by following several steps. Recent studies evaluating the ease-of-use of these kits have shown that in 80% of cases, users fail to correctly reconstitute and/or administer the recommended dose<sup>23</sup>.

By using proprietary BioChaperone<sup>®</sup> technology, Adocia intends to develop a stable aqueous solution of human glucagon. Such a solution could both be used as part of the emergency treatment of hypoglycemia (in a ready-to-use device) and in the context of a dual hormone artificial pancreas (DHAP). In the latter, using glucagon may help to significantly increase the time spent within the targeted glycemic range. Additionally, the joint use of glucagon and insulin may help bring about devices that are completely autonomous, using algorithms that react automatically to glycemic variations, without the patient directly intervening. Recently, several research groups (academic and

<sup>22</sup> Cf. Calculation for human insulin premixes. The proportion of prandial human insulin is estimated here to be 40% of reported sales. Once again, the turnover figures for local players (Gan & Lee, DongBao, Fosun WangBang, Biocon, R-Pharm, BioMM, Bioton, etc.) have not been reported, suggesting that this figure is probably underestimated.

<sup>23</sup> Locemia, 2015

industrial, such as Beta Bionics or Inreda Therapeutics) have developed such “smart” pumps and have clinically demonstrated their potential benefits in comparison to pumps using insulin alone<sup>24</sup>, particularly with regards to reduced glycemic variability and the reduced risk of hypoglycemia. However, all these teams are currently limited by the absence of a commercially available glucagon solution. Most of the studies up until now have been conducted using lyophilized glucagon reconstituted every day, what would not be acceptable for a daily use, or with developing products which are not yet approved by a regulatory authority Adocia is also seeking to develop BioChaperone Glucagon for other indications, including congenital hyperinsulinism and chronic hypoglycemia following bariatric surgery.

Adocia hopes to be able to soon offer an aqueous solution of human glucagon. Using human glucagon also presents Adocia the additional advantage of being able to take advantage of the track record of this approved peptide compared to glucagon analogs developed by some competitors (e.g. Eli Lilly, Zealand Pharma).

## ▪ Clinical results obtained with BioChaperone Glucagon

### Phase 1 clinical results – Evaluation of the safety, pharmacokinetics, and pharmacodynamics of BioChaperone Glucagon in patients with type 1 diabetes (n=24)

In November 2017, Adocia announced positive topline results for this first study of BioChaperone Glucagon in human participants. A subcutaneous injection of 1 mg BioChaperone Glucagon showed acceptable safety and tolerability profiles, validating the primary objective of the study. In all groups, the most common adverse event was nausea, with eight events observed in 25 patients with BioChaperone Glucagon vs. five events in 24 patients with Glucagen® HypoKit®. The median time to reach a clinically risk-free level of glucose of 70 mg/dL was 11 min for BioChaperone Glucagon and almost 7 min for the reconstituted commercial product Glucagen®. All patients achieved hypoglycemic resolution within 35 minutes of injection.

## ▪ Next steps

Adocia plans to initiate a second Phase 1/2 study during the second quarter of 2019. This study could be the last one before starting the program in Phase 3 development. In parallel, Adocia is selecting a high quality and easy-to-use injection device for BioChaperone Glucagon.

## ▪ Competition

Two major applications are envisaged for the BioChaperone Glucagon formulation.

- Treatment of severe hypoglycemia
- Chronic use (bi-hormonal artificial pancreas, indications in need of a glucagonotherapy)

For the treatment of severe hypoglycemia, there are currently two products on the market: Glucagon® (**Eli Lilly**) and GlucaGen® Hypokit® (**Novo Nordisk**). These both come in emergency kits and require the real-time reconstitution of lyophilized glucagon and injection with a syringe. There are between seven and nine stages to the procedure. In a real emergency situation, wherein the patient is unconscious, these devices have proven to be extremely difficult to use for third parties, even more so if they have not been trained in their use. In a study of 130 parents of people with type 1 diabetes in a simulated hypoglycemic emergency, 69% of them had difficulty handling the emergency kit (Glucagen Hypokit)<sup>25</sup>. Due to the difficulty using these products, they remain underprescribed and underused, leading to frequent interventions by emergency teams. The response time can be fatal. Severe hypoglycemia results in more than 300,000 hospitalizations in the United States each year<sup>26</sup>. Several companies, including Adocia, are developing ready-to-use alternatives for emergency treatment.

<sup>24</sup> For example, c.f. El Khatib et al., 77-OR, ADA 76th Scientific Sessions June 10–14th, 2016, USA. et Russell et al, *The Lancet* (2016) 4(3):233-2

<sup>25</sup> Harris, G et al *Practical Diabetes Int.* 2001; 18:22-25.

<sup>26</sup> Report from the CDC, 2014

Locemia has developed a single-use nasal spray presentation which in principle is easier to use for the untrained user. This product was acquired by **Eli Lilly**, for an undisclosed sum, in October 2015. Lilly filed this product for registration with the US and European regulatory authorities during the second quarter 2018. Meanwhile, Lilly ended in 2018 the development of a soluble glucagon analog formulation.

Furthermore, several companies are developing liquid forms for use in emergency situations or for use with an artificial pancreas.

**Xeris** developed a human glucagon liquid formulation with the help of the organic solvent DMSO. It intends to develop this product in the form of a pen for emergency situations, a mini-pen for moderate hypoglycemic episodes, and a cartridge for use in pumps (artificial pancreas or other chronic uses of glucagon). At this stage, two Phase 3 studies and a Phase 3b study have been successfully completed. Xeris entered pre-registration stage in the US in Q2 2018. Furthermore, the company completed a Phase 2 study using glucagon pumps to treat post-bariatric hypoglycemia and initiated in April 2018 a Phase 2 study using glucagon pumps in people with type 1 diabetes with hypoglycemia unawareness. Xeris has also obtained the 'orphan medicinal product' indication from the FDA for use in the treatment of congenital hyperinsulinemia and started a Phase 2 for this indication in December 2018.

**Zealand Pharma** is developing a glucagon analog, dasiglucagon, for three main indications: for the treatment of severe hypoglycemia; for use in a DHAP; and for the chronic treatment of congenital hyperinsulinism (in a glucagon pump). At the end of 2017, it started Phase 3 studies on HypoPal<sup>®</sup>, a prefilled ready-to-use pen for the emergency treatment of severe hypoglycemia. Preliminary positive results for this study were announced in February 2018. Zealand plans to market HypoPal<sup>®</sup> in Europe and the United States in 2020/2021. Furthermore, it recently announced the preparation of a Phase 2b study using the Beta-Bionics artificial pancreas, iLet<sup>™</sup>. Finally, it has obtained an 'orphan drug' indication by the FDA for the use of dasiglucagon to treat congenital hyperinsulinism, a project which entered Phase 3 in December 2018.

Compared to an analog, BioChaperone Glucagon should offer the advantage of using human glucagon, the safety and efficacy of which have been demonstrated with the Glucagon<sup>®</sup> and Glucagen<sup>®</sup> products.

### 1.3.3.8 BioChaperone Pramlintide Insulin: multi-hormonal prandial combinations for the treatment of type 1 diabetes

- Provide high-performance, easy-to-use multi-hormone therapy for people with type 1 diabetes to improve long-term outcomes

Although insulin is a vital treatment for people with type 1 diabetes, even the best-controlled patients present significant glycemic variations and frequently do not achieve the targets set by their physician. This may result in an increase in the risk of severe complications in the long term, such as cardiovascular disease, retinopathy, renal failure and neuropathy.

In fact, in people who do not have diabetes, insulin is secreted synchronously and acts in synergy with other hormones, such as amylin and GLP-1, to control glycemia. In type 1 diabetes, ultimately, neither insulin nor amylin are secreted, and GLP-1 secretion is deficient. It is therefore possible that the use of insulin alone cannot address all the metabolic deficiencies related to diabetes.

Pramlintide (Symlin<sup>®</sup>, AstraZeneca), a rapid-acting amylin analog, was approved in 2005 for the treatment of diabetes (type 1 and 2) as a supplement to intensive insulin therapy. In phase 3 clinical studies, this molecule has been shown, when used as a supplement to insulin therapy, to improve HbA1c (-0,2% by people with type 1 after 6 mo.) and reduce prandial insulin use (-22% in the same study) and weight gain compared to insulin alone (-3 kg in the same study)<sup>27</sup>.

<sup>27</sup> Guthrie R and al Diabetes 2005, 54(Suppl 1):A118. See also Pullman J and al Vasc Health Risk Manag. 2006, 2 (3), 203-212



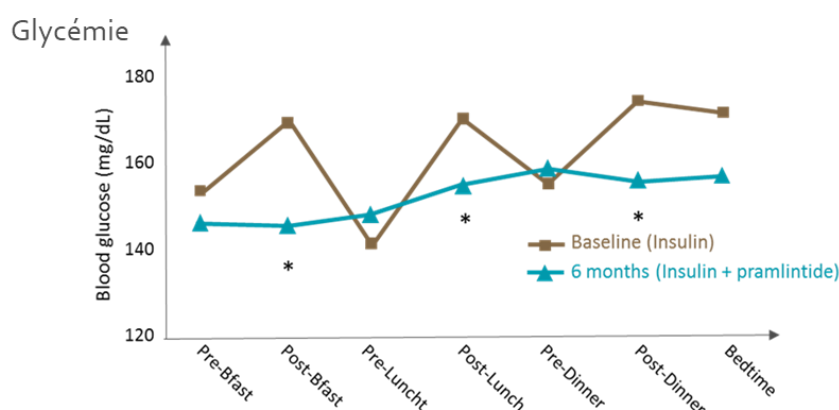


Figure 10 : Average daytime glycemia in people with type 1 diabetes, treated by insulinotherapy alone (brown curve) or by insulinotherapy + Symlin® (pramlintide, blue curve), after a 6 months treatment period. Adapted from Guthrie R and al Diabetes 2005, 54(Suppl 1):A118, \*P <.05. See also Pullman J and al Vasc Health Risk Manag. 2006, 2 (3), 203-212. And for type 2 diabetes : Karl D, and al. Diabetes Technol Ther 2007; 9(2):191-199 and the label of Symlin.

Unfortunately, to the extent that insulin therapy for type 1 diabetes requires high patient compliance, with frequent glycemia monitoring and at least four injections of insulin daily, the introduction of an additional injectable treatment is often synonymous with a significant deterioration in quality of life and an increase in the cost of treatment, which can lead to its abandonment.

The combination of this molecule with insulin could therefore prove to be an elegant solution to maximize the medical benefit whilst maintaining patient compliance and controlling health costs. Developing such a combination is Adocia's objective for the BioChaperone Pramlintide Insulin program.

Currently, the prandial insulin and pramlintide formulations are not compatible. Adocia has therefore used its expertise to develop BioChaperone so pramlintide can be solubilized and stabilized in neutral pH solution, enabling it to be combined with prandial insulin.

Our BioChaperone formulation strategy, based on actual clinical results, showing a clear medical benefit when hormones are administered separately, could reduce development time. The BioChaperone Pramlintide Insulin project could also support a competitive pricing strategy, taking advantage proteins already approved and in the public domain.

### ▪ Clinical results obtained by BioChaperone Pramlintide Insulin

#### Phase 1 clinical results – Evaluation of safety, pharmacokinetics and pharmacodynamics of BioChaperone Pramlintide Insulin in people with type 1 diabetes (n=24)

In September 2018, Adocia announced positive pharmacodynamic and safety topline results from the Phase 1 study of BioChaperone Pramlintide Insulin (BC Pram Ins), the ready-to-use co-formulation of pramlintide and human insulin. This randomized, double-blind, active comparator-controlled, three-period cross-over study, enrolled 24 participants with type 1 diabetes. Subjects were randomly allocated to a sequence of three treatments, administered at the time of the intake of a standardized mixed meal. This study aimed to investigate the pharmacokinetics, pharmacodynamics, and the safety and tolerability of a single fixed dose of BC Pram Ins (containing 7.5U insulin and 45 µg pramlintide), compared on the one hand to separate and simultaneous injections of human insulin (7.5U, Humulin®, Eli Lilly) and pramlintide (45 µg, Symlin®, AstraZeneca), and on the other hand to an injection of rapid-acting insulin analog lispro (7.5U, Humalog®, Eli Lilly).

Treatment with BC Pram Ins resulted in a statistically significant 97% reduction of blood glucose excursions over the first two hours compared to Humalog (Mean(±SD) DeltaAUCGIR 0\_2h = 4 (63) mg\*h/dL vs. 126(74) mg\*h/dL; p<0.0001) and a comparable postprandial glycemic control to that of the separate injections of Humulin and Symlin (LS- Mean DeltaAUCGIR 0\_2h = 21 (66) mg\*h/dL, n.s.)

All treatments were well tolerated. Notably, the overall number of hypoglycemia was similar between treatments (BC Pram Ins: n=4; Symlin + Humulin: n=3; Humalog: n=3) and there were no warnings on gastro-intestinal side-effects with any of the administered treatments. As a reminder, hypoglycemia and gastro-intestinal side effects have been previously associated with Symlin® clinical use.

### ▪ Next steps

Adocia plans to initiate a second phase 1 /2 study during the first semester of 2019.

### ▪ Competition

To date and to our knowledge, only **Biozeus**, a Brazilian biotechnology company, and **Xeris** Pharmaceuticals, a biotech company known for its ready to use glucagon program for different indications, are developing at the preclinical level a combination of insulin and amylin.

**AstraZeneca**, which owns the commercial product Symlin (pramlintide), has successfully conducted Phase 1 clinical trials on the joint administration, with two independent pumps, of prandial insulin and pramlintide. These studies were partially funded by the Juvenile Diabetes Research Foundation (JDRF). These results support Adocia's approach of combining the two products in a single formulation for better results<sup>28</sup>.

**Novo Nordisk** is also developing a new long-acting amylin analog, which is currently tested in 2 Phase 1 clinical trials, alone and in combination with Novo Nordisk's last generation GLP-1, semaglutide. This product is intended for use in overweight or obese patients, but not in patients with diabetes.

**Zealand Pharma** in collaboration with Boehringer Ingelheim, is also developing a long-acting amylin analog for people with obesity as well as for people with type 2 diabetes. A phase 1 study planned in 2017 was cancelled and the project is registered as in preclinical development.

### 1.3.3.9 BioChaperone Glargine GLP-1

#### ▪ Combinations to intensify treatment in people with type 2 diabetes using basal insulin

Basal insulin remains an essential treatment for patients with uncontrolled type 2 diabetes using oral antidiabetic agents. However, according to some estimates, 50% of people with diabetes using basal insulin alone as an injectable treatment do not meet their glycemic target<sup>29</sup>.

As the underlying mechanisms of action of basal insulin and GLP-1 receptor agonists (GLP-1s) are complementary, combinations of the two agents have been developed as one product, once-daily treatment intensification options for these patients. In Phase 3 clinical studies, these combinations demonstrated improved glycemic control whilst reducing the incidence of adverse reactions compared to each agent used separately (hypoglycemia level similar to or lower than basal insulin alone and less gastrointestinal adverse reactions GLP-1 alone)<sup>2</sup>. Two basal insulin-GLP-1 combinations were approved by the FDA in November 2016 (Xultophy<sup>®</sup> by Novo Nordisk and Soliqua<sup>®</sup> by Sanofi).

In September 2016, Adocia announced the launch of a new BioChaperone program to combine basal insulin and GLP-1. This program benefits from the expertise gained through the BioChaperone Combo project because it relies on BioChaperone's ability to solubilize insulin glargine at physiologic pH. This makes it possible to combine it with the two GLP-1 market leaders: liraglutide (Victoza<sup>®</sup>, Novo Nordisk, daily administration) and dulaglutide (Trulicity<sup>®</sup>, Eli Lilly, weekly administration), in order to develop two potential candidates:

- BioChaperone<sup>®</sup> Glargine Liraglutide, with a strong potential price advantage, as it is based on two proteins in, or about to enter, the public domain, and
- BioChaperone<sup>®</sup> Glargine Dulaglutide, with a strong potential for best-in-class performance, based on the excellent pharmacologic profile of dulaglutide and glargine.

<sup>28</sup> Control of Postprandial Hyperglycemia in Type 1 Diabetes by 24-Hour Fixed-Dose Coadministration of Pramlintide and Regular Human Insulin: A Randomized, Two-Way Crossover Study, Riddle et al., *Diabetes care*, 2018

<sup>29</sup> Sanofi, JP Morgan Healthcare Conference Presentation, San Francisco, January 12, 2015.

These two candidates, which are intended for daily use, may help improve glycemic control whilst also reducing the number of injections and limiting costs for the patient.

- **Preclinical results and next steps**

Adocia generated positive stability and preclinical results for the program BioChaperone Glargine GLP-1.

- **Competition**

Two combinations of basal insulin and a GLP-1 agonist were recently approved for the treatment of type 2 diabetes. Xultophy® (insulin degludec and liraglutide, **Novo Nordisk**) was approved in Europe in September 2014 and in the United States in November 2016. Soliqua®/Suliqua® (basal insulin and lixisenatide, **Sanofi**) was approved in the United States and Europe in November 2016.

In both cases, these products may be used to intensify treatment after using basal insulin or a GLP-1 agonist alone. The two combinations demonstrated in phase 3 clinical studies significant advantages compared to basal insulin: lower HbA1c, weight loss, less nausea than GLP-1 used alone. In the case of Xultophy, the product helps patients to lose weight. In the case of Soliqua, the product is neutral with regard to weight gain (compared to the increase in weight when using insulin). Furthermore, using a combination makes it possible to limit the number of injections to one per day and, in the American healthcare system, to also limit the cost borne by the patient (by requiring only a single "copay" payment per product).

The two companies launched their products on the US market in early 2017. While Novo Nordisk fixed a price for Xultophy corresponding to the sum of the Victoza and Tresiba prices, less a reduction of about 20%, Sanofi was more aggressive, fixing a pricing structure which is equivalent to the average price of a GLP-1, a price (before negotiations) about 33% lower than that of Xultophy. Indeed, as Sanofi had already amortized its investments in insulin glargine (now in the public domain), it has more leeway to set its prices. Conversely, Novo Nordisk must recoup the investments in the development of insulin degludec and liraglutide and must also protect the independent Tresiba (insulin degludec) and Victoza (liraglutide) brands.

Compared to these products, BioChaperone Basal GLP-1 formulations could be positioned at potentially similar performance levels. Moreover, in the case of BioChaperone Glargine Liraglutide, the product could have an advantage in terms of pricing similar to, or even higher than, Soliqua, by using two molecules that are going to be in the public domain.

One last competitor product in development is the combination developed by the Korean company **Hanmi** of a weekly insulin (LAPS-Insulin, currently in the phase 1) and a weekly GLP-1 (efpeglenatide). This combination was licensed to Sanofi in November 2015, as well as each component independently (including a once-monthly version of efpeglenatide), under an agreement including an initial payment of \$434 million (€400 million) and expected to total \$4.2 billion (€3.5 billion). In January 2017, Sanofi announced its was relinquishing the rights to LAPS-insulin and concentrating on the development of efpeglenatide (the weekly injectable version entered phase 3 in 2017). This announcement resulted in Hanmi refunding Sanofi \$250 million (€196 million) and a reduction of the total potential amount of the agreement to €2.72 billion. For its part, Hanmi is responsible for the development of the weekly LAPS-insulin/efpeglenatide combination, a product for which Sanofi retains a licensing option. Hanmi also has to bear some of the development costs of efpeglenatide, which was not the case in the initial agreement. This combination of insulin and GLP-1 is currently in preclinical development.

### 1.3.4 BioChaperone Glucagon GLP-1 for the treatment of obesity

- **Providing a powerful and easy-to-use multi-hormonal treatment to optimize lasting weight loss in obese people**

Obesity is defined as an excessive accumulation of fat in adipose tissue negatively impacting the well-being and health of the person. A person is diagnosed as obese when his or her body mass index (BMI) is more than 30 kg/m<sup>2</sup>.

## Presentation of Adocia and its activities

The increase in weight is the consequence of an imbalance between energy intake and expenditure. This imbalance results from a complex combination of environmental, behavioral and genetic factors.

The World Health Organization (WHO) estimates that there were 650 million obese adults in the world in 2016, or 13% of the world's population. This number has nearly tripled since 1975 and continues to grow<sup>30</sup>. The obesity rate varies from one country to the next with, for example, 39.2% of adults obese (and 65% overweight) in the United States<sup>31</sup>.

Obesity increases the risk of developing many other diseases, including type 2 diabetes, non-alcoholic steatohepatitis (NASH), dyslipidemia, sleep apnea, cardiovascular disease and several types of cancer. These risks increase for overweight people (BMI > 25 kg/m<sup>2</sup>) and increase with weight gain. The World Obesity Federation estimates that obesity and its complications led to nearly \$800 billion in healthcare expenditure worldwide in 2017. This expenditure could reach \$1,200 billion by 2025<sup>32</sup>.

It is generally accepted that a 10–15% loss of body mass significantly reduces the comorbidities associated with obesity.<sup>33</sup> To lose weight, the first recommendation is to have enough regular physical activity and to follow a special diet. However, weight loss is often difficult to maintain, both because it requires often significant behavioral changes, and because the body tends to return to the original weight, for various physiological reasons, which results in discouragement in obese people. Medical treatment is prescribed to patients with BMI greater than 30 kg/m<sup>2</sup> or, if there are two cardiovascular risk factors, a BMI > 27 kg/m<sup>2</sup>. In the event of morbid obesity, bariatric surgery may be prescribed. This consists of reducing the volume of the stomach.

Today, only 2% of obese patients use medication. This low percentage is due to the limited efficacy of the medicinal products available and the lack of persistence of their effects over time. These treatments, oral or injected subcutaneously, can lead to a rapid loss of 3 to 10% of body weight, but this loss is rarely stabilized in the long term. Some of these treatments are also associated with adverse reactions (nausea, cardiac risk, diarrhea, etc.). Mechanisms of action include a decrease in the food bolus, a limitation of nutrient absorption, or an increase in energy expenditure.

Among the available treatments, one of the most effective is **Saxenda**<sup>®</sup> (liraglutide, GLP-1 receptor agonist, Novo Nordisk)<sup>34</sup>. Saxenda<sup>®</sup> is currently the only GLP-1 treatment for obesity and has met with significant commercial success.

Recent studies have shown that a multi-hormonal approach targeting both GLP-1 receptors and other metabolic hormone receptors, such as glucagon or GIP, could increase energy expenditure, promote significant weight loss and improve blood glucose control in obese people<sup>35</sup>. Based on these results, several companies have initiated the development of co-agonists or combinations allowing this multi-hormonal approach.

Based on this promising research and its BioChaperone Glucagon formulation, Adocia has developed BioChaperone Glucagon GLP-1, a two-in-one combination of human glucagon and exenatide (Byetta<sup>®</sup>, AstraZeneca), a GLP-1 receptor agonist. It has been previously shown that the combination of glucagon and GLP-1 RA works by increasing satiety, slowing gastric emptying and increasing energy expenditure (Figure 11). In contrast to the multi-agonist approaches, Adocia's formulation approach makes it possible to rely on the efficacy and safety profiles of two approved molecules, while favoring the choice of the best ratio between these two molecules to optimize the product profile.

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30 Key facts about being obese and overweight, WHO, October 2017

31 NCHS Data Brief, Prevalence of obesity among adults and youth: United States, 2015–2016

32 World Obesity Federation, 2017

33 Glandt & Raz, J. Obes, 2011;2011:636181

34 Liraglutide is also the active ingredient, used at a lower dose, in the hypoglycemic treatment Victoza<sup>®</sup> (Novo Nordisk) for the treatment of type 2 diabetes.

35 Cegla G. et al, Diabetes 2014;63:3711–3720 ; Henderson SJ. et al , Diabetes, Obesity and Metabolism 2016; 18: 1176–1190; Evers A. et al, J Med Chem. 2017 May 25;60(10):4293-4303.

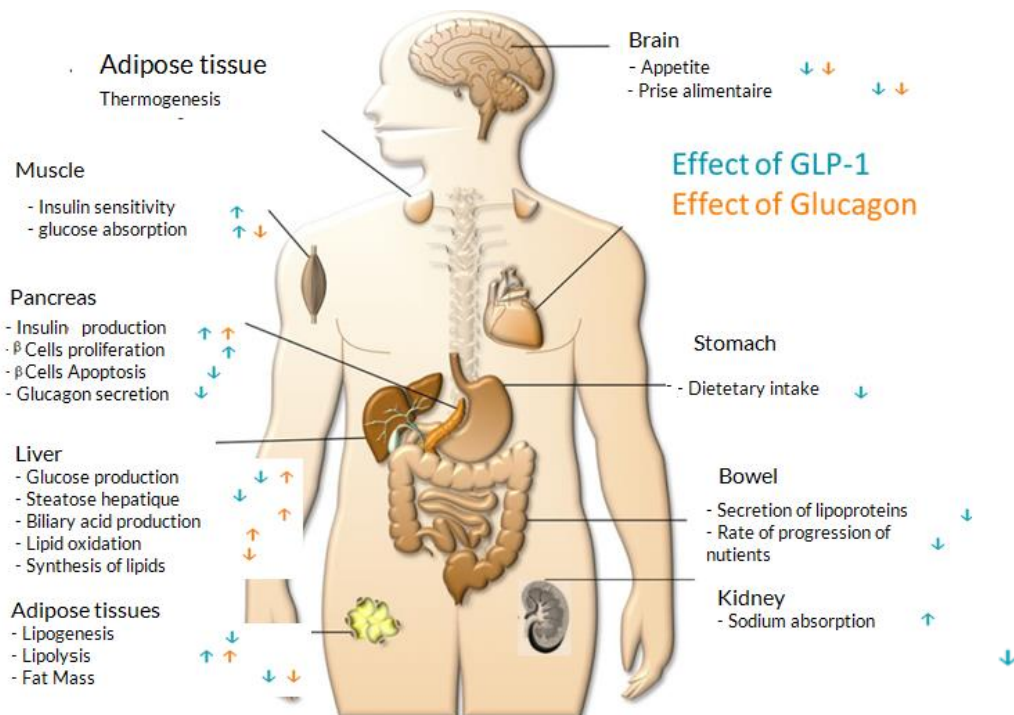


Figure 11: Combined effects of glucagon and GLP-1 on the human body

### ■ In vitro results and next steps

On the basis of promising in vitro stability results, BioChaperone Glucagon GLP-1 is currently in preclinical development, with the goal of starting the first human clinical trial in the second semester of 2019

### ■ Competition

The competition includes both products already approved for the treatment of obesity, and multi-hormonal treatments currently under development.

This market of the treatment of obesity is growing strongly (+120% per year since the end of 2015), due to the rapid increase of the obese population, the emergence of more effective products like Saxenda® (liraglutide, Novo Nordisk) and growing awareness of the value of drug approaches. Five products are currently approved for the treatment of obesity, for a global market still relatively limited, \$500 million in 2017.

- Saxenda® (liraglutide, Novo Nordisk), the only injectable treatment approved in the US since 2015, currently accounts for 75% of the value of the US market<sup>36</sup>. In clinical trials, Saxenda showed a decrease in body weight of 5-7.5% over 12 months.
- BelviQ® (API, Arena/Eisai) is an oral appetite suppressant enabling limited weight loss (around 3%). This treatment is only available in the United States.
- Qsymia® (phentermine and topiramate, Vivus) is an oral combination showing the best weight loss efficacy among oral treatments, but the effect disappears on average less than one year after the start of treatment.
- Xenical® (API, Roche) blocks the absorption of triglycerides.
- Contrave® (bupropion and naltrexone, Nalpropion) is an oral combination that reduces appetite and increases energy expenditure. Following the bankruptcy of Orexigen. The company Nalpropion acquired their assets (including Contrave) in April 2018.

There are currently 33 products in clinical development to treat obesity, with various approaches in terms of mechanism of action and expected efficacy.

<sup>36</sup> Analysis of sales in the third quarter of 2017. \$101 million in sales for Saxenda in a \$139 million market (BelviQ + Saxenda + Qsymia + Contrave).

Among the products in development, semaglutide from Novo Nordisk, a new GLP-1 agonist already approved for the treatment of diabetes, has shown positive weight loss results in Phase 2 studies. This product recently approved for patients with Type 2 diabetes entered into a Phase 3 for treating obese patients.

Eli Lilly also presented promising results of a co-agonist GLP-1 and GIP (the tirzepatide) by patients with type 2 diabetes during the EASD international conference in October 2018. Eli Lilly plans to start soon the clinical development of this product for obese patients.

### 1.3.5 BioChaperone Teduglutide for the treatment of short bowel syndrome

- Simplifying chronic treatment injections for people with severe short bowel syndrome

Short bowel syndrome (SBS) is a serious disease caused by either a congenital defect, intestinal obstruction or extensive surgical resection of the intestinal tract, resulting in a functional small intestine less than 200 cm in length (the average length of the small intestine is 6.1 m in a healthy person). Sufferers have an intestine which is too short to absorb enough ingested food, leading to not only malnutrition and weight loss but also dehydration, severe diarrhea, abdominal pain, and fatigue. In the long term, various complications may occur including anemia or hyperkeratosis. Short bowel syndrome is most often the result of resection of the small intestine, which is itself a result of inflammatory diseases or intestinal tumors. More rarely, there are cases of congenital short bowel syndrome (birth with a small intestine less than 75cm long).

In its most severe forms (intestine less than 1 m), SBS requires supplementary parenteral or enteral nutrition to compensate for the effects of diarrhea, malabsorption of nutrients, intestinal dilatation and intestinal dysmotility. This supplementary nutrition can also sometimes lead to severe complications, particularly involving the liver. Approximately 20,000 people with SBS in the United States and Europe need parenteral nutrition. In these individuals, Gattex®/Revestive® (teduglutide, GLP-2 analog, Shire) can be prescribed to improve intestinal absorption and reduce the need for parenteral nutrition, which seriously disrupts patients' lives.

Indeed, GLP-2 promotes the growth of intestinal villi, reduces intestinal flow and reduces acid secretions in the stomach. However, teduglutide is unstable in aqueous solution and is only available in the form of a lyophilized powder to be reconstituted before each daily injection. Reconstituting the product before injection involves 22 steps and the use of 6 different objects (syringes, needle, vial, Figure 13). This complicated procedure takes time and can result in mishandling, misinjection, or even injury. A ready-to-use solution could therefore have significant benefits for people with short bowel syndrome.



Figure 13: Detail of the material necessary for the reconstituting of Gattex®/Revestive® before injection. (Excerpt from the instruction leaflet).

- In vitro results and next steps

On the basis of promising in vitro results, BioChaperone Teduglutide is currently in preclinical development, with the goal of starting the first human clinical trial in the second semester 2019.

## ▪ Competition

Today, the only competitor product on the market is Gattex® (teduglutide) itself, which has recently addressed a significant medical need. Sales reached \$219.4 million in 2016, and \$335 million in 2017. The market has been growing strongly since the launch of Gattex and is expected to reach in excess of \$500 million at its peak. The annual cost for medication with Gattex® is approximately \$350,000 per year in the United States and €240,000 per year in France.

Two GLP-2 analog projects are currently in clinical development for the treatment of short bowel syndrome. Zealand Pharma is developing glepaglutide, a stable analog of GLP-2 in liquid form. Gelpaglutide entered Phase 3 in October 2018. In addition, Therachon acquired in September 2018 the apraglutide formerly developed by Glypharma. Apraglutide is a long-acting GLP-2 analog with the potential to reduce injections to once or twice a week. This compound has the same disadvantage as teduglutide i.e., instability in liquid form, and is being developed as a powder for reconstitution. Glypharma had announced positive toxicity and safety results in Phase 1 clinical study in healthy subjects. A new analog GLP-2 announced by Hanmi in January 2019 entered in Phase 1 during Q1 2019.

## 1.3.6 Intellectual property

### 1.3.6.1 Innovation policy

Adocia's mission is to create and develop inventions that are subsequently licensed.

These inventions involve in particular innovative therapeutic treatments based on the combination of our processing technology (BioChaperone®) with therapeutic protein agents.

Since its founding, Adocia has created inventions in several therapeutic domains based on its BioChaperone® technology, such as the healing of chronic wounds and the treatment of diabetes with insulin therapy. In 2016 the Company refocused its business on the treatment of diabetes, which is reflected in its patent portfolio.

The Company's innovation policy consists of all measures the Company takes in this area. The Company's innovative mission guides the recruitment of management employees and technicians, employee training, and its work methods. More specifically, researchers receive both internal and external training related to IP.

The inventions that Adocia develops are cross-disciplinary and cover various scientific fields, in particular chemistry, physical chemistry, analytics and biology. Teams of experts have therefore been formed, and then expanded, in each discipline. The various teams are coordinated during regular working meetings held for each project. In addition, each lead scientist presents a bimonthly report on scientific advances every two weeks.

Mr. Gérard Soula has significant research and innovation management experience, with over 30 years' experience in this field. Mr. Olivier Soula, Vice President and R&D Director has more than 15 years of experience in R&D management, first with Flamel Technologies and then with Adocia.

### 1.3.6.2 Procedures for the protection of intellectual property

#### ▪ IP department and external Industrial Property consultancy

The Intellectual Property department reports to the Business Development and legal department under the responsibility of Rémi Soula, BD and Legal Director. The Intellectual Property department is under the responsibility of Walter Roger, IP Director and comprises three people at the date of this registration document.

The Intellectual Property department, in collaboration with an intellectual property consulting firm, evaluates the patentability of inventions and, if applicable, conducts studies of freedom to operate for the products intended to be utilized, in particular via a license. Patent applications and examination procedures are conducted in collaboration with this consulting firm.

## Presentation of Adocia and its activities

This intellectual property firm, Cabinet Tripoz, manages the Company's portfolio of patents.

### ▪ Designation of inventor and remuneration

An invention declaration form has been created to describe the invention and designate its inventor(s), specifying their respective contribution.

Besides, Adocia has set up an attractive compensation policy for inventions in order to promote innovation within the Company. An internal memorandum explains the conditions under which employee-inventors are entitled to the additional compensation prescribed by the French Intellectual Property Code, and provides for payment of attractive lump-sum fixed compensation after submission of a first patent application and granting of a patent in Europe or the United States, as well as variable compensation that increases in accordance with sales generated by the relevant invention.

Mr. Gérard Soula has assigned to the company, without any financial consideration, all of the rights he held for inventions within the Company's field of business at the date of this registration document. Assignment agreements are signed whenever required by national law (in particular, in the USA and Canada). Furthermore, Mr. Gérard Soula has undertaken to assign to the Company, also without any financial consideration, all new intellectual property rights within the company's field of business that he may hold in the future during the time he continues to be an officer of the Company.

### ▪ Communication and confidentiality

It is essential for an innovation company such as Adocia to manage communication and control the confidentiality of information.

Technical communication is therefore approved by the Intellectual Property department and, if applicable, subject to contracts suitable to the situation (see chapter relating to Contracts below).

## 1.3.6.3 Patents and patent applications

### ▪ Intellectual property protection policy

The success of the Company depends at least in part on its ability to protect its inventions, primarily by obtaining and renewing patents in Europe, the United States and the rest of the world.

Since March 16, 2013, priority applications are only submitted in France since it is no longer necessary to apply for a US patent in order for protection to be recognized in this country. Before the new regulation took effect in the United States on March 16, 2013, priority applications were filed simultaneously in France and the United States to implement protection as rapidly as possible.

However, direct extensions in the United States are often conducted simultaneously with PCT extensions to ensure direct and rapid US procedures.

### ▪ Offensive, alternative and defensive strategies

An active policy is pursued to protect products under clinical development (offensive strategy) as well as products derived from alternative solutions (alternative strategy) and products corresponding to defensive solutions (defensive strategies). Patent applications are qualified as (i) protection of core business, (ii) protection of alternative solutions and (iii) defensive applications.

### ▪ Territories

Patent coverages are examined with respect to the importance of inventions, and three predetermined strategies are implemented by the Company concerning the choice of countries in which the national phase of PCT applications are in force (no later than 30 months after submitting the priority application). These three predetermined strategies are:



- Strategy 1 for defensive applications: United States and Europe;
- Strategy 2 for alternative solutions: United States, Europe, China, India, and possibly Brazil, Canada, Japan, Australia and/or Israel;
- Strategy 3 for the core business: United States, Europe, Canada, China, Japan, India, Australia, Israel, Mexico, Brazil, Russia (or Eurasia), South Africa, Singapore and South Korea, even additional territories depending on the market

#### ▪ Patents Applications in the sole name of Adocia

Patents applications submitted by the Company are filed in the name of the Company if their inventors are all employees, with the exception of Mr. Gérard Soula. In the case of company employees, every employment contract for staff contributing to invention contains a clause covering inventions, and all inventions legally belong to the Company as stipulated in article L.611-7 of the French Intellectual Property Code. Transfer agreements are systematically signed for each invention whenever required by government regulation.

#### ▪ Types of patent application

There are two main types of patent:

- Patents concerning an object (also known as “composition of matter” patents) may involve polymers, composites or compositions;
- Patents concerning actions, such as utilizations or procedures.

#### ▪ Portfolio

A review of the portfolio was carried out in 2018 and notably led to the discontinuation of certain patents granted which were no longer relevant to ongoing projects. This explains the decrease in the number of patents issued compared to the latest figures released.

To date inventions are protected by patent application filings comprising 47 distinct families. Adocia's portfolio contains more than 200 patents and patent applications belonging to the Company, of which 157 are being examined by patent authorities. The table below indicates the number of patents granted as well as the patent applications currently underway, by territory, as of December 31, 2018:

## Presentation of Adocia and its activities

Territoires	Patents	Ongoing patent application
France	14	25
USA	14	27
Europe (Brevet Européen)	8	21
South Africa	0	4
Saudi Arabia	2	3
Australia	1	5
Brazil	0	8
Cambodge	0	1
Canada	0	4
China	4	6
South Korea	0	4
Egypt	0	1
Eurasia (Eurasian patent)	0	4
Hong Kong	1	3
India	0	6
Indonesia	0	1
Israël	0	3
Japan	2	4
Malaysia	0	1
Mexico	1	6
New Zealand	0	2
Pakistan	0	2
Philippines	0	1
Russia	1	0
Singapour	1	5
Taiwan	0	2
PCT	NA	14
<b>TOTAL</b>	<b>49</b>	<b>163</b>

Adocia's portfolio is primarily composed of "composition of matter" patents. More specifically, the families involving prandial or basal insulin, amylin receptor agonists (RA) and glucagon rely on polymers, composites and/or compositions.

The FAST insulin project (BC Lispro and HinsBet) comprises 13 families of patent that include many delivered patents.

It includes in particular, the WO2014076422 and WO2014076423 families currently under review for which patent applications have been submitted in Australia, Brazil, Canada, China, Eurasia, Europe, Hong Kong, Israel, India, Japan, South Korea, Mexico, Saudi Arabia, Singapore, the United States and South Africa. The WO2014076423 application led indeed to the issuance of the patents US9700599 in the United States, CN104902922 in China, EP2918804 in Europe and JP6322642 in Japon.

The patents for these families, subject to their delivery and to payment of annuities, will confer protection until 2033.

The project for the combination of basal insulin, notably glargine insulin, and prandial insulin, comprises 14 families of patents.

We can cite among these the WO2017211916 and WO201721903 applications submitted in 2017, involving new composites and new compositions combining a basal insulin, like glargine uinsulin and a prandial insulin. These families have patents pending in the following countries or regions: South Africa, Saudi Arabia, Brazil Cambodia, China, Egypt, Europe, India, Indonesia, Japan, Mexico, Eurasia, Singapore and United States. Subject to payment of annuities, the patents of this family will provide protection until 2037.

The glucagon project involves in particular the applications WO2017211917 et WO2017211917 submitted in 2017. These families have patents pending in the following countries or regions: Australia, Brazil, Canada, China, South Korea, Europe, Japan, Mexico, New-Zealand, and Singapore. Subject to payment of annuities, the patents of this family will provide protection until 2037.

ADOCIA is still developing a project involving a composition combining amylin, an agonist of amylin or an agonist of amylin receptor, in particular Pramlintide, formulated at physiological pH value. This project involves notably the application WO2018122278.

Finally, the project involving the combination of prandial insulins with GLP-1 RA includes the application WO2019020820.

It should be noted that published patent applications and patents granted can be found on the internet using free patent databases, such as Espacenet or USPTO.

- **Portfolio management**

The portfolio is examined periodically for patent applications made for inventions that are no longer under development and that can neither be sold nor licensed. These are terminated to reduce costs. This is the case of applications concerning nanoparticles, for example.

## 1.3.7 Legal

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### 1.3.7.1 Major Contracts

- **Protection of proprietary technologies**

Before any exchange of information or material of a confidential nature with a third party, a suitable contract is drafted that systematically includes confidentiality and restriction of use clauses. A confidentiality contract is generally signed first when assessing the relevance of entering into a possible commercial relationship or collaboration. There will follow, depending on the situation, one or more contracts for transfer of equipment, service provision, consulting or collaboration, which will ensure, among other provisions, that Adocia retains full ownership of the results (related to Adocia's proprietary technologies) arising from these contracts and of the intellectual property rights attached to these results.

- **Cooperation agreements**

Starting in November 2007, the Company began signing cooperation agreements with various major pharmaceutical groups.

The Company did not assign intellectual property rights to its technology with any of the agreements it signed, and no implicit license can arise from any of the cooperation agreements with its partners, as this is a prerequisite demanded by Adocia upon signing any such agreement.

Partners may hold rights only to inventions developed strictly within the scope of the cooperation that is the subject of these agreements, and to no other inventions. Depending on the partner, title may be held jointly with the company or outright by the partner.

Most of these cooperation agreements involve evaluating BioChaperone® technology with respect to active pharmaceutical ingredients that are already marketed or are under pharmaceutical development.

## Presentation of Adocia and its activities

Studies are conducted in either the Company's or the partners' laboratories, and the costs of such trials are either fully paid by the Company's partners or shared between the partner and Adocia.

Because the Company's partners have demanded confidentiality about the very existence of these agreements, neither the areas of cooperation nor the partners' identities may be disclosed in this reference document.

### 1.3.7.2 Licenses

#### ▪ License granted by Adocia to Eli Lilly

On December 14, 2011, the Company signed a licensing and cooperation agreement with the Eli Lilly group. This agreement concerned the development and marketing of Lispro rapid-acting insulin analog in conjunction with BioChaperone® technology ("BioChaperone® Lispro"). The company granted Eli Lilly exclusive worldwide rights to BioChaperone® for the purpose of developing, manufacturing and marketing BioChaperone® Lispro. This agreement covered all potential indications for BioChaperone® Lispro. The license rights granted were based on the WO2008038111 and WO2010122385 families of patent applications and patents. In July 2013, Adocia and Eli Lilly decided to terminate their licensing and cooperation agreement, and Adocia recovered its rights to develop ultra-rapid insulin analogs.

On December 19, 2014, Adocia and Eli Lilly announced the signature of a licensing agreement for the development of an ultra-rapid insulin based on insulin lispro (commercial product from Eli Lilly, Humalog®) with BioChaperone® technology ("BioChaperone Lispro").

Adocia's and Eli Lilly's goal was to develop BioChaperone Lispro with the goal of optimizing glucose levels during and after meals. The expected benefits of BioChaperone Lispro for patients with diabetes included greater flexibility in the timing of insulin injections, lower variability of postprandial glycemic levels, lower rates of hypoglycemia and better overall glycemic control.

Under the terms of the agreement, Lilly was responsible for future development, manufacturing, and commercialization of BioChaperone Lispro. The total upfront and milestone payments could have reached \$570 million. Adocia had received an upfront payment of \$50 million, and a \$10 million milestone payment in December 2015.

No joint patent applications were submitted during this collaboration.

By letter dated January 26, 2017, Eli Lilly announced its decision to terminate the 2014 licensing contract. As a result, the rights that Adocia has licensed to Lilly reverted to Adocia at no cost (see Adocia press release of January 27, 2017).

#### ▪ Licenses granted by Adocia to Tonghua Dongbao Pharmaceuticals Co. Ltd

April 26<sup>th</sup>, 2018, Adocia and Tonghua Dongbao Pharmaceuticals Co. Ltd Pharmaceuticals a strategic partnership, whereby Adocia granted the exclusive development and commercialization rights to Tonghua Dongbao Pharmaceuticals Co. Ltd for the fixed-ratio insulin glargine and insulinlispro combination, BioChaperone® Combo, and ultra-rapid insulin, BioChaperone® Lispro, in China and other designated Asian and middle -East countries.

Under the terms of the Licensing Agreements, Tonghua Dongbao is responsible for the future development, manufacturing, and commercialization of BioChaperone Combo and BioChaperone Lispro in China and certain other countries. Adocia received a total upfront payment of \$50 million, including \$40 million for BioChaperone Combo and \$10 million for BioChaperone Lispro. Additionally, Adocia is entitled to receive development milestone payments up to \$85 million, including \$50 million for BioChaperone Combo and \$35 million for BioChaperone Lispro. Finally, Adocia is expected to receive double-digit royalties on the sale of both products in the territories. Tonghua Dongbao will also reimburse some of Adocia's expenses for research and development activities performed during the terms of the agreements.

Adocia retains the rights to develop and license these two insulin programs in worldwide markets outside of the territories covered by these agreements, including the United States, Europe and Japan. Adocia remains responsible for the development and the manufacturing of BioChaperone® pharmaceutical excipients.

Tonghua Dongbao Pharmaceutical Co., Ltd. is a China-based company with over 2.000 employees, principally engaged in the research and development, manufacture and distribution of pharmaceuticals. The Company provides biological products, traditional Chinese medicines and chemical supplements, applied in the treatment of diabetes and cardiovascular and cerebrovascular diseases, among others. The Company produces 10 different types of products with over 100 specific pharmaceutical products in production. Tonghua Dongbao Pharmaceutical Co., Ltd. main products portfolio consists, at the time of the signature of the partnership with Adocia, of recombinant human insulin crystal API, regular recombinant human insulin injection Gansulin R, isophane protamine recombinant human insulin injection Gansulin N, 30/70 mixture recombinant human insulin injection Gansulin 30R, 3 50/50 mixture recombinant human insulin injection Gansulin 50R, 40/60 mixture recombinant human insulin injection Gansulin 40R, Zhen Nao Ning capsules and Dongbao Gantai tablets, among others. Tonghua Dongbao Pharmaceutical Co., Ltd. also provides medical instruments. The Company distributes its products within domestic markets and to overseas markets.

### 1.3.7.3 Litigation

#### ▪ Arbitrations

In October 2017, Adocia announced in a press release its filing of an arbitration claim against Eli Lilly & Co related to a research and licensing agreement signed in 2014. This proceeding concerns some \$11 million and other specific compensation for changes made to the development plan during the collaboration. The arbitration court finds in favor of Adocia in first phase of arbitration against Eli Lilly in August 2018 and Adocia announced via a press release the same month that the company will separately seek interest, litigation fees and costs in addition to the damages awarded. In October 2018. The arbitration court granted Adocia fees' interests on the amount cited above accruing from March 30, 2017.

In February 2018 Adocia announced additional arbitration claims against Eli Lilly & Company arising out of Lilly's misappropriation and improper use of Adocia's confidential information and discoveries as well as Lilly's breaches of several collaboration and confidentiality agreements. Adocia is seeking monetary damages in excess of \$1.3 billion (before taking into account the interests pre-and post judgement) as well as others specific relief. In this second phase of this arbitration, Lilly has filed counterclaims against Adocia seeking approximately 188 million including prejudgment interest. These counterclaims are based on an allegation that Adocia concealed its discoveries and confidential information which are at issue in Adocia's claims. Adocia denies Lilly's claims. Hearings were held in December 2018. Adocia expects a decision in the third quarter of 2019 on this second phase of this arbitration proceedings, as well as the reimbursement of the fees and lawyers' fees paid as such.

#### ▪ Civil Action

Eli Lilly and Company ("Lilly") filed a complaint against Adocia in the United States District Court of the Southern District of Indiana on October 9th, 2018. Lilly's complaint seeks a declaratory judgment that "the designations of inventorship currently appearing on [Lilly's] United States Patent Nos. 9,901,623 and 9,993,555 are complete and correct, as required by the patent laws of the United States." US Patent No.9,901,623 is entitled "Rapid-acting insulin compositions" and was issued February 27, 2018. US Patent No 9,993,555 is entitled "Rapid-acting insulin compositions" and was issued June 12, 2018. Lilly contends in its complaint that it filed the action because Adocia has asserted that Lilly's patents reflect Adocia's inventive contributions. The agenda of this proceeding is not known at date of the current reference document (please see Adocia's Press release published on October 11<sup>th</sup>, 2018).

### 1.3.7.4 Insulin supply agreements

Adocia and Tonghua Dongbao Pharmaceuticals Co. Ltd announced on June 1<sup>st</sup>, 2018 an expansion of their strategic alliance with Tonghua Dongbao. "(see section 1.3.8.2 « Licences granted by Adocia to Tonghua Dongbao Co.Ltd »

above) by signing with the Chinese company two supply agreements in insulin, under the terms of the agreements, Tonghua Dongbao Pharmaceuticals Co. Ltd will manufacture and supply insulin lispro and insulin glargine APIs to Adocia worldwide, excluding China in accordance with Adocia's specifications and established quality standards.

Local leader on the Chinese insulin market, Tonghua Dongbao Pharmaceuticals Co. Ltd can currently produce several tons of insulin per year divided on numerous outstanding production plants. While the Chinese company commercializes already human insulin products in China and in other market, Tonghua Dongbao Pharmaceuticals Co. Ltd develop in parallel several insulin analogs. Notably, its insulin glargine is under commercial approval in China, and its insulin lispro is expected to enter Phase 3 trials in the near future. Insulin lispro from Tonghua Dongbao Pharmaceuticals Co. Ltd. is produced in the same plant as human insulin used in its commercial products; this plant has recently passed a cGMP standard audit allowing Phase 3 entry into Europe of this human insulin from Tonghua Dongbao Pharmaceuticals Co. Ltd.

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### 1.3.7.5 OSEO Innovation agreements of April 25, 2012

As part of the Insulin project, the company signed an agreement with OSEO on April 25, 2012 under which the company received a reimbursable advance totaling €800,000 for the development of a fast-acting "human" insulin formulation and the Phase 2a clinical trial. After fulfilling all the technical and financial conditions, the company received the full amount of this reimbursable assistance on April 30, 2012.

**In the event of the program's success**, the company agreed to repay OSEO the sum of €800,000 according to the following terms:

The company agreed to repay OSEO the full amount lent based on the following payment schedule:

- €130,000 for the year 2017 (€32,500 per quarter),
- €150,000 for the year 2018 (€37,500 per quarter),
- €200,000 for the year 2019, and
- €320,000 for the year 2020.

In the event of assignments of licenses or marketing, the company agreed to pay OSEO, by March 31 of each year and starting on January 1, 2014:

- 44.82% of income, excluding tax, from assignments or concessions of licenses, patents or know-how received during the previous calendar year, when such assignments or concessions concern all or part of the results of the financed program, and
- 44.82% of income, excluding tax, generated by the marketing and particularly the sale to a third party or the use by the company for its own purposes of the prototypes, pilot products and samples developed under the financed program.

In this case, the sums paid will first be deducted, by the same amount, from the last payment owed to OSEO Innovation, as specified in the above payment schedule, and, where applicable, from the next to last payment.

**In the event of the program's commercial failure**, even if such failure is partial, given the nature of the work carried out under the fast-acting human insulin project, the company agreed to repay OSEO a minimum sum of €280,000 corresponding to the amounts due for 2017 and 2018 as described above. In 2017 and 2018, the Company reimbursed accordingly to the plan.

If the company fails to fulfill its obligations, OSEO would have a right to demand the repayment of the advance granted.

### 1.3.7.6 Coface – International business development insurance agreement of October 1<sup>st</sup>, 2012

As part of its business development in new markets (India and China), the company signed a business development agreement with Coface (French insurance company for foreign trade) on October 26, 2012 in return for the payment of a premium equivalent to 2% of the annual budget.

Under the terms of the agreement, Coface guarantees the reimbursement of 75% of the expenses incurred during the four-year guarantee period, which runs from October 1, 2012 to September 30, 2016.

The company agreed to repay the sums received from Coface according to the Terms and Conditions set out in the agreement during an amortization period that runs until September 30, 2021. The repayment terms are as follows:

- 14% of the billing amount of services provided
- 30% of the sums received from the assignment of intellectual property rights

The sums repaid will first be deducted, by the same amount, from the amount of the advance granted for the first guarantee period and then for the following periods, it being understood that such repayments:

- are limited in time (repayment of the advance over a period ending on September 30, 2021),
- will not exceed the principal amount of the total advance received.

For the expenses incurred during the first insured period, i.e. from October 1, 2012 to September 30, 2013, the company received the sum of €91,000 on December 17, 2013.

During the period between October 1, 2013 and September 30, 2014, the Company has not committed exploration expenditures on target markets and the contract has been canceled. Therefore, the Company entered into the amortization period on amounts received previously, meaning €91 thousand and as provided in the contract and listed above. By letter received on November 27, 2014, Coface declared the guarantee period extended by two years, i.e. from October 1, 2013 to October 1, 2018.

Over the year 2018 and following the signature of the partnership with the Chinese Company Tonghua Dongbao Pharmaceuticals Co. Ltd, the Company proceeded to reimburse the totality of the amount advanced ie €91 thousand, according to the terms of the agreement

## 1.4. Analysis and comments on activities during the year

Readers are invited to read this analysis of the Company's financial position and results along with the financial statements prepared under IFRS for the fiscal years ended December 31, 2017 and December 31, 2018, as well as the notes to the consolidated financial statements prepared under IFRS and presented in section 4.1 of this registration document and all other financial information included herein. Readers may also review the description of the Company in section 1.2 "Presentation of Adocia and its activities."

The consolidated financial statements prepared under IFRS are presented in section 4.1 of this registration document. Only the corporate financial statements prepared under French GAAP have legal force and are reproduced in the notes to this registration document along with the statutory auditors' reports.

### 1.4.1. Main activities during the year

2018 was marked by the signature of a strategic alliance with the company Tonghua Dongbao Pharmaceuticals Co. Ltd (« THDB »), Chinese leader of the production and commercialization of insulin. In April 2018, Adocia and THDB announced the signature of two licenses to develop and commercialize BioChaperone® Lispro and BioChaperone® Combo in China and other Asian and Middle-East territories. Under the terms of the Licensing Agreements, THDB is responsible for the future development, manufacturing, and commercialization of BioChaperone Combo and BioChaperone Lispro in China and certain other covered territories. Adocia received a total upfront payment of \$50

## Presentation of Adocia and its activities

million and is entitled to receive development milestone payments up to \$85 million, as well as double-digit royalties on the sale of both products in the territories. Since the signature, the two companies actively worked on technology transfer to enable the manufacturing of the two products. THDB envisaged in 2019 to start a Phase 3 for BioChaperone Lispro in 2019 and a first clinical study for BioChaperone Combo at the end of 2019.

In June 2018, the partnership with THDB, was reinforced by two global supply agreements for insulin lispro and insulin glargine. Under the terms of the Supply Agreements, THDB will manufacture and supply insulin lispro and insulin glargine (APIs) to Adocia worldwide, excluding China. These agreements offer Adocia the opportunity to further develop the BioChaperone Lispro and BioChaperone Combo projects and open additional collaboration opportunities. Adocia is preparing a « bridging » clinical study to qualify the insulin lispro from THDB as a source equivalent to Lilly's insulin lispro. This study should be the only one required by regulatory agencies to enable BioChaperone Lispro to enter in phase 3.

From a clinical perspective, in 2018 Adocia initiated a first-in-human clinical trial of BioChaperone<sup>®</sup> Pramlintide Insulin (BC Pram Ins). This trial in people with type 1 diabetes, which positive topline results were announced in September 2018, showed a significant 97% decrease in blood glucose excursion over the first two hours after the meal with BC Pram Ins compared to Humalog<sup>®</sup>. The product was well tolerated. Adocia plans to initiate a second, repeated administration trial in Q2 2019.

The development of our varied portfolio products to date revealed unique properties of the BioChaperone technology, which notably enables to significantly improve single agents and to combine multiple therapeutic proteins. In order to expand the use of this technology, Adocia announced early in 2018 that BioChaperone<sup>®</sup> would now be deployed in a selected range of injectable therapeutics across numerous therapeutic areas. Initial programs added to the portfolio include a ready-to-inject version of teduglutide for the treatment of short bowel syndrome and a fixed dose combination of glucagon and exenatide for the treatment of obesity, both in preclinical stage.

Lastly, regarding legal proceedings, the first phase of the arbitration procedure initiated by Adocia against Lilly concluded in favor of Adocia. The Arbitration Tribunal awarded Adocia USD 11.6 million, as well as interests.

Adocia's additional claims against Lilly for a revalued amount of USD 1.3 billion and the counterclaims of Lilly for an amount of USD 188 million, remain pending, with a decision of the court expected in the third quarter of 2019.

Finally, in October 2018, Lilly filed a civil complaint against Adocia in the United States District Court of the Southern District of Indiana to seek a declaratory judgment for two of its US patents regarding ultra-rapid insulin formulation (Lilly's United States Patent Nos. 9,901,623 and 9,993,555 entitled "Rapid-acting insulin compositions"). Lilly contends in its complaint that it filed the action because Adocia has asserted that Lilly's patents reflect Adocia's inventive contribution. We do not expect the matter to be resolved during this fiscal year

### 1.4.2. Presentation of the financial statements

#### 1.4.2.1. General information

The Company's principal activity is research and development of innovative formulations of pre-approved therapeutic proteins. It has a high level of expertise in the field of insulin. The proprietary technology platform, called BioChaperone<sup>®</sup>, aims to improve the efficacy of therapeutic proteins and their ease of use for patients.

#### 1.4.2.2. Main accounting principles

- Revenue recognition

Adocia generates revenue from collaboration and licensing agreements signed with other companies operating in its sector and from public funding of research costs (grants and research tax credit).



## ▪ Research and development costs

Research and development costs are recognized as expenses on the income statement in the year in which they are incurred. Development costs are capitalized only when the conditions required by IAS 38 are met. As of the date of this registration document, these conditions had not been met and the Company therefore did not capitalize its development costs.

### 1.4.3. Financial position and appropriation of profit

#### 1.4.3.1. Components of income

The table below summarizes the Company's income statement under IFRS for the fiscal year ended December 31, 2018 and provides a comparison with fiscal year 2017.

<i>In (€) thousands</i>	<b>FY 2018 (12 months)</b>	<b>FY 2017 (12 months)</b>
<b>Revenue (a)</b>	<b>47 389</b>	<b>19 469</b>
Research and collaborative agreements	0	650
Licencing revenues	47 389	18 819
<b>Other revenue (b)</b>	<b>6 541</b>	<b>7 708</b>
Research tax credit	6 368	7 535
Grants, public financing, others	173	173
<b>Operating revenue (a) + (b)</b>	<b>53 930</b>	<b>27 177</b>
Research and development expenses	(25 760)	(27 074)
General and administrative expenses	(18 463)	(8 284)
<b>Operating expenses</b>	<b>(44 223)</b>	<b>(35 358)</b>
<b>OPERATING INCOME (LOSS)</b>	<b>9 707</b>	<b>(8 180)</b>
<b>FINANCIAL INCOME (LOSS)</b>	<b>2 051</b>	<b>(335)</b>
Tax	(4 144)	(35)
<b>NET INCOME (LOSS)</b>	<b>7 615</b>	<b>(8 550)</b>
Base earning per share (€)	1,1	(1,2)
Diluted earning per share (€)	1,0	(1,2)
<b>GROUP NET PROFIT (LOSS)</b>	<b>7 615</b>	<b>(8 550)</b>

## ▪ Operating income

The Company's operating income resulted from collaboration and licensing agreements and public funding of research costs. In 2018, operating income amounted to €53.9 million compared to €27.2 million in 2017 based on the following breakdown:

<i>In (€) thousands</i>	<b>FY 2018 (12 months)</b>	<b>FY 2017 (12 months)</b>
<b>Revenue (a)</b>	<b>47 389</b>	<b>19 469</b>
Research and collaborative agreements	0	650
Licencing revenues	47 389	18 819
<b>Grants, public financing, others (b)</b>	<b>6 541</b>	<b>7 708</b>
<b>OPERATING REVENUE (a) + (b)</b>	<b>53 930</b>	<b>27 177</b>

## Presentation of Adocia and its activities

Revenue of €47.4 million in 2018 resulted up to €37.1 million from the partnership and licensing agreement signed with Tonghua Dongbao Pharmaceuticals Co. Ltd (THDB) in April 2018. The non-refundable upfront payment provided for in the contract in the amount of 50 million dollars, or €41.1 million, is partially recognized as revenue (i.e. €37.1 million) in 2018. It reflects the rights thus granted to THDB to develop, manufacture, and commercialize BioChaperone® Lispro and BioChaperone® Combo in China and other territories in Asia and the Middle-East. The remaining non-amortized amount of the initial payment will be recognized upon provision of research and development services by Adocia related to the transfer and development of the products.

By the end of December 2018, licensing revenues also included an amount of \$11.6 million (€10.3 million) corresponding to a contractual milestone payment contested by Lilly, for which Adocia obtained a favorable arbitration judgement in August 2018. The payment is expected to be received in 2019.

Last year, revenue for 2017 was impacted by the end of the collaboration with Lilly which resulted in the recognition of the not-yet-amortized balance of the \$50 million upfront payment received in 2014 (no cash impact as payment had been received upon contract signature in December 2014).

Other operating income includes the research tax credit in the amount of €6.4 million at December 31st, 2018 compared to €7.5 million at December 31st, 2017. This decrease by €1.1 million is in line with the reduced amount of research and development expenses recorded this year.

### ▪ Operating expenses

The table below shows a breakdown of operating expenses by function for the fiscal years ended December 31st, 2017 and December 31st, 2018:

<i>In (€) thousands</i>	<b>FY 2018 (12 months)</b>	<b>FY 2017 (12 months)</b>
Research and development expenses	(25 760)	(27 074)
General and administrative expenses	(18 463)	(8 284)
<b>OPERATING EXPENSES</b>	<b>(44 223)</b>	<b>(35 358)</b>

Research and development expenses mainly include payroll costs of research and development employees, subcontracting costs (including preclinical studies and clinical trials), intellectual property costs and purchases of materials (reagents and other consumables), pharmaceutical products and other raw materials. In 2018, these expenses amounted to €25.8 million compared to €27.1 million in 2017.

The activities carried out during the 2018 financial year focused mainly on the preparation of clinical studies and support for the Company's Chinese partner for the development of the two products licensed in April 2018. In 2017, research and development, and more specifically clinical expenses were impacted by the costs of three clinical studies.

General and administrative expenses mainly include payroll costs of non-research and development employees, as well as the cost of services related to the management and business development of the Company and its subsidiary in the United States. They also include fees and expenses related to the arbitration procedure launched against Lilly. These general costs amounted to €18.5 million in 2018 compared to €8.3 million in 2017. This increase of €10.2 million is mainly due, for an amount of €8.3 million, to the legal expenses related to the current litigation proceedings and, for an amount of €1.5 million, to the increase in staff expenses, notably following the payment of performance bonuses to employees, as a result of the signature of the partnership with THDB. As a reminder, in 2017 salaries and bonuses were frozen due to the termination of the contract with Lilly.

R&D expenses represented in 2018 76.4% of the operating expenses compared to 81% in 2017, once restated for the costs related to the arbitration proceedings against Lilly.

The table below shows a breakdown of operating expenses by type of expense for the fiscal years ended December 31<sup>st</sup>, 2017 and December 31<sup>st</sup>, 2018:

<i>In (€) thousands</i>	<b>FY 2018 (12 months)</b>	<b>FY 2017 (12 months)</b>
Purchases used in operations	(2 188)	(1 740)
Payroll expense	(13 327)	(10 843)
Share-based payments	(1 574)	(2 525)
External expenses	(25 537)	(19 019)
Taxes and contributions	(553)	(217)
Depreciation, amortization & provisions	(1 044)	(1 013)
<b>OPERATING EXPENSES</b>	<b>(44 223)</b>	<b>(35 358)</b>

The cost of materials, products and supplies consumed increased in 2018 compared to 2017 up to €2.2 million, as a result of additional purchase of the raw materials needed for the manufacturing of clinical batches. This increase of €0.5 million is mostly due to the increase in raw material purchase necessary to manufacture clinical batches.

Payroll expenses totaled €13.3 million in 2018 compared to €10.8 million in 2017. Given the recruitments conducted last year, the average workforce rose from 126.1 full-time equivalents (FTE) in 2017 to 129.4 FTE in 2018, an increase of nearly 3%. The €2.5 million increase in personnel expenses mainly reflects the payment of performance bonuses to employees, as a result of the signature of the partnership with THDB.

The share-based payments item of €1.6 million in 2018 mainly includes the impact of the plans implemented in previous years. The €0.9million decrease in this item is related to the vesting of several share-based plans in 2018. In accordance with IFRS 2, these expenses correspond to the fair value of the equity instruments granted to managers and employees. These elements had no impact on the Company's corporate financial statements or cash position.

External charges mainly included the costs of preclinical studies, clinical trials, subcontracting expenses, intellectual property costs, professional fees and administrative expenses. These expenses amounted to €25.5 million and increased by € 6.5 million in 2017. This is mainly due to the intensification of the legal fees incurred for the procedures against Lilly. Restated of these fees, external charges amounted to €15 million in 2018, versus €16.8 million in 2017.

Taxes totaled €0.6 million in 2018, versus €0.2 million in 2017.

Depreciation and amortization remained stable over both years totaling more than €1 million.

#### ▪ Net financial income/expense

The net financial result was a profit of €2 million in 2018, compared to a loss of €0.3 million in the previous year. This is explained by the recognition of the accrued interest of €1.6 million calculated on the contractual milestone payment of \$11.6 million, which cash payment is expected in 2019 after the second phase of the arbitration procedure against Lilly is concluded.

The Company's investment policy focuses on liquidity, the absence of capital risk and, to the extent possible, guaranteed performance.

#### ▪ Corporation tax

The 2018 tax amount recorded in the consolidated income statement for €4.1 million refers to the corporate income tax calculated on the fiscal benefit subject to a reduced tax rate of 15%. This tax will be paid in full by charging the withholding tax paid in China on the initial upfront payment.

## Presentation of Adocia and its activities

The amount of carryforward tax losses, after allocation of the fiscal deficit subject to the standard tax rate for the 2018 financial year, was €115.5 million. This carryforward loss is not limited in time. Since the company cannot determine with sufficient reliability when it will be able to absorb its accumulated tax loss, it did not recognize a deferred tax asset for this loss.

### ▪ Net profit/loss

The net profit for 2018 totaled €7.6 million compared to a loss of €8.6 million in 2017. The net profit per share for 2018 amounts to €1.10, compared to a net loss of €1.25 per share in 2017.

## 1.4.3.2. Balance sheet analysis

### ▪ Non-current assets

Between 2017 and 2018, non-current assets have remained stable at €9.1 million. The investments in 2018 of €0.8 million are mainly due to ongoing renovation work of the two 450 m<sup>2</sup> floors by December 31<sup>st</sup>, 2018 dedicated to the analytical department (for an amount of €0.4 million), as well as the purchase of scientific and computer hardware material (for €0.3 million). These cumulative investments, added to the increase of the valuation of the liquidity agreement in the financial assets of €0.25 million, are compensated by the depreciation of the year, which amounts to €1 million.

### ▪ Current assets

Current assets amounted to €61 million at December 31<sup>st</sup>, 2018 compared to €44.7 million at December 31<sup>st</sup>, 2017. They consisted of the following items:

- "Cash and cash equivalents" increased from €34.8 million at December 31<sup>st</sup>, 2017 to €39.8 million at December 31<sup>st</sup>, 2018. The €5 million increase on the year reflects the initial upfront payment of THDB for €37.2 million (\$ 45 million) net of Chinese withholding taxes, as well as a level of expenditure similar to that of last year, after restating expenses related to the legal proceedings against Lilly.
- « Other current assets » amounted to €9.8 million at December 31<sup>st</sup>, 2017 and consisted mainly of the receivable related to the research tax credit (CIR) of €7.5 million. At December 31<sup>st</sup>, 2018, this item amounted to €21 million. The €11.2 million increase is mainly due to the favorable outcome of the first phase the arbitration proceedings initiated by Adocia against Lilly. The Arbitration Tribunal ordered Lilly to pay the disputed milestone payment of \$11.6 million, or €10.3 million, plus interests (accrued end of December for \$1.6 million). The payment of this total receivable of €11.9 million at the end of December 2018 is expected in 2019. The research tax credit amounts to €6.4 million at the end of 2018.

### ▪ Current and non-current liabilities

Liabilities consisted mainly of four items presented on the balance sheet according to their maturity:

- "Trade payables" under current liabilities in the amount of €7.5 million compared to €4.9 million at end-December 2017, which reflect the intense activity at the end of the year 2018 and the lawyers' fees incurred in connection with the proceedings against Lilly.
- "Financial debt" totaling €7.1 million at end-December 2018, decreasing by €0.5 million compared to the previous year. This decrease related mainly to the repayment of the loans taken out to finance the building. The short-term portion, shown under "Current financial liabilities", totaled €2.2 million at end-December 2018 compared to €1.8 million a year earlier.
- "Long-term provisions" mainly comprise provisions for retirement benefits, which totaled €2.8 million for fiscal year 2018 versus €2.2 million for fiscal year 2017.
- The "other liabilities" item for 2018 mainly includes tax and social security liabilities which amounted to €2.7 million, an increase by €0.6 million from the previous year given the increase of the accrual for paid

vacation and the value-added contribution (CVAE) tax. In 2018, other liabilities also included €4 million in deferred revenue related to the agreement signed with THDB in 2018.

## 1.4.4. Cash, financing and equity

Readers are invited to review notes 9 and 10 to the consolidated financial statements prepared under IFRS for the fiscal years ended December 31, 2017 and December 31, 2018, which are presented in section 4.1.6 and Chapter 5 of this registration document.

### 1.4.4.1. Debt financing

As of the date of this registration document, the Company received non-interest-bearing repayable aid for its research from Bpifrance and COFACE, for a total amount of €4.1 million. At December 31, 2018, the amount still owed on these advances was €0.5 million. The details of each of the repayable advances received and the repayment terms are provided in section 1.3.7 of this registration document.

The Company also uses other types of financing to finance the purchase of laboratory equipment and a company car. As of December 31, 2018, short-term future obligations under these finance leases totaled €0.4 million.

In 2016, the Company took out a loan to finance the purchase of the building that it has occupied since its creation as well as adjoining parking. At the end of 2018, the principal balance was €4.9 million.

Finally, in 2017 the Company funded part of the legal costs incurred in the arbitration against Lilly. This financing, obtained from two banks, took the form of two lines of credit, each in an amount of \$1.5 million each. At December 31, 2018, one of the two cash lines was renewed and Adocia's financial debts were impacted by €1.3 million (\$1.5 million).

At end-December 2018, debt totaled €7.1 million, with a portion due in less than one year of €2.2 million.

### 1.4.4.2. Cash flows

<i>In (€) thousands, Consolidated financial statements, IAS/IFRS</i>	<b>FY 2018 (12 months)</b>	<b>FY 2017 (12 months)</b>
Net cash flow generated by operating activities	6 313	(22 227)
Net cash flow in connection with investment transactions	(1 034)	(1 685)
Net cash flow in connection with financing transactions	(216)	653
<b>Changes in net cash</b>	<b>5 063</b>	<b>(23 259)</b>
Cash and cash equivalents at the start of the year	34 778	58 037
Cash and cash equivalents at year-end	39 841	34 778

#### ▪ Net cash flow from operations

For fiscal year 2018, net cash inflows related to operations amounted to €6.3 million compared to a net cash outflow of €22.2 million in the previous year.

Net cash flow includes the cash proceeds from THDB's initial payment of €37.2 million (or \$45 million), net of Chinese withholding tax.

#### ▪ Net cash flow from investments

Cash consumption related to investment transactions was €1 million, compared to €1.7 million in the previous year.

## Presentation of Adocia and its activities

In 2018, the Company acquired equipment and made some renovation for an amount of €0.8 million. It also increased by €0.25 million the resources made available under the liquidity contract entrusted to Kepler Cheuvreux.

### ▪ Net cash flow from financing transactions

In 2018, net cash flow from financing transactions resulted primarily from the repayment of the two lines of credit obtained in 2017 to finance the legal costs incurred for legal proceedings against Lilly, as well as the renewal in December 2018 of one of its two lines. At the same time, the Company continued to repay its mortgages as well as its conditioned advances, according to the planned deadlines.

### 1.4.4.3. Funding sources needed in the future

With nearly €40 million in cash and cash equivalents at December 31, 2018, the Company believes that it has the necessary resources to finance its operating expenses for at least the next 12 months from the date of this registration document.

Including financial debt, net cash at the end of 2018 was €37.2 million. This level of cash enables the Company to fund its planned clinical development (see section 1.3.2 of this registration document) and the development of its new programs.

The Company believes that it is able to make its next repayments of the loans and the Bpifrance repayable advances, which are estimated at €2.2 million for 2018 being precised that no reimbursements are expected within Bpifrance (see note 10 to the Company's consolidated financial statements prepared under IFRS in section 4.1 of this registration document).

## 1.4.5. Growth prospects, outlook and significant events after the close of the fiscal year

### 1.4.5.1. Trend information

See section 1.3 of this registration document which describes the epidemiological data for the pathologies targeted by the BioChaperone® technology platform, and, for certain pathologies, market trends and size.

### 1.4.5.2. Profit forecasts and estimates

The Company does not plan to make profit forecasts or estimates.

### 1.4.5.3. Significant change in the financial or trading position

None.

## 1.5. Risk factors

Investors are invited to consider all information contained in this reference document, including the risk factors described in this chapter, before deciding to purchase or subscribe for the company's shares.

The Company has reviewed the risks that may have a material adverse impact on the Company, its business, financial position, income, outlook or ability to achieve its objectives, and it considers that there are no significant risks other than those described herein.

In addition, the Company may be subject to other risks that, as of the date of this presentation, are unknown to the Company or which the Company deems immaterial at this time, and which may have a material adverse impact on the Company, its business, financial position, income or outlook.

In each section below, the risk factors are presented in order of decreasing importance, according to the Company's assessment as at the date of this Registration Document. The occurrence of new facts, either internal to the Company or external, may change this order of importance in the future.

## 1.5.1. Risks associated with implementation of the Company's strategy

### 1.5.1.1. The Company is dependent on its BioChaperone® technology platform.

The Company does not plan to develop or market therapeutic products directly. The Company's main strategy is to develop innovative formulations for various therapeutic proteins based on its BioChaperone® technology, and then to license use thereof to major players in the pharmaceutical, biotechnology and medical devices industries for the development and marketing of therapeutic products.

Research programs to identify new product candidates require substantial technical, financial and human resources. Research programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development that would be attractive to potential partners, for a number of reasons, including:

- The research methodology used may not be successful in identifying potential product candidates; or
- Product candidates may, on further study or through clinical trials, show inadequate efficacy, harmful side effects, undifferentiated features or other characteristics suggesting that they are unlikely to be effective or safe products.

If the Company is unable to develop suitable innovative formulations for various therapeutic proteins based on its BioChaperone® technology through its research programs or otherwise, the Company might have difficulty finding partners and its medium and long-term business, financial position, income, expansion and outlook would be materially adversely affected.

### 1.5.1.2. In order to carry out its medium-term strategy, the Company must enter into agreements with partners.

The Company's medium-term strategy depends on its ability to enter into lasting partnership agreements with major players in the pharmaceutical, biotechnology and medical devices industries, on the basis of the results of feasibility studies and clinical trials it conducts.

The Company does not plan to produce or market its products and does not have the human, material and financial resources necessary to develop, manufacture and market therapeutic products using its technology.

As part of its strategy, when proof of concept has been obtained for humans or animals, the Company intends to license products derived from its BioChaperone® technology to industrial partners in the pharmaceutical, biotechnology or medical device markets who have the human, material and financial resources necessary to conduct and successfully complete the clinical trials required by law, apply for market authorization, and produce and market the products. Accordingly, the Company plans to sign licensing and collaboration agreements under which its partners will be responsible for developing, manufacturing and marketing products incorporating the Company's technology, and will agree to pay royalties to the Company on any sales of such products, once commercialized.

However, the research and results of clinical trials that the Company carries out itself may fail to yield product candidates or may fail to yield candidates that are sufficiently safe, efficacious and innovative to attract major players

## Presentation of Adocia and its activities

in the pharmaceutical, biotechnology and medical devices industries to sign licensing and collaboration agreements for the Company's products and technologies.

In addition, other factors including general market demand for particular product candidates or therapeutic areas, market competition or other reasons, the Company may be unable to attract partners for future licenses and/or collaborations and/or the terms of those licensing and collaboration agreements the Company enters into may not be favorable to the Company.

If the Company is not successful in its efforts to enter into licensing and collaboration agreements, the Company may not have sufficient funds to further develop its product candidates internally. In addition, the inability to enter into licensing and collaboration agreements could delay or preclude the development, manufacture and/or commercialization of the relevant product candidate or any other product candidates and could have a material adverse effect on the Company's financial condition and results of operations, as revenues from product candidate licensing arrangements could be delayed or never materialize. If so, the Company may elect not to commercialize or further develop the product candidate.

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### 1.5.1.3. The commercialization of the Company's product candidates is often dependent on the actions of the Company's partners, which are largely outside of the Company's control.

The Company is structurally dependent on its partners' interest in its technology, as well as on their diligence in continuing the development of products incorporating the Company's technology.

Furthermore, the Company's current and future partners could encounter difficulties in obtaining technical and clinical approvals for the products using the Company's technology. Any resulting delays or refusals may hinder or impede marketing of the relevant products.

The success of our partnership agreements will depend on the efforts and activities of the Company's current and potential partners, who may have significant discretion in determining how to pursue planned activities and the quality and nature of the efforts and resources that they will apply to the partnership agreements, and who otherwise may be unable to complete the development and commercialization of the Company's product candidates.

The Company cannot be certain that it will be able to initiate and maintain partnerships, that any partnerships will be scientifically and/or commercially successful or that the Company will receive revenues from any of these agreements. For example, in December 2011, the Company entered into a first licensing and collaboration agreement with Eli Lilly for the development of a formulation of a rapid-acting insulin analog. In 2013, the Company and Eli Lilly agreed to terminate such an agreement. In 2014, given the clinical results, Eli Lilly signed a new licensing agreement with Adocia for the formulation of an ultra-rapid insulin lispro analog, BC Lispro. In January 2017, Eli Lilly announced its decision to terminate this collaboration.

Factors that may affect the success of the Company's collaborations include the following:

- partners may not employ all the resources necessary to obtain the results expected from the agreements entered into with the Company. In particular, if these partners experience budgetary restrictions or give priority to other development programs, this could delay or prevent altogether approval of potential products incorporating the Company's technology, which is an indispensable stage for the success of its commercial policy;
- conflicts could arise between the Company and certain of its industrial partners. In particular, the Company cannot guarantee that none of its partners will design or attempt to set up a commercial business that uses a technology that competes with that of the Company, or uses all or part of the Company's technology, or decide to prioritize internal development of products in markets that compete with the Company's product candidates, and which would therefore compete with the Company's business (see the section below on risks associated with competition);



- current or future partners could limit or terminate their relationships with the Company, which could lead to additional costs, delays, and difficulties in the development of, or in obtaining approval by regulatory authorities for, or successfully commercializing, our product candidates which could have a material adverse impact on the Company's business, financial position, income, expansion and outlook. Limitation or termination of an agreement could make it difficult for the Company to attract new partners or adversely affect its reputation in the business and financial communities, cause the Company to lose expertise and even lead to the disclosure of key confidential information derived from the Company's research and development program, despite the fact that the relevant partners may be contractually bound to the Company by a confidentiality obligation.

Furthermore, the Company's current revenues in 2018 depended in large part on the licensing and collaboration agreement signed with the Chinese Company Tonghua Dongbao Pharmaceuticals Co. Ltd. Upon signature in April 2018 of these two licencing and collaborative agreements focused on the development of an ultra-rapid insulin, known as BioChaperone Lispro and a combination of a basal and rapid insulin named BoChaperone Combo, Adocia received an upfront payment of \$50 million. According to the terms of the agreement, there had been potential for future payments of up to \$85 million if the product reached certain development and regulatory milestones, (ii) sales royalties (for more information on this partner, please refer to section 1.3.7.2 "licenses granted by Adocia to Tonghua Dongbao Co Ltd").

The Company cannot guarantee that collaboration with a partner will meet the development and regulatory milestones that would enable it to receive the anticipated revenues. Thus, when Eli Lilly decided to terminate the contract in January 2017, the Company faced a difficult situation forcing it to review its development plan. Any decision by a future partner to discontinue its agreement with the Company could have a material adverse effect on its business, operational results and prospects.

If the Company does not realize the anticipated benefits from its partners, its business, results of operations, and prospects would be materially adversely affected.

## 1.5.2. Risks associated with the Company's business

### 1.5.2.1. Research programs and clinical studies are lengthy, time consuming, expensive and have uncertain outcomes.

Research programs are designed to identify new product candidates and require substantial technical, financial and human resources. Only a small minority of all research programs result in product candidates, and completion of preclinical studies does not guarantee that we will initiate additional studies or trials for our product candidates.

If a product candidate passes the preclinical stage, the Company must then develop and design clinical trials to test specific characteristics of the candidate. In order to carry out clinical trials, the Company must first obtain appropriate authorizations to conduct clinical trials in the countries where the Company will seek market authorization. The Company cannot predict the time that will be necessary for regulatory authorities to review the trial protocol and approve the files submitted to them. For example, for its phase 3 clinical trials for the treatment of diabetic foot ulcers conducted in India, the Company submitted the authorization request to the Drug Controller General of India (Indian drug regulation body) in September 2012. However, processing of this request was delayed by the internal restructuring of the Indian regulatory agency, and the Company was only granted final authorization in August 2014.

The completion of clinical trials will depend on various factors, such as the therapeutic indication in question, the size of the population affected, clinical trial design, qualification and initialization of clinical trial sites, availability of the investigational product, the proximity of patients to clinical test sites, the eligibility criteria for trials, recruitment rates and competition for the recruitment of patients, and compliance with and changes in regulatory requirements.

Moreover, the Company cannot guarantee that clinical trials that are authorized will be completed within the planned timeframes. In addition, the data obtained from these clinical trials may be subject to differing

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interpretations, which may delay, restrict or prevent obtaining regulatory authorization, in particular if the clinical data is deemed incomplete.

Lastly, at each stage of a product's progress through the clinical trials, there will be a significant risk of failure that may prevent continued development of a drug candidate, such as intolerance to the product, insufficient therapeutic benefits, and inability to meet prespecified primary endpoints or side effects. Even if the Company obtains positive results from preclinical or early clinical studies, the Company may not achieve success in future studies. Furthermore, the Company, its relevant partners or the regulatory authorities may suspend or terminate clinical trials if they deem that the subjects participating in the trials are exposed to health risks.

The innovative therapeutic protein formulations that the Company currently provides and intends in the future to provide its current and future industrial partners for incorporation into their own products may also not prove to be sufficiently effective and/or have a sufficient safety profile to justify marketing them.

The inability of the Company and/or its partners to successfully complete the necessary clinical trials, including obtaining positive results, and meet certain other requirements for regulatory approval, could cause the development of the Company's research programs and technologies to be delayed or abandoned. As a result, the Company may never realize revenues from certain product candidates, despite significant investments.

The Company's medium and long-term business, financial position, income, expansion and outlook could be materially impacted by the occurrence of one or more of these risks.

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### 1.5.2.2. The products developed based on the Company's current or future technologies may take significant time to gain regulatory approval and reach the marketing stage, if at all.

The technologies developed by the Company have not yet led to the marketing of products. The Company and its partners must obtain regulatory approval for each product candidate before marketing or selling any of them. In Europe, the United States and Japan, as well as in many other countries, access to the drug market is controlled and marketing must be authorized by a regulatory authority.

The Company's product candidates must undergo preclinical trials on animals and clinical trials in humans in order to be approved by the regulatory authorities with jurisdiction before they may be placed on the market. Obtaining marketing authorization requires compliance with strict rules imposed by the regulatory authorities, as well as providing the authorities with extensive preclinical and clinical data and supporting information about the new product and for each indication, such as its toxicity, dosage, quality, effectiveness and safety. The approval process is lengthy, time consuming, expensive and has uncertain outcomes.

Factors that can impact the approval process include: failure of the Company's and its partners' product candidates to meet a regulatory agency's requirements for safety, efficacy and quality, disagreements over interpretations of results of clinical trials, unforeseen safety issues or side effects, failure of trials to be conducted with internationally recognized requirements for good laboratory practice and good clinical practice, disapproval of manufacturing processes or facilities of third-party manufacturers with which the Company and its partners contract for clinical and manufacturing supplies, and changes in governmental regulations or regulatory delays.

Regulators can refuse marketing approval or can require the Company or the Company's partners to repeat previous clinical studies or conduct further clinical studies. A pre-approval inspection of manufacturing facilities by regulatory authorities may need to be completed before marketing approval can be obtained, and such facilities will be subject to periodic inspections that could prevent or delay marketing approval or require the expenditure of financial or other resources to address.

Moreover, both the approval process and the requirements governing the conduct of clinical trials, product manufacturing, safety profiles and other criteria vary significantly from country to country and the fact that the regulatory authorities in one country grant approval does not guarantee that approval will be obtained in other countries.

If a partner of the Company is unable to obtain marketing authorization for one or more products incorporating its technologies, or succeeds only after delays, this could have a material adverse effect on the Company's ability to generate revenues.

Delays in obtaining regulatory approvals may:

- adversely affect the successful commercialization of any product that the Company or its partners develop;
- impose costly procedures on the Company or its partners;
- diminish any competitive advantages in the marketplace that the Company or its partners may attain; and
- adversely affect the Company's receipt of revenues or royalties.

As a result, it may take several years before products are available to end users, if at all, primarily due to the time periods necessary to conduct clinical trials, develop products and obtain marketing authorization.

Even if marketing authorization is obtained, there is a risk that the approved indication is narrower than originally sought and/or contains restrictions regarding its use such as those set out in black box warnings, and there is no guarantee that the authorization will not be subsequently suspended, for example in the event of non-compliance with manufacturing rules or if undesirable side effects are discovered. All of these risks may have a material effect on the ability of the Company and its partners to generate revenues.

### 1.5.2.3. Even if the Company and its partners' product candidates obtain regulatory approval, they may not gain market acceptance.

Even if the Company's and its partners' product candidates obtain regulatory approval, they may not gain market acceptance by the relevant medical community. The rate at which products incorporating the Company's technologies are marketed by its partners and the success thereof depends on various factors, such as:

- the results of ongoing and future clinical trials or delays thereof;
- their acceptance by the relevant medical community; and/or
- the intensity of sales efforts deployed by the Company and/or its partners.

The Company cannot guarantee that products incorporating its technologies will be placed on the market at all or within the estimated time periods, that the medical community will view them favorably, or that its partners will employ the resources necessary to successfully market such products. If the Company and its partners are unsuccessful in commercializing the product because of lack of market acceptance or resources employed for marketing or other post-commercialization problems, the Company and its partners will have spent valuable time and development and financial resources on research programs that ultimately do not yield commercially viable products. As a result, the Company's business, results of operations and prospects could be materially adversely affected.

### 1.5.2.4. There is significant competition in the Biotechnology, pharmaceutical and medical devices industries.

The research into products incorporating the Company's technologies targets markets in which there already exist therapeutic products, some of which are very widely used. In addition, therapeutic products or competing technologies, whether in existence, in development or unknown to date, could at some point in the future gain significant market share and limit the ability of the Company and its partners to successfully market products that incorporate the Company's technologies.

The markets in which the Company and its current and future partners compete and intend to compete are undergoing, and are expected to continue undergoing, rapid and significant technological changes. New therapeutic products or technologies developed by the Company's and its current and future partners' competitors may be more effective, safer and/or less expensive than those that the Company or its partners have developed,

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which could render the Company's current or future product candidates and/or technologies non-competitive, obsolete or non-economical.

The Company's competitors may have:

- significantly greater financial, technical and human resources than the Company has at every stage of the discovery, development, manufacturing and commercialization process;
- more extensive experience in preclinical testing, conducting clinical studies, obtaining regulatory approvals, commercializing drugs, challenging patents and in manufacturing and marketing pharmaceutical products;
- products that have been approved or are in late stages of development;
- for products of similar efficacy, more favorable recommendations or decisions in relation to reimbursement or pricing of their products;
- stronger patent protection;
- more innovative technologies or delivery devices; and/or
- collaborative arrangements in the Company's target markets with leading companies and research institutions.

The Company's and its current or future partners' competitors may be more successful in developing and commercializing their products than the Company, which could materially adversely affect the medium- and long-term business, financial position, income, expansion and outlook of the Company.

### 1.5.3. Risks associated with the Company's organization

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#### 1.5.3.1. The Company could lose key employees and be unable to attract new qualified personnel.

To a large extent, the Company's success depends on the involvement and expertise of its managers and expert scientific staff, in particular its three founders, Gérard Soula, Olivier Soula and Rémi Soula.

The Company has taken out a "key person" insurance policy covering its chairman and founder Gérard Soula (see section 1.5.7 of this registration document, "Insurance and risk coverage").

His departure or the departure of Olivier Soula and/or Rémi Soula or other key employees of the Company could cause:

- a loss of know-how detrimental to certain activities, a risk that would be even greater in the event of a move to the competition; or
- a lack of technical skills that could cause slowdowns in the business and ultimately compromise the Company's ability to achieve its objectives.

Furthermore, in light of the Company's current development, the Company is in the process of expanding its workforce and actively recruiting expert scientific staff to expand its activities. The Company is in competition, in particular with other companies, research organizations and educational institutions, to recruit and retain highly qualified scientific, technical and management staff. Because the Company faces significant competition in recruiting and retaining personnel, the Company may be unable to attract or retain these key staff members under financially acceptable terms.

The Company's inability to attract and retain key staff members could prevent it from achieving its global objectives and could have a material adverse impact on its business, income, financial position, expansion and outlook.

### 1.5.3.2. Company's inability to manage internal growth

In connection with its development, the Company is in the process of recruiting additional staff and expanding its operating capacity significantly, which could make high demands on its internal resources.

In this respect, the Company will notably have to:

- train, manage, motivate and retain a growing number of employees;
- plan for the expenses associated with this growth and the corresponding financing requirements;
- anticipate the demand for its products and the revenue they may generate; and
- increase the capacity of its existing operating, financial and management IT systems.

In addition, the Company is in the process of significantly expanding its research and development facilities, including renovating and equipping these facilities. Unexpected issues related to the Company's expansion could divert management attention from other business concerns or be potentially disruptive to employees.

The Company's inability to manage its growth, or if it encounters unexpected difficulties during its expansion, could have a material adverse impact on its business, income, financial position, expansion and outlook.

### 1.5.3.3. As part of its growth and development, the Company and its partners will need to find new supply sources for certain of the proteins it uses in its product candidates.

In connection with the progression of the Company's pipeline and the initiation of later stage clinical trials for BC Lispro U100, BC Combo and other product candidates, the Company will need to purchase greater quantities of the specific proteins required to develop its formulations to meet the needs of larger clinical trials. The Company may be unable to find suppliers able to supply the appropriate quantities and qualities of proteins at a competitive price, which could delay the start or completion of clinical trials.

In addition, the innovative therapeutic protein formulations that the Company develops require an association of polymers developed by the Company with specific proteins supplied by third parties. The Company's general policy is to diversify its supply sources and to identify at least two suppliers for each type of purchase. Nevertheless, for certain proteins, the various sources of supply are not interchangeable due to the specificities of each protein. Consistent with current practices in the Company's business sector, a single supply source is maintained for each protein. The Company has developed alternative solutions but implementing them could delay the development of its innovative formulations and generate additional costs.

As a result, the Company may not always have access to the specific proteins necessary for the future development of its projects, nor can it guarantee access thereto under acceptable terms.

The inability of the Company or its partners to obtain, on financially acceptable terms, or at all, one or more specific proteins of sufficient quality necessary for the development of its projects could have a material adverse impact on the Company's business, income, financial position, expansion and outlook.

### 1.5.3.4. The Company relies on third parties to conduct clinical trials on its product candidates.

The Company relies on specialized healthcare institutions, including clinical research organizations and clinical investigators to conduct clinical trials of its product candidates, which are necessary to obtaining proof of concept in order to license the Company's technologies. Although the Company relies on these parties for high quality execution of the Company's clinical trials, the Company is unable to control all aspects of their activities.

If these third parties do not carry out their contractual duties or obligations or meet expected deadlines, if the third parties need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to failure

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to adhere to the Company's clinical protocols or good clinical practices or for other reasons, the Company's current or planned clinical studies may be extended, delayed or terminated.

Any extension, delay or termination of any of the clinical trials would have a significant negative impact on the Company's business and would compromise the Company's ability to license or commercialize its product candidates. Distance from or geographical distribution of the clinical or preclinical trial centers may also create operating and logistical difficulties, which may generate additional costs and delays.

### 1.5.4. Regulatory and legal risks

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#### 1.5.4.1. Risks associated with obtaining regulatory approvals

The Company has only limited experience in filing and pursuing applications necessary to obtain regulatory approval or authorization.

It also cannot ensure that its product candidates will be approved or licensed for marketing, even in circumstances where the Company is collaborating with a partner who has more experience in seeking market authorization. The process of applying for regulatory approval is expensive, often takes many years and can vary substantially based upon the type, complexity and novelty of the product candidates involved.

If any of the Company's product candidates are not approved, this could have a material adverse effect on the Company's business, results of operations and prospects and the value of the Company's shares.

#### 1.5.4.2. Risks associated with an increasingly restrictive regulatory environment for the pharmaceutical industry

One of the most significant challenges faced by a growth company like Adocia is to succeed, with the assistance of its partners, in developing products incorporating its technologies in an increasingly strict regulatory environment.

The statutory and regulatory provisions adopted by the AFSSAPS\*, European Commission, EMA\*, FDA\* and equivalent regulatory authorities in other countries govern research and development work, preclinical trials, clinical trials, the regulation of institutions, and the production and marketing of drugs.

The trend toward stricter statutory and regulatory supervision is worldwide, although requirements vary from one country to another. The health authorities, in particular the FDA and EMA, have imposed increasingly strict requirements to prove the effectiveness and safety of products, in particular with respect to the volume of data requested.

Accordingly, the authorization process is long and costly. It may last several years, and its outcome is unpredictable.

Thus, whether in the United States, Europe or other countries, this strict regulatory framework may result in:

- increased costs in connection with the development, testing, production and marketing of products incorporating the Company's technologies;
- a restriction as to the indications or restrictions regarding use such as those set out in black box warnings for products incorporating the Company's technologies; and
- significant delays in obtaining marketing authorization for products incorporating the Company's technologies and, consequently, in the generation of revenue for the Company.

### 1.5.4.3. Risks associated with uncertain protection of the Company's patents and other intellectual property rights

To protect its innovative therapeutic protein formulations and technologies, the Company relies on the protection afforded by intellectual property rights, such as patents, patent applications, trademarks and trademark applications, as well as the protection afforded to its trade secrets and know-how by confidentiality agreements and other contracts. However, these means offer only limited protection and may not be successful in preventing unlawful use of the Company's products or technologies.

The patents and patent applications that the Company has filed and that aim to protect its technologies are recent and many are still being examined by patent authorities. These patents and patent applications afford protection that varies in duration from one country to another. For example, in France and in Europe, this duration is 20 years from the date patent applications are filed. The Company devotes significant financial and human resources to protecting its technologies, and employs means commonly used in the industry (such as filing additional results to expand one or more patent claims) to extend the protection of its technologies beyond application periods, although it cannot guarantee the results thereof.

The outcome of patent applications for biotechnology and pharmaceutical products are generally very uncertain, raising complex legal and scientific questions. The standards applied by patent offices to grant patents in different countries, or to define the subject and scope of admissible applications, are not always applied in a predictable or uniform manner, and may be amended without warning. Neither the Company nor its partners can be assured that the Company was the first to claim a given invention among its current patent applications, nor that it or its partners were the first to submit applications to protect these inventions. The Company may therefore encounter difficulties in gaining approval for some of its current or future patent or trademark applications currently under examination or that may be examined in the future.

In addition, the Company regularly files trademarks. These trademarks have been registered or are currently undergoing examination. When the Company files any of its trademarks in a country in which it is not already covered, the Company could discover that the trademark in question is not available in that country. In such case, a new trademark would have to be found for such country. The Company does not yet use its trademarks because it is still in the development stage. Nevertheless, the trademarks are not yet vulnerable, such as being subject to revocation for non-use, and no affidavits of use are currently required to maintain them.

Furthermore, the fact that a patent or trademark is granted does not guarantee that it will be valid or enforceable. In fact, the Company's competitors could at any time successfully challenge the validity or enforceability of the Company's patents, patent applications, trademarks and trademark applications before the courts or in other proceedings, which, depending on the outcome of such disputes, may result in their scope being limited, their revocation or their circumvention by competitors. Consequently, the Company's rights under its patents, patent applications, trademarks and trademark applications may not afford the expected protection from competitors.

In addition, the Company may also in-license certain technologies, such as the DriveIn® technology which it has since abandoned. The patents licensed to the Company could be challenged, discovered to have been issued on the basis of insufficient and/or incorrect documentation or disclosure, or held to be unenforceable.

Therefore, the Company cannot guarantee with certainty that:

- the Company's patent and trademark registration applications undergoing examination will, in fact, result in patents and trademarks being granted; and
- the patents and trademarks granted to the Company will not be disputed or revoked.

If the Company fails to obtain and maintain intellectual property protection of its products or product candidates and protection of its trade secrets, the Company could lose its competitive advantage, and the increased competition the Company may face could materially adversely affect its business, results of operations and prospects.

#### 1.5.4.4. Risks associated with the inability to protect its intellectual property rights

The Company cannot guarantee that its technologies and the innovative therapeutic protein formulations developed using its technologies, which are closely tied to its know-how and trade secrets, are adequately protected from competitors or that competitors cannot misappropriate or circumvent them. Pursuant to the cooperation and research agreements that the Company enters into, the Company may be required to provide its contractual partners, in various forms, with certain elements of its know-how, whether or not protected by patents, particularly information, data and facts concerning its research, technologies or products.

The Company attempts to limit disclosure of key elements of its know-how to third parties solely to information that is strictly necessary to its collaboration with such third parties. Through contractual provisions, in particular confidentiality clauses, the Company ensures that such third parties undertake not to misappropriate, use or disclose such information. Nevertheless, the Company cannot guarantee that such third parties will comply with these agreements, that the Company will be aware of a breach of these clauses, or that any compensation that may be subsequently obtained will be sufficient in light of the loss sustained.

Furthermore, the Company faces the risk that its contractual partners may claim ownership of intellectual property rights in the Company's inventions, knowledge or results, based on these cooperation and research agreements. Lastly, these agreements may lead to the creation of intellectual property rights that are jointly owned or to exclusive rights of use granted to the Company on unfavorable terms.

Therefore, the Company cannot guarantee with certainty that:

- its know-how and trade secrets cannot be misappropriated or circumvented;
- its competitors have not already developed a technology or products similar to its own;
- the scope of the protection afforded by patents and trademarks is sufficient to protect it from the competition or third-party patents and trademarks that cover similar products or devices; and
- no contracting partner will claim ownership of intellectual property rights in the Company's inventions, knowledge or results.

The Company incurs significant costs in protecting intellectual property rights, in particular, filing fees and the costs of maintaining patents in force and managing its other intellectual property rights. These costs could increase, in particular if the Company is obliged to take legal action to protect its rights. In addition to these costs, if legal action becomes necessary to enforce the Company's intellectual property rights, protect its trade secrets or know-how, or establish the validity and scope of its intellectual property rights, this could have material adverse impact on the Company's income and financial position and may not provide the protection sought.

Thus, the Company is currently engaged in legal proceedings against its former partner Eli Lilly in order to defend its rights following the appropriation and misuse by Lilly of confidential information and discoveries belonging to Adocia, as well as Lilly's breach of several collaboration and confidentiality agreements.

Moreover, monitoring unauthorized use of products and technologies is difficult, and the Company cannot be sure that it will be able to prevent misappropriation or unauthorized use of its products and technologies, in particular in foreign countries where its rights may not be as well protected.

#### 1.5.4.5. Risks associated with license holders that may affect the Company's relations with its current or potential licensees

The Company may infringe or violate the intellectual property rights of others with technologies, product candidates or products that the Company or its partners seek to use, target or develop and commercialize. These third parties could bring claims against the Company or the Company's collaborative partners, which could cause the Company to incur substantial expense, and if successful, could require the payment of substantial damages. The Company or its partners could be forced to cease or delay research, development, manufacturing or sales of the product or product candidate or technology that is the subject of the suit.



The Company cannot guarantee that there are no prior patents owned by third parties that may provide grounds for an infringement action against the Company.

In addition, the Company cannot guarantee that there are no prior third-party trademark rights that may provide grounds for an infringement action against it.

The Company's domain names could also be the subject of Uniform Dispute Resolution Policy (UDRP) proceedings or an infringement action brought by a third party claiming prior trademark rights. Therefore, the Company cannot guarantee with certainty that its products do not infringe patents or trademarks owned by third parties.

The Company can also not guarantee that there are no trade secrets or know-how owned by third parties that may provide the grounds for a misuse action against the Company.

#### 1.5.4.6. Risks associated with liability arising from products

The Company's business exposes it to potential liability, in particular to patients or healthy volunteers who take part or have taken part in clinical trials conducted under its direction, if they suffer side effects in connection with such trials, even when the instructions in the protocols have been followed.

The Company may also be liable in the event of commercial use of products incorporating its technologies. Criminal or civil actions could be filed or initiated against the Company by users (patients, practitioners, researchers and other healthcare or research professionals), the regulatory authorities, distributors or any other third party that uses or markets products incorporating its technologies.

Product liability claims may be expensive to defend and may result in judgments against the Company that are material. Although the Company has taken out specific insurance policies to cover the resulting financial risk (see section 1.5.7 of the registration document, "Insurance and risk coverage"), and believes that this coverage is appropriate for its business and stage of development, it cannot be certain that the insurance policies will be sufficient to cover all claims made against it. Product liability insurance is expensive, difficult to obtain, and may not be available in the future on acceptable terms. However, any such claims, regardless of merit, could be time-consuming and expensive to defend, could divert management's attention and resources, and could materially adversely affect the Company's reputation, business, results of operations and prospects.

#### 1.5.4.7. Risks associated with litigation and claims

From time to time, the Company may become subject to litigation and claims or become otherwise involved in litigation, arbitration proceedings or similar disputes. In addition, the Company regularly includes indemnification provisions in its contractual arrangements and, from time to time, may be subject to claims by its contractual counterparties or third parties with respect to these obligations. The Company has no reason to believe that the Company's contracting partners, or other interested parties in its agreements, would raise any claims against the Company. However, any such claims, regardless of merit, could be time consuming and expensive to defend, could divert management's attention and resources, and could materially adversely affect the Company's business, results of operations and prospects.

#### 1.5.4.8. Risks associated with evolving reimbursement and drug pricing policies

The process of setting the sale price of drugs and their reimbursement rate begins when marketing authorization has been granted.

The ability of the Company's partners to achieve acceptable levels of reimbursement for drug treatments by governmental authorities, private health insurers and other organizations will have an effect on its ability to successfully commercialize its product candidates. In many markets, including France, this process depends on decisions made by public commissions and bodies on the basis of pharmacological and financial data submitted by applicants. In connection therewith, the Company's partners may be requested to carry out additional studies of

their products incorporating the Company's technologies. Such studies would generate additional costs for the relevant partners and marketing delays.

The price, as set by governmental authorities, private health insurers and other organizations, will depend on a rate deemed acceptable for the community, applying a policy that seeks to control health costs. The price set will condition the ability of the Company's partners and, indirectly, the Company to earn profits on the sale of the corresponding products.

If reimbursement is not available or is available only at limited levels, the Company's partners may not be able to successfully commercialize its product candidates and may not be able to obtain a satisfactory financial return on products that the Company may develop. Furthermore, the Company's level of remuneration may change during the period in which products incorporating its technologies are marketed by its partners, in particular due to the reimbursement rate for such products, which may change significantly over time.

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### 1.5.4.9. Risks associated with health, safety of use of hazardous substance, technical facilities and the environment

Research and development activities in the biology field require the use of certain hazardous biological or chemical substances. Although the Company has adopted a policy appropriate for the types of risks generally identified in biological research laboratories, it cannot rule out all risk of accidents in its laboratories resulting in contamination or injury to its research teams. In the event of an accident, the Company could be held liable and be ordered to pay significant damages to affected employees.

Furthermore, the laws currently in force may be amended significantly, which could cause the Company to incur considerable expenses to comply therewith.

The Company's medium- and long-term business, financial position, income, expansion and outlook could be materially impacted by the occurrence of one or more of these risks.

### 1.5.5. Financial risks

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#### 1.5.5.1. History of operating losses – Risks associated with projected losses

The Company has posted operating losses every year since its creation in 2005. As of December 31, 2018, its cumulative net losses presented under IFRS rules (including losses carried forward) were €41.3 million.

These losses are mainly due to internal and external research and development expenses, in particular in connection with the numerous in vivo and clinical trials conducted. As its research and development activities continue, the Company may experience additional operating losses in future years, which may be higher than in the past, in particular due to:

- increased research and development costs associated with the development of its projects as they progress (due, in particular, to the need to conduct clinical trials, without any guarantee as to the point at which such costs may be assumed by the partners with which the Company plans to enter into license agreements);
- stricter regulatory requirements governing the manufacturing of its products;
- a larger project portfolio; and
- expanded research and development activities and, perhaps, the acquisition of new technologies, products or licenses.

An increase in such expenses could have a material adverse impact on the Company and its business, financial position, income, expansion and outlook.

To become profitable, the Company must sign successful license and collaborative agreements and/or successfully develop and obtain regulatory approval for its product candidates. The Company may never generate significant revenues and, even if it does, it may never achieve profitability.

However, the signature of an important agreement with a licensing and collaborative partner could have an immediate effect on profitability for a given fiscal year.

In addition, as a result of recent changes to French tax law, the amount of operating losses a company may carry forward in a given fiscal year is now limited to €1 million plus 50% of the income before tax per fiscal year. As a result, the Company could become profitable more quickly than prior to such changes, particularly in a situation where the Company enters into one or more major agreements with a licensing and collaborative partner.

Nevertheless, to become and remain profitable, the Company must succeed in developing and commercializing products with significant market potential. This will require the Company to be successful in developing its current product candidates, some of which are only in the preliminary stages of development, signing agreements with partners, obtaining regulatory approval and marketing, manufacturing and selling the products. The Company may never succeed in these activities and may never generate revenues that are significant or large enough to achieve profitability. Even if the Company does achieve profitability, the Company may not be able to sustain or increase profitability in the long term. The Company's failure to become and remain profitable may cause the market price of its shares to decrease and could impair the Company's ability to raise capital, expand its business, diversify its product offerings or continue its operations.

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#### 1.5.5.2. Uncertain capital resources and additional financing

In the future, the Company will continue to have significant financing needs in order to develop its technologies and pursue its strategy. The Company may be unable to finance its growth itself, which would require it to seek other sources of financing, such as increasing its equity through capital increases and/or taking out bank loans.

The Company's financing needs and the timing thereof depend on factors that are largely beyond the Company's control, such as:

- higher costs and slower progress than anticipated for its research and development programs and clinical trials;
- the costs of preparing, filing, defending and maintaining its patents and other intellectual property rights;
- the scope of preliminary research work and the time periods necessary to conclude licensing agreements with industrial partners;
- the costs of keeping up with technological developments and markets;
- higher costs and longer time periods than anticipated to obtain regulatory authorizations, including the time required to prepare applications to be submitted to the authorities with jurisdiction; and
- new development opportunities for new products or the acquisition of technologies, products or companies.

The Company may be unable to procure additional capital when needed or such capital may not be available on financial terms acceptable to the Company. If the necessary funds are unavailable, the Company may be required to:

- delay, reduce or cancel research programs;
- obtain funds by entering into partnership agreements, which may oblige it to give up the rights to certain of its technologies or products;
- grant licenses to all or part of its BioChaperone® technological platform to partners or third parties; or
- enter into new cooperation agreements, which may be less favorable to the Company than those it would have been able to negotiate in a different context.

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Furthermore, if the Company raises capital by issuing new shares, the stakes of its shareholders may be diluted. In addition, debt financing, if available, could impose restrictive terms on the Company and its shareholders.

The occurrence of one or more of these risks could have a material adverse impact on the Company and its business, financial position, income, expansion and outlook.

### 1.5.5.3. Risk of dilution

Pursuant to its policy to motivate its managers, directors and employees, since its creation, the Company has issued or granted stock warrants and business founders' stock warrants (BSPCE) and has granted bonus shares. The maximum possible dilution from financial instruments in existence as of December 31, 2018 is 7.3% on a fully diluted capital basis.

In the future, the Company may issue or grant additional financial instruments that confer equity rights in the Company.

Any grant or issue of additional shares or other financial instruments conferring equity rights would dilute, potentially significantly, the equity stakes of the Company's shareholders.

### 1.5.5.4. Risks associated with access to public subsidies and to the research tax credit

Since its creation, the Company has received grants from the French government, French public and private research assistance organizations, and the European Union. The Company may request additional grants or advances in the future.

As of December 31, 2018, and since its creation in 2005, the Company has received the following financial assistance:

<i>In (€) thousands</i>	<b>Amount granted and cashed in</b>	<b>Amount reimbursed</b>	<b>Amount granted as a subvention</b>
OSEO repayable advances	3 470	1 900	1 050
OSEO FEDER subvention	605		605
COFACE repayable advances	91	91	
<b>TOTAL ADVANCES</b>	<b>4 166</b>	<b>1 991</b>	<b>1 655</b>

The amounts and payment dates of current and future grants depend on various factors beyond the Company's control, such as a decision not to distribute or to freeze credits. Delays in paying or the non-payment of these grants, which finance part of the Company's growth, could materially adversely impact its business, financial position, income, expansion and outlook.

### 1.5.5.5. Risks associated with access to public subsidies and to the research tax credit

To finance its activities, the Company has also opted for the research tax credit, pursuant to which the French government grants a tax credit to companies that make significant investments in research and development. Research expenses eligible for the research tax credit include salaries and wages, depreciation of research equipment, services subcontracted to accredited research organizations (public or private) and intellectual property expenditures.

The Company has been entitled to the research tax credit each year since its creation, and the amount thereof has been systematically reimbursed to the Company upon submission of the corresponding application.

In 2018 the Company received a total reimbursement of €7.6 million under the research tax credit for expenditures generated in fiscal year 2017.

For fiscal year 2018, the Company recorded an amount of €6.5 million under the research tax credit that appears in its receivables, for which it will seek reimbursement in 2019.

With respect to 2018 and subsequent years, it cannot be ruled out that the tax authorities may dispute the methods that the Company uses to calculate its research and development expenses, or that the research tax credit may be lost due to statutory amendments or a dispute with the tax authorities, despite the fact that the Company feels it is in compliance with the expense documentation and eligibility requirements. Such occurrence could have a material adverse impact on the Company's income, financial position and outlook.

## 1.5.6. Market risks

### 1.5.6.1. Liquidity risk

Historically, the company has financed its growth primarily by increasing its equity through capital increases. For the acquisition of the building completed in February 2016, the Company took out bank loans. However, it is not exposed to liquidity risks from the application of early repayment clauses in bank loans.

The Company's cash and cash equivalents totaled € 35million as of December 31, 2017 and almost € 40 million as of December 31, 2018.

The Company conducted a specific review of its liquidity risk and considers that it is in a position to meet its financial obligations that will fall due within the next 12 months. With integration of its financial debt and loans in the amount of €7.1 million at end-December 2018, net cash flow for this period was €32.7 million. This level of cash enables the Company to fund its planned clinical development (see section .1.3 of this registration document) and the development of its new programs.

In particular, the Company believes that it is able to make its next repayments of its loans and Bpifrance repayable advances, being precised that no reimbursment are expected for 2019 (see note 10 to the Company's consolidated financial statements prepared under IFRS in chapter 4.1 of this registration document).

The company supports the development of the projects licensed to Tonghua Dongbao and pursues its research and development activities while nevertheless focusing its expenses on projects and priority activities. The recovery of damages awarded under the first part of the arbitration proceeding against Lilly (\$ 11.6 million plus interest) is expected in 2019, following the conclusion of the second part of the arbitration. Pending the cash receipt of this amount, the possibility of an advanced payment of the research tax credit allows the Company to finance the defined operational plan and thus to meet its financial commitments for at least the next 12 months. Therefore, the going concern assumption has been retained.

### 1.5.6.2. Foreign exchange risk

Foreign exchange risk is the risk that the fair value or future cash flows of a financial instrument will fluctuate due to changes in foreign exchange rates. The Company's strategy is to enter into agreements denominated in euros, because its expenditures are also largely denominated in euros.

However, as a result of the agreement signed with Tonghua Dongbao Pharmaceuticals Co. Ltd in April 2018, a major part of the Company's revenues, such as the upfront payment received in connection with that agreement, were denominated in US dollars. As a result, the Company was exposed to risk in relation to fluctuations in the euro-US dollar exchange rate.

If the Company signs further licensing and collaboration agreements with US pharmaceutical companies, it may be exposed to additional euro-US dollar exchange rate risks.

## Presentation of Adocia and its activities

The Company cannot rule out that significant growth in its business may create greater exposure to exchange rate risk. In such case, the Company will consider adopting a new policy appropriate to hedging such risk such as currency hedging transactions and the purchase of currency forwards.

The company cannot rule out the possibility that a significant increase in its activity may result in greater exposure to foreign exchange risk. The company will therefore again consider developing an appropriate policy to hedge these risks.

### 1.5.6.3. Interest rate risk

In 2015 the Company took out a loan from two banks to finance the acquisition of the building in which its research center and headquarters are located. These loan agreements were negotiated at a fixed rate for a 12-year term.

The Company is exposed to changes in interest rates in the course of managing its cash and cash equivalents. The Company's cash and cash equivalents totaled €35 million as of December 31, 2017 and almost €40 million as of December 31, 2018. This item includes term deposits, accounts that pay fixed interest and investments in money market mutual funds. The Company's policy is to invest exclusively in liquid products with no risk to capital.

The Company strives to reduce the credit risk to which its cash and cash equivalents are exposed by monitoring the quality of the financial institutions with which it deposits its funds.

The Company has no guarantee that it will obtain the same interest rates when it renews its time accounts at maturity.

### 1.5.6.4. Equity risk

None.

### 1.5.6.5. The price of the Company's shares is subject to significant volatility.

The price of the Company's shares is subject to significant volatility. For example, on December 31, 2017 the Company's share price traded at €14.35, compared with €16.54 on December 31, 2018. The average daily trading volume of 36,265 shares traded per day in 2017 decreased to 19,615 shares traded per day in 2018. The public float remained steady in 2018 and was around 60% at the end of December 2018.

As of April 9<sup>th</sup>, 2019, shares traded at €14.14 with an average volume of 13,329 shares traded since the beginning of the year.

In addition to the occurrence of the risks described herein, the market price of the Company's shares could be significantly affected by various factors that may impact the Company, its competitors, general economic conditions and the biotechnology sector. In particular, the following factors may have a significant impact on the share price:

- an unfavorable movement in market conditions specific to the Company's business sector;
- announcements by the Company, its competitors or other companies that engage in similar businesses and/or announcements concerning the biotechnology market, including announcements about the financial and operating performance or scientific results of such companies;
- changes, from one period to another, in the forecasts or outlook of the Company or its competitors;
- changes concerning patents or intellectual property rights of the Company or its competitors;
- announcements regarding results of the Company's clinical trials or other scientific developments;
- changes in the political, economic and monetary context, in particular unfavorable changes in the applicable regulatory environment in countries or markets specific to the Company's business sector or to the Company itself;

- announcements concerning changes to the Company's shareholder structure;
- announcements concerning the signature of new partnership agreements or the end of existing partnership agreements;

### 1.5.7. Insurance and risk coverage

The company has adopted a policy to cover the main risks to which it is exposed, when possible, by taking out coverage amounts that it deems consistent with its cash consumption requirements.

For all of the insurance policies referred to above, the company's total expenses remained stable in the fiscal years ended on December 31, 2017 and 2018.

The main insurance policies are:

- a "property damage" policy, which generally covers the risks of fire, explosion, lightning, electrical damage, special risks, IT risks, loss of goods in refrigerated chambers, goods in transit, theft, machinery breakdowns and loss of use;
- a "business liability" policy, which covers risks in connection with business operations for all damage, including bodily injury;
- a "key person" insurance policy that insures against the death of the chairman and chief executive officer due to illness or accident;
- a "directors' and officers' liability" insurance policy, which covers the liability of the company's senior managers if their liability is alleged in connection with the performance of their duties.

For all the policies, the Company and the insurer determine together the maximum coverage in adequacy with the specificities of the Company and in line with the practices of companies in a similar field of activity.

The company's liability in connection with clinical trials is covered by specific policies whose rates and coverage amounts depend on the local laws applicable to the relevant clinical research center. The total amount of premiums and coverage taken out for these trials depends in particular on the number of trials, their location and the number of patients to be included in each trial.

The company considers that these insurance policies adequately cover the insurable risks inherent to its business activities, and that its policy with respect to insurance is consistent with practices in its business sector. The company does not foresee any particular difficulty in maintaining adequate insurance levels in the future, subject to market conditions.

Nevertheless, the company cannot guarantee that it will always be able to maintain or, if necessary, obtain similar insurance coverage at an acceptable cost, which may oblige it to take out more expensive insurance policies and/or to assume greater risks, in particular as its business activities expand.

### 1.5.8. Extraordinary events and disputes

**Except as noted below**, during the 12-month period preceding the filing date of this registration document, the company has not been involved in any administrative, criminal, judicial or arbitration proceedings that may have a material adverse impact on the company, its business, financial position, income or expansion and that is not reflected in its financial statements. Furthermore, to the company's knowledge, as of the date of this registration document, the company is not threatened with any such proceedings.

To the Company's knowledge, no exceptional event arose during the same period that would generate additional risk or additional unplanned costs.

**However, it must be noted** that in October 2017, Adocia announced in a press release its filing of an arbitration claim against Eli Lilly & Co related to a research and licensing agreement signed in 2014 and terminated in January

## Presentation of Adocia and its activities

2017 at the initiative of Eli Lilly & Company. In August 2018, the first phase of the arbitration procedure initiated by Adocia against Lilly concluded in favor of Adocia. The Arbitration Tribunal awarded Adocia \$ 11.6 million, as well as interests.

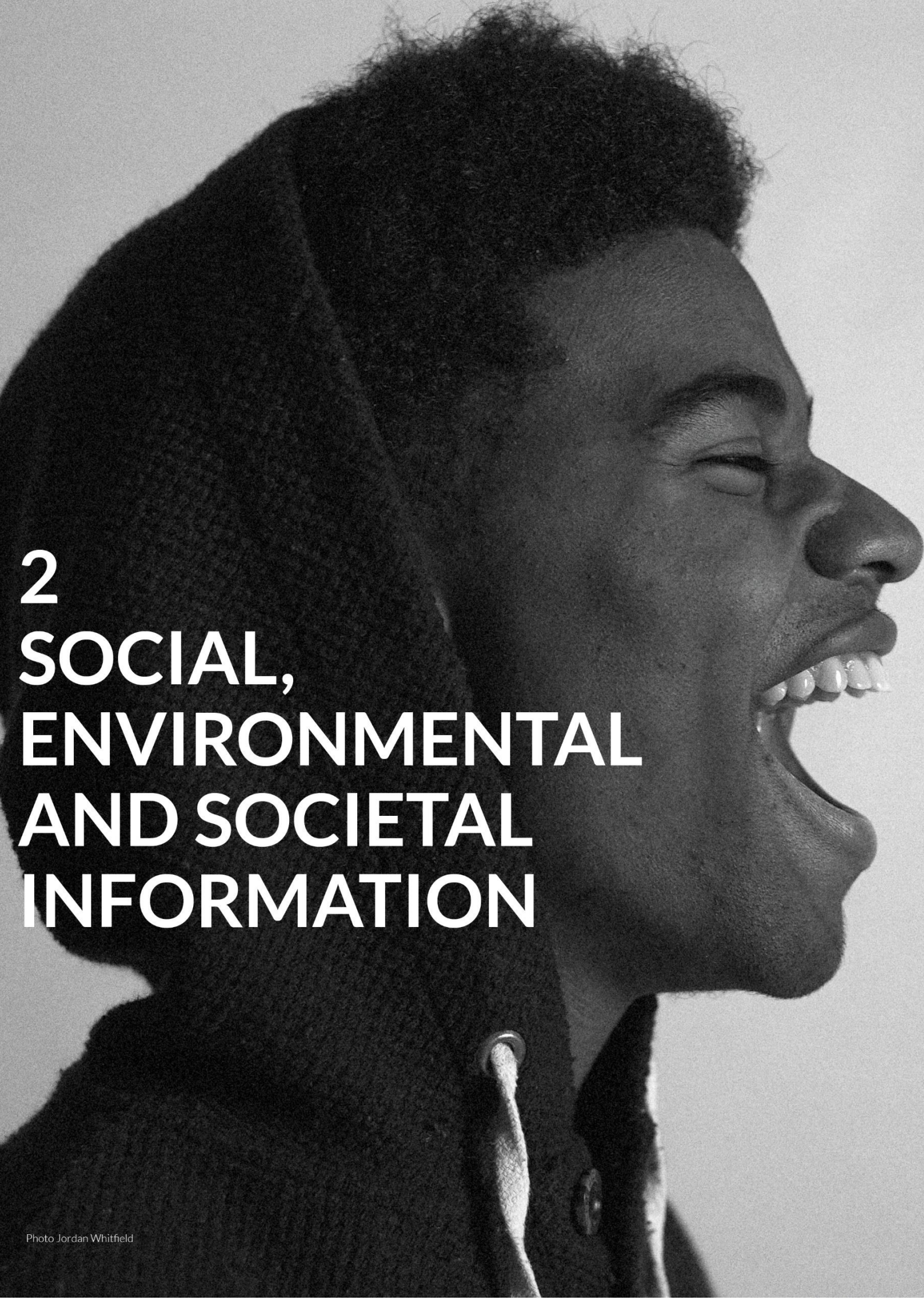
The arbitration proceeding is continuing, in particular related to Adocia's additional claims against Lilly, filed in February 2018, for a revalued amount of USD 1.3 billion and the counterclaims of Lilly for an amount of USD 188 million, remain pending, with a decision of the court expected in the third quarter of 2019.

Finally, in October 2018, Lilly filed a civil complaint against Adocia in the United States District Court of the Southern District of Indiana to seek a declaratory judgment for two of its US patents regarding ultra-rapid insulin formulation (Lilly's United States Patent Nos. 9,901,623 and 9,993,555 entitled "Rapid-acting insulin compositions"). Lilly contends in its complaint that it filed the action because Adocia has asserted that Lilly's patents reflect Adocia's inventive contribution. Adocia does not expect the matter to be resolved during this fiscal year.

1







**2**  
**SOCIAL,  
ENVIRONMENTAL  
AND SOCIETAL  
INFORMATION**

# Chapter 2

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## 2 SOCIAL, ENVIRONMENTAL AND SOCIETAL INFORMATION

### 2.1 Methodology note

This report uses indicators selected to represent the main economic, social and environmental impacts of the Company's activities.

The social, environmental and safety indicators that were collected, calculated and consolidated may be subject to inherent limits in terms of the practical modalities of collection and consolidation of this data.

The data presented covers all the Company's activities and all the group's employees, unless otherwise indicated.

2

#### 2.1.1 Definition of labor indicators

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**Workforce:** Number of employees on staff at December 31 of the year N, under permanent or fixed term contract (including work-study contracts). Contracts terminating on December 31 are not included in the workforce. This calculation is not prorated for part-time workers.

**New hires:** Number of employees hired under permanent or fixed term contract between January 1 and December 31 of the year N. This calculation is not prorated for part-time workers. Transitions from fixed term to permanent contracts are not included in new hires. A transition from a work-study to a fixed term or permanent contract is counted as a new hire.

**Departures:** Number of employees who left the company between January 1 and December 31 of the year N. This calculation is not prorated for part-time workers.

**Absenteeism rate:** The ratio of the number of days of absence due to illness, sick child or workplace accident to the number of theoretical days worked. This figure only covers the France scope.

**Number of hours worked:** This indicator only covers the Company's activities located in France from January 1 to December 31 of the year N. It corresponds to the number of hours of effective work. Interns are excluded from the calculation.

#### 2.1.2 Definition of safety indicators

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These indicators only cover the Group's activities located in France.

**Frequency rate (FR):** (number of workplace accidents and commuting accidents resulting in medical leave / hours worked) x 1,000,000

**Severity rate (SR):** (number of days lost due to temporary disabilities as a result of a workplace accident or commuting accident / hours worked) x 1,000,000

## 2.2 Social data

### 2.2.1 Group remuneration policy

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#### 2.2.1.1 Remuneration

The Company has to be competitive and attractive to attract and retain top talent. It therefore applies an ambitious remuneration policy, reflected in particular in a payroll of €9.3 million (French GAAP) for 2018 and significant annual increases. Over the last three years, average general and individual increases fell within a 2% to 4% range (excluding corporate officers), plus bonuses based on collective and individual performance. However, in a more challenging economic environment, the Company reserves the possibility of revising its remuneration policy to adapt to economic and financial constraints and issues.

Allocation of pay raises and/or bonuses is based on objective criteria and individual merit. Employees enjoy workplace equality regardless of race, sex, color, religion, disability, family status, sexual orientation, age and ethnicity.

Adocia supplements its remuneration policy with plans launched in 2008 to award free corporate shares and BSPCE founders' warrants. Initially intended for key Company managers (directors and service line heads), and then project managers, this policy was extended to technicians and managers at the expert and senior level in 2015.

#### 2.2.1.2 Equity interests held by employees

To the Company's knowledge, at December 31, 2018, the Company's employees (including Olivier Soula and Rémi Soula) held 716,335 shares, i.e. 10% of equity and 14.2% of voting rights in the Company. The proportion of capital represented by the shares held by Company employees, including corporate officers, that are subject to collective management (PEE or FPCE accounts), calculated in accordance with Article L. 225-102 of the French Code of Commerce, was zero. The shares held by employees or corporate officers following free allocation as per Article L. 225-197 of the French Code of Commerce represented 1.5% of equity.

#### 2.2.1.3 Employee savings

ADOCIA has implemented various employee savings schemes. Such schemes are instruments in the company's labor policy that can meet various objectives, such as strengthening the connection between employee performance and business results, retaining and motivating employees.

- Profit sharing (*participation*) implemented by an agreement signed December 11, 2013 between management and the employees represented by the Single Employee Representative Body. There was no profit sharing at December 31, 2018, given the fiscal loss registered for fiscal year 2018.
- A company savings plan (PEE) and collective retirement savings plan (PERCO) created on July 28, 2014 by agreement of management and the employees represented by the Single Employee Representative Body.
- The time savings account (CET) set up by an agreement signed June 30, 2014 between management and the employees represented by the Single Employee Representative Body.

The Company has not signed a profit sharing (*intéressement*) agreement to date.

### 2.2.2 Employment

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The main objectives of Adocia's human resources policy are to:

## Social, environmental and societal information

- attract, retain and motivate the best talent to support the development of the company's ambitious and innovative projects;
- provide training opportunities to employees;
- promote internal mobility and promotions, so as to offer employees a broader scope of activities and enable them to gain new expertise.

### 2.2.3 Workforce

At the end of December 2018, the Company had 132 employees (full-time and part-time), of which 130 work in France in the parent company and two are based in the US subsidiary Adocia Inc. At December 31, 2018, the breakdown of the workforce by socio-professional categories and gender is as follows:

<i>Effectif total et répartition des salariés par CSP et par sexe</i>	<b>31/12/2018</b>	<b>31/12/2017</b>
<b>Executives</b>	<b>74</b>	<b>70</b>
of which permanent contracts	72	68
<b>Non executives</b>	<b>58</b>	<b>59</b>
of which permanent contracts	46	46
<b>Workforce (number)</b>	<b>132</b>	<b>129</b>
<b>Workforce breakdown by gender M/F (in %)</b>	<b>52/48</b>	<b>50/50</b>
Men (number)	69	65
Women (number)	63	64

At the end of December 2018, the company employed 52 researchers who hold a doctorate in science, medicine or pharmacy, or more than one-third of the total.

As of December 31, 2018, close to 80% of the workforce was assigned directly to research and development, with the remaining employees performing support functions, such as finance, administrative services, quality, security and human resources.

At December 31, 2018, the average employee age was 36 years and the breakdown of the workforce by age bracket was as follows:

<i>Age pyramid 2018</i>	<b>Men</b>	<b>Women</b>	<b>Total</b>	<b>Percentage</b>
Younger than 25 years old	7	7	<b>14</b>	<b>11%</b>
25 to 34 years old	22	27	<b>49</b>	<b>38%</b>
35 to 44 years old	26	16	<b>42</b>	<b>33%</b>
Older than 44 years old	14	13	<b>27</b>	<b>21%</b>

The Company's R&D and SG&A workforce has evolved as follows:

	<b>12/31/2018</b>	<b>12/31/2017</b>
R&D workforce	104	101
G&A workforce	28	28
<b>Total workforce</b>	<b>132</b>	<b>129</b>

### 2.2.4 Personnel movements in 2018

The table below presents the evolution of the workforce from January 1 to December 31, 2018:

	12/31/2018	12/31/2017
<b>Number of hires</b>	<b>25</b>	<b>22</b>
<b>Number of employee departures</b>	<b>22</b>	<b>18</b>
<b>Net increase of the workforce</b>	<b>+3</b>	<b>+4</b>
of which permanent contracts	0	1
of which short-term contracts for additional activity	3	0
of which short-term contracts for replacement	0	3
of which work-study contracts	0	0

The Company registered 22 departures during 2018, including:

- 12 departures at the end of fixed term contracts (including 7 work-study contracts)
- 9 resignations
- 1 dismissal

## 2.2.5 Work organization

The employment contracts of the French employees are governed by that country's collective bargaining agreement for pharmaceutical industries.

Those employed by the Adocia Inc. subsidiary are governed by US law.

On July 22, 2010 the Company reached an agreement on the organization of working time with employee representatives, whose details were developed with a view to the agility and flexibility needed in the research field. This agreement was approved by the French National Joint Committee for the pharmaceutical industry on September 29, 2010.

Pursuant to this agreement, the working time of management-level employees (groups VI to IX of the pharmaceutical industries collective bargaining agreement classification) is counted in days and the working time of technicians (employees in groups I to V) is counted in hours. For these latter, effective working time is 36.25 hours per week, with allocation of compensatory days to result in an average working time of 35 hours per week.

In 2018, 13 employees worked part time, 4 of which under a parental leave contract. All these employees choose to work part time to deal with family responsibilities.

The main reasons for absences in 2018 were illness and maternity or paternity leaves.

The absenteeism rate was 1.62% in 2018 compared with 1.95% in 2017. The number of days of absence due to sickness, workplace accident and sick child for 2018 was 522 days, compared with 613 days the previous year. The 15% decrease is primarily due to the decrease of the sick leaves exceeding 40 days, which impacted the year 2017. Planned absences such as maternity leave or paternity leave are not included in this calculation.

## 2.2.6 Labor relations

The Company decided to create a single employee representative body in 2013 after arriving at the legal thresholds in 2012. This single employee representative body was renewed in November 2016.

This new single representative body, in accordance with the Rebsamen Act of August 18, 2015, combines the attributes of employee representatives, works council and health, safety and working conditions committee within a single elected delegation. The Single Employee Representative Body had 5 members and 5 alternates at end-2018, among them 5 executives and 5 non-executives.

Social, environmental and societal information

The company ensures that the rights and freedoms of the delegates to employee representative bodies are scrupulously respected, and that these delegates enjoy the same career prospects and training opportunities as other employees.

Management and the employee representative bodies jointly and freely decide the common measures to be taken to guarantee the development of a progressive, high quality industrial relations policy by maintaining ongoing and constructive labor-management dialogue.

The company complies with the fundamental conventions of the International Labor Organization on 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 abolition of child labor.

2.2.7 Health and safety



The Company has a Health, Safety and Environment department comprising three people. This department also relies on 16 individuals with occupational first aid training in the various departments of the Company. Individual and collective safety equipment has been installed and is inspected regularly. Evacuation drills are held according to a predetermined schedule. Fire safety equipment and electrical systems are inspected annually by certified organizations.

Since November 2016, the missions of the health, safety and working conditions committee have been assigned to the single employee representative body.

Quarterly meetings are held, which are attended by the Health and Safety department.

A workplace accident means any accident that is suffered due to or during work by any person who is a company employee or who is performing work for the company. Workplace accidents also include commuting accidents that occur in the course of ordinary travel by an employee between their home and workplace (round trip).

The Company registered 46 accidents during the year. In relation to the average workforce in 2018, the rate of workplace accidents per employee is 0.36 compared with 0.40 the previous year, remaining at a rate that is considered as low. Four of these accidents resulted in medical leave of maximum one week, compared with 3 days in 2017 for a maximal duration of 8 days, compared to 7 in 2017.

The frequency rate in 2018 was 21.56 and the 2018 severity rate was 0.09.

	12/31/2018	12/31/2017
Frequency rate	21.56	16.22
Severity rate	0.09	0.08

No occupational or work-related illness was reported in 2018 or during the previous three fiscal years. An occupational illness means an illness due to a person’s exposure to a risk in connection with his/her employment position. The company has not been informed of any permanent disability in this fiscal year or prior fiscal years.

The Company provides a medical examination for all of its workers, with different frequencies depending on the nature of the position: laboratory staff are examined at least once every two years; administrative staff have a medical visit at least once every five years.

To date, no agreement on occupational health and safety has been signed with the labor unions or employee representatives.

2.2.8 Training

Staff members have extensive training and the company places particular importance on maintaining each employee’s knowledge and expertise at a high level. Continuing education is primarily focused on scientific and



technical training to develop the skills of laboratory staff (researchers and laboratory technicians) but it can also involve all staff on topics such as management, communication in English, the use of computer software, accounting and human resources training, training for new tools and materials, or regulatory monitoring. Each year, employees also receive general training targeting all staff around a theme whose underlying focus has been the same for several years: "better self-knowledge, better knowledge of others."

A total of 1,344.50 hours of training were dispensed in 2018.

<i>Number of employees trained in 2018</i>	<b>Men</b>	<b>Women</b>	<b>Total</b>
Executives	31	26	<b>57</b>
Non executives	17	23	<b>40</b>
<b>Total workforce</b>	<b>48</b>	<b>49</b>	<b>97</b>
Breakdown by gender (in %)	49	51	

<i>Personnel in the Company as of 12/31/2018</i>	<b>Men</b>	<b>Women</b>	<b>Average number</b>
Average number of training actions taken per employee in 2018	1.54	1.11	<b>1.33</b>
Average number of training hours per employee in 2018	11.67	7.76	<b>9.72</b>

To develop individual skills and maintain a high level of expertise, the company also encourages all researchers to attend international conferences and seminars. In 2018, Adocia participated in 43 conferences and scientific seminars (involving 68 participants).

## 2.2.9 Workplace equality

### 2.2.9.1 Measures taken to support gender equality

After consultation with the Single Employee Representative Body in December 2013, an action plan took effect on January 1, 2014, in accordance with Article L. 2242-5-1 of the French Labor Code and Decree no. 2011-822 of July 7, 2011 on the implementation of companies' gender equality obligations (Articles R. 2242-2 to R. 2242-8 of the French Labor Code).

This plan focuses primarily on three points:

- Workforce: The Company will continue to hire its employees on the basis of objective expertise criteria and individual merit, keeping in mind gender equality.
- Training: The Company will ensure that training, whether to develop each employee's business skills or to enable them to adapt to changes in the company, is accessible to and equal for both men and women.
- Compensation: The Company will continue its policy of compensating men and women equally.

The Company seeks to ensure that there is no discrimination in employment and career, via annual performance and skill reviews.

At December 31, 2018, the breakdown of men and women in the workforce was perfectly balanced, with 63 women and 69 men.

### 2.2.9.2 Measures taken to support employment and integration of workers with disabilities

To promote the recruitment of workers with disabilities, the company has taken steps to such workers, in particular holding meetings with CAP Emploi, the French national placement network for people with disabilities. Despite these actions and the fact that all positions are open to people with disabilities, the company has received few

applicants (an issue of skills not matching the position profile). At the end of December 2018, the Company had one employee in its workforce recognized as having disabled worker status.

The Company utilizes supported employment agencies for workers with disabilities (ESAT) for its supply of stationery, maintenance and cleaning of green spaces, and also began outsourcing its paper recycling to a company in the supported employment sector in 2017.

## 2.3 Environmental data

### 2.3.1 General environmental policy required by Article R225-105-1 of the French Code of Commerce

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In light of its business (drug research and development) and its geographical location (laboratories located at a single site in Lyon), the Company considers that its environmental impact is low. No provisions or guarantees for environmental risks have been recognized to date. Its activities do not include industrial production or distribution, or significant discharges of effluents into the environment. Its activities do not require the use of the ground as a resource and employ few raw materials.

On February 21, 2016, the Company acquired the building located at 115, avenue Lacassagne, Lyon, in which its laboratories and offices are located. The building has a total surface area of 6,874 m<sup>2</sup> (excluding the basement) of which 1,602 m<sup>2</sup> is occupied by three companies to which Adocia has granted commercial leases.

On June 28, 2017, the Company completed its installation on the site with the purchase of a storage building with delivery bay, with a total surface area of 2,092 m<sup>2</sup>, of which 1,650 m<sup>2</sup> underground. Following this acquisition, the Company converted the former courtyard into a garden.

In 2018, the Company initiated the development of two floors of 450 m<sup>2</sup> each, previously unoccupied. One will be destined for offices and the other for laboratories for the Analysis Department. The works are carried out with a view to improving energy consumption with an interior insulation made with 45 cm of hemp, new exterior joinery and lighting provided by LED luminaires.

The following factors are not discussed in this report because they were deemed irrelevant or because the Company does not have significant information in light of the quantities and interests at stake:

- Greenhouse gas emissions
- Adaptation to climate change
- Biodiversity
- Ground use
- Visual environmental impact of the business

The two employees based in the subsidiary Adocia Inc. have a low environmental impact due to their activity, limited to business travel. These two employees are excluded permanently from environmental indicators.

Despite the Company's low environmental impact, from the outset, it has focused on environmental protection and appointed two individuals to manage environmental aspects, one of whom, the HSQE manager, is a member of senior management.

The Company has made the treatment and recycling of chemical substances one of its priorities.

## 2.3.2 Pollution and waste management

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The Company purchases chemicals that are used in research and development operations. However, given the Company's size, only limited quantities of chemicals are handled, all of which are carefully monitored. The traceability of chemicals is strictly ensured from the time they arrive (a register kept by each department tracks raw materials). After their use in research operations, waste is recovered and stored under specific conditions until it is collected by a specialized company.

The Company has no regulatory obligation to monitor solvents used or emissions of volatile organic compounds (VOC) for effluents linked to the use of volatile solvents used with extractors. The Company has appointed a service provider that specializes in removing and recycling chemical waste. Before collection, which takes place at least once per month, the Company stores its waste in appropriate containers in dedicated premises and in compliance with the relevant safety standards.

In 2018, the quantity of hazardous laboratory waste sent to a specific center (soiled packaging and glass, chemical waste) totaled 33.9 metric tons. The Company considers that the quantity of waste that it discharges into the city of Lyon's wastewater treatment system is low, as most waste is recovered during handling. The Company emits no liquid effluent in wastewater.

Furthermore, the Company has initiated the following recycling actions:

- sorting of plastics and caps
- sorting of paper and cardboard
- sorting of ink cartridges
- sorting of coffee pods
- recycling of vials, and
- sorting of batteries.

In 2018, the quantity of paper and cardboard removed totaled approximately 5.554 metric tons. Sorting and packaging is undertaken by the company ELISE for recycling in the paper industry, which generated in average 104 hours of work for employees with disabilities in 2018.

The resources devoted to waste management issues are of two types:

- external resources, comprising purchases of specific containers and expenses associated with services subcontracted to waste specialists, amounting to €48 thousand in 2018;
- internal resources, consisting of involving all employees in sorting waste and reducing energy consumption.

Training is regularly provided, in particular at the time employees are hired. Each new employee receives onboarding during which the Safety/Environment Department provides information on environmental practices that are implemented. During this training, employees are provided with a waste management procedure.

The Company has set up a shared space that includes refrigerators for meals. This favors meal brought from home rather than the establishment of a catering service, to limit food waste.

Since 2016, under the impetus of the employee representative body (DUP), the Company installed a composter for the organic waste employees create during their lunchtime meals. This initiative was carried out with the help of a local firm.

In terms of noise pollution, only the laboratories' fume chamber extractors are potential sources of noise. This equipment, which is installed on the roof, is fitted with a soundproofing casing. Accordingly, the Company deems that it has minimized the risk of noise pollution.

### 2.3.3 Sustainable use of resources

The Company is attentive to management of its water and energy consumption.

#### 2.3.3.1 Water

The company’s consumption of municipal water is mainly for sanitary purposes.

The Company also uses water for its research activities, and in particular for cleaning its laboratory equipment. Water is thus used to supply the washing machines and sinks installed in the various laboratories and shared spaces in the Company. It is discharged after use in conventional drainage systems. For some of its activities, the Company also consumes water for the production of distilled water.

Until 2015, the Company purchased bottled water for the staff to drink. Since 2016, to reduce its environmental impact, drinking fountains are available in the lobby, considerably reducing the use of water bottles and hence plastic waste. As a result, the quantities purchased are negligible and are no longer monitored. Running water consumption is calculated from actual consumption based on invoices. Lastly, certain research operations require purified water, which the Company purchases in canisters.

<i>Consumption in M<sup>3</sup></i>	<b>12/31/2018</b>	<b>12/31/2017</b>
Bottled water	NS	NS
Distilled water	12	12
Current consumption water (*)	2 919	3 486
<b>Water total</b>	<b>2 931</b>	<b>3 498</b>

(\*) prorated to the surface occupied by the Company

The significant decrease in the consumption of running water is the result of various actions undertaken in 2018 to identify high-consumption appliances and limit their use.

#### 2.3.3.2 Electricity and natural gas

With respect to energy, the Company consumes electricity only.

Electrical invoices received are for the entire building. In the absence of individual meters for each of the tenants, the company estimated its own consumption according to the occupied surface area:

<i>Consumption in KWh</i>	<b>12/31/2018</b>	<b>12/31/2017</b>
<b>Electricity total (*)</b>	<b>1 275 467</b>	<b>1 360 363</b>

(\*) prorated to the surface occupied by the Company

The decreased consumption is due to improved practices despite a level of activity that remains stable. Gas consumption is negligible.

The Company has set up a consumption monitoring program and, at the end of each day, has a person check and turn off electrical equipment that has been left on and adjust the temperature of heating and cooling systems. Motion detectors that automatically turn off lights have been installed in some locations. The Company has also adopted and is gradually implementing a plan to replace older light bulbs with new generation low consumption bulbs.



### 2.3.3.3 Climate change

According to an initial analysis, the Company's production of greenhouse gas emissions is primarily from its purchasing of raw materials and consumables. In 2018, the Company received from its provider its emissions related to business travel (607 metric tons of CO<sup>2</sup>).

Given the elements above, the Company's impacts were judged too minimal to justify recognition of provisions or guarantees for environmental risks.

## 2.4 Social data: information on social responsibility in favor of sustainable development

### 2.4.1 Territorial, economic and social impact of business

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Because of its activity (drug research and development), the Company considers that its environmental impact is low. The activities of the Company generate no particular noise or visual pollution for its employees or for neighboring residents.

Adocia has been based in Lyon since its creation and endeavors to be active and involved in its local area. In 13 years, the company hired over 130 people, most of them are coming from the Lyon area. The company's ongoing policy is to recruit and train young people. Each year, the company accepts workers under apprenticeship or work-training contracts (8 at the end of December 2018) and a certain number of trainees (10 during 2018). The Company is therefore attractive to and offers professional prospects for scientists, researchers and technicians in the life sciences.

In 2018, the Company's payroll expenses and social security contributions accounted for nearly 30.1% of the operating expenses.

The company maintains close ties with education institutions. In this regard, it is sponsoring the 135th graduating class of ESPCI Paris Tech in order to create and maintain multiple contacts with students during their four-year course of study, i.e. till 2020.

### 2.4.2 Relations with its shareholders and investors

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The Company's financial communication is intended to guarantee access to complete, transparent and clear information for all. To this end, the Company publishes a number of documents for its shareholders to explain its strategy, research being conducted, and the results obtained.

These documents are accessible on the Company's website in the Investors section, in French and in English. An email address ([contactinvestisseurs@adocia.com](mailto:contactinvestisseurs@adocia.com)) is also available for investors.

The Company also complies with its obligations as a listed company. It disseminates annual information supplemented by periodic information and press releases to the financial community and more generally to the public. It also organizes regular telephone conferences to comment on its results and answer questions from shareholders.

In 2018, the Company participated in the Actionaria trade show, which took place in Paris last November, and in the Biotech conference last June to meet individual shareholders. It has also participated in multiple investor salons in France, Europe and the United States, to meet institutional investors.

## 2.4.3 Subcontracting and suppliers

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The Company appoints external suppliers to perform a significant portion of its activities, in particular, activities that require specific accreditations (Good Laboratory or Manufacturing Practices), particular facilities (animal housing unit) or organizations specialized in conducting clinical trials, known as contract research organizations (CROs). These external expenses account for 22% in average of the Company's total expenses.

The supplier selection process complies with pharmaceutical regulations and takes into account criteria such as proximity, excellence and research ethics. Due to its size and the corresponding social and environmental stakes, the Company does not audit its suppliers on CSR issues.

At the local level, the Company has created partnerships with the Lyon Veterinary School and Namsa for conducting its preclinical studies. The main service provider, Namsa, as well as ICB (dependent on the veterinary school of Lyon) are AAALAC accredited.

These two organizations comply with ethics legislation and have an animal welfare structure, an independent ethics committee and socialization and enrichment programs for the two models used by the company (dog and pig). They also have programs for animal outplacement to comply with the 3Rs rule when study conditions permit.

The Company also uses the services of numerous consulting firms in the region (patents, finance, lawyers).

## 2.4.4 Fair practices

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The Company has set up mechanisms to prevent risks of corruption. Separating tasks associated with payments is one of the means put in place for avoiding possible errors or misappropriation.

Concerning the choice of suppliers, comparative bids are requested above a certain expenditure threshold. As part of its research and development activities, the company is obliged to comply with current standards (Good Laboratory Practice, Good Manufacturing Practice), as well as with the regulations adopted by public health protection agencies, such as the European Medicines Agency (EMA) and the Food and Drug Administration (FDA) in the United States.

The Company has been listed on the regulated Euronext stock exchange in Paris since February 2012. Accordingly, purchases and sales of securities and, in particular, bonus shares and business founders' stock warrants (BSPCE), are subject to strict rules.

Adocia has adopted a corporate disclosure policy and a code of ethics, which are in compliance with AMF recommendation no. 2010-07 of November 3, 2010, as well as the MiddleNext guide, which set forth and explain the rules applicable to privileged information and the duties owed by insiders.

## 2.4.5 Public health issues

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Health and consumer safety is at the core of the Company's business: developing innovative medicines for everyone, all over the world.

The Company develops drugs based on therapeutic molecules that have already been approved. Using its proprietary BioChaperone technology, it improves the effectiveness of such molecules, thereby simplifying and expanding their therapeutic use, while improving patients' quality of life.

In a worldwide pharmacological and economic context marked by the adoption of policies designed to control health costs, the products that Adocia develops may improve the effectiveness of therapeutic molecules, while reducing the dosage, number of applications and/or duration of treatment.

Lastly, despite the fact that the demand for pharmaceutical products in emerging countries is expanding, access to healthcare and drugs remains problematic, even critical, in certain countries. The World Health Organization

estimates that over 80% of the deaths due to chronic pathologies occur in low- or medium-income countries. By offering pharmaceutical products destined to become best-in-class and at lower prices than existing products, Adocia's strategy seems particularly suited to meet the mass needs of these emerging countries.

Given the stage of development of its entire project portfolio, no drug containing BioChaperone technology developed by the Company has been marketed to date.

The development of the Company's projects is strictly regulated. Thus, for studies using animal models (preclinical development) and studies using human participants (clinical development), it submits its dossiers to various approval committees: regulatory affairs authorities (e.g. Bfarm for clinical studies in Germany) and ethics committees.

## 2.4.6 Actions taken to promote human rights

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The Company endeavors to comply with prevailing regulations and is not aware of any specific issues in this regard.

The information concerning labor issues required by Article R. 225-105-1 of the French Commercial Code is provided in sections 2.2 and 2.3 of this registration document.



3  
CORPORATE  
GOVERNANCE





## Chapter 3

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## 3 CORPORATE GOVERNANCE

### 3.1 Governing, management, supervisory and executive management bodies

#### 3.1.1 Methods of corporate governance

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Until October 24, 2011, the Company was incorporated as a *société par actions simplifiée* (simplified joint stock company). At the time of its initial public offering, the Company was converted, on October 24, 2011, into a *société anonyme* (corporation) with a Board of Directors, and adopted new governance rules. Shareholders appointed a six-member Board of Directors, five of whom had been members of the Board of Directors of the Company in its previous form as a *société par actions simplifiée*.

The Board of Directors, at its meeting of October 24, 2011, adopted its own Rules of Procedure which specify, *inter alia*, the role and composition of the Board, the principles of conduct and the obligations of members of the Company's Board of Directors, and the operating procedures of the Board of Directors and its committees, as well as the rules for determining the compensation received by their members. The Board's Rules of Procedure can be accessed on the Company's website ([www.adocia.fr](http://www.adocia.fr)).

To structure its governance, the Company has chosen to refer to the corporate governance code for small and midcaps as published in September 2016 by MiddleNext (the "MiddleNext Code").

At its meeting of March 7, 2017, the Board of Directors familiarized itself with the Code's keys points to be monitored and undertook to review them on a regular basis, in line with recommendation no. 19. This review was made by the Board at its meeting held on March 11<sup>th</sup>, 2019.

The Board has put in place a program to achieve gradual compliance with the MiddleNext Code recommendations, and to that effect amended the Board's Rules of Procedure at its meeting of March 7, 2017.

On October 24, 2011, the Board of Directors decided to appoint Mr. Gérard Soula as Chairman of the Board of Directors and Chief Executive Officer. As Chairman, he is responsible for organizing and directing the work of the Board of Directors, reporting on this to the Shareholders' Meeting, and for ensuring the proper functioning of the Company's bodies. As Chief Executive Officer, he is responsible for the executive management of the Company, represents the Company in its relations with third parties, and has the powers granted to him by law to act in all circumstances on the Company's behalf.

On December 19, 2012, the Board of Directors decided to appoint Mr. Olivier Soula as Deputy General Manager. The Deputy General Manager has the same powers as the Chief Executive Officer with regard to third parties.

A brief description of the main provisions of the Company's Articles of Incorporation and Bylaws and its Rules of Procedure governing its specialized committees is provided in this registration document, in section 5.3 'Articles of Incorporation' and section 3.1.5 'Operation of the governing and management bodies' .

#### 3.1.2 Members of the Board of Directors

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As of the filing date of this reference document, the members of the Company's Board of Directors are:

Name	Office	Main functions within the Company	Main functions outside the Company	Starting and ending dates of terms of office
<b>Mr. Gérard Soula</b>	Chairman of the board of directors	Chairman and chief executive officer	None	Appointed director by the shareholders' meeting held on October 24, 2011.
				Renewed by the combined shareholders' meeting of June 27, 2017 for a term of three years which will expire at the conclusion of the shareholders' meeting convened to vote on the financial statements for the fiscal year ending December 31, 2019.
				Renewed as chairman and chief executive officer by the board of directors' meeting held on June 27, 2017 for the duration of his term of office as director.
<b>Mr. Olivier Soula</b>	Deputy chief executive officer, Director	R&D Director VP	None	Appointed director by the shareholders' meeting held on October 24, 2011.
				Renewed by the combined shareholders' meeting of June 27, 2017 for a term of two years which will expire at the conclusion of the shareholders' meeting convened to vote on the financial statements for the fiscal year ending December 31, 2018.
				Renewed as deputy chief executive officer by the board of directors' meeting held on June 27, 2017 for the duration of his term of office as director.
<b>Mr. Olivier Martinez</b>	Director	Member of the audit committee	Investment Manager, Bpifrance Investissement	Appointed director by the shareholders' meeting held on October 24, 2011.
				Renewed by the combined shareholders' meeting of June 27, 2017 for a term of two years which will expire at the conclusion of the shareholders' meeting convened to vote on the financial statements for the fiscal year ending December 31, 2018.
<b>BPI France Investissement, represented by Mr. Laurent Arthaud</b>	Director	President of the remuneration committee	Deputy Chief Executive Officer, Bpifrance Investissement	Appointed director by the shareholders' meeting held on October 24, 2011.
				Renewed by the combined shareholders' meeting of June 27, 2017 for a term of three years which will expire at the conclusion of the shareholders' meeting convened to vote on the financial statements for the fiscal year ending December 31, 2019.
<b>Ms. Dominique Takizawa</b>	Director (*)	President of the audit committee	Secretary General, Institut Mérieux	Appointed director by the shareholders' meeting held on October 24, 2011.
				Renewed by the combined shareholders' meeting of June 27, 2017 for a term of three years which will expire at the conclusion of the shareholders' meeting convened to vote on the financial statements for the fiscal year ending December 31, 2019.
<b>Ms. Ekaterina Smirnyagina</b>	Director (*)	Member of the remuneration committee	Investment Director, Capricorn Venture Partners	Appointed director by the shareholders' meeting held on June 18, 2013.
				Renewed by the shareholders' meeting of June 21, 2016 for a term of three years which will expire at the conclusion of the shareholders' meeting convened to vote on the financial statements for the fiscal year ending December 31, 2018.

\* Independent board member

### 3.1.2.1 Business address

The business address of the Chairman and Chief Executive Officer and of the Deputy General Manager is the address of Company's registered office.

The business addresses of the other directors are:

- Mr. Olivier Martinez, c/o Bpifrance Investissement, 6-8 Boulevard Haussmann, 75009 Paris;
- Mr. Laurent Arthaud, c/o Bpifrance Investissement, 6-8 boulevard Hausman, 75009 Paris;
- Ms. Dominique Takizawa, c/o Institut Mérieux, 17 rue Bourgelat, 69002 Lyon ;
- Ms. Ekaterina Smirnyagina, c/o Capricorn Venture Partners, De Jonge Saint Jacob, Lei 19/1-B-3000 Leuven, Belgium.

## 3

### 3.1.2.2 Gender balance

Two of the Board's six members are women, which is consistent with the Law of January 27, 2011 on the gender balance on boards, as the difference in terms of the number of male and female board members is not greater than two.

### 3.1.2.3 Independent directors

In accordance with its Rules of Procedure, the Board of Directors has decided to apply the definition of independence proposed in the MiddleNext Code's recommendation no. 3 "Composition of the Board", which requires satisfaction of the following five criteria:

- the director is not an employee or executive corporate officer of the Company, nor an employee or executive corporate officer of a company in its group, and must not have held such a position within the last five years;
- the director is not, and must not have been within the last two years, in a significant business relationship with the Company or its group (client, supplier, competitor, service provider, creditor, banker, etc.);
- the director is not a reference shareholder of the Company and does not hold a significant percentage of its voting rights;
- the director does not have close family ties with a corporate officer or reference shareholder of the Company; and
- the director has not been an auditor of the Company within the last six years.

At its meeting of March 11, 2019, the Board of Directors confirmed that two of its members met all the above criteria, namely Ms. Dominique Takizawa and Ms. Ekaterina Smirnyagina. Every year, the Board of Directors reviews the position of each of its members in light of the above criteria.

### 3.1.2.4 Term of office

Members of the Board of Directors are appointed by an Ordinary General Shareholders' Meeting for a three-year term of office. In line with recommendation no.9 of the MiddleNext Code a first staggered renewal of the directors was carried out last year following the resolutions adopted by the General Meeting held in June 2017.

### 3.1.2.5 Rules of Conduct

The Rules of Procedure, the Code of Conduct and the Financial Reporting Charter have been approved by the Board of Directors. These documents set out the rules to be followed by Board members, in line with recommendation no. 1 of the MiddleNext Code.

### 3.1.2.6 Choice of Directors

When a Director is appointed or reappointed, information on his or her experience, skills and offices held is published in the reference document and presented to the Shareholders' Meeting. This information is also published on the Company website, in line with recommendation no. 8 of the MiddleNext Code. A separate resolution is put to the shareholders for the appointment or reappointment of each individual Director. These persons have gained expertise and management experience in the various salaried and management positions they have previously held (see section 3.1.4 "Biographies of the directors").

There are no family ties between the persons listed above, except in the case of Messrs. Gérard Soula and Olivier Soula, who are both members of the Board of Directors.

Furthermore, to the best of the Company's knowledge as of the date of this reference document, no member of the Board of Directors:

- Has been convicted of fraud during the past five years;
- Has been associated in his/her capacity as corporate officer or director with any bankruptcy, receivership or liquidation during the past five years;
- Has been publicly and officially accused or penalized by any statutory or regulatory authority during the past five years.

Lastly, to the best of the Company's knowledge as of the date of this reference document, no member of the Board of Directors has been deprived of the right to hold a seat on a governance, management or supervisory body of an issuer or to take part in the management or running of an issuer during the past five years.

There are no service contracts between the members of the Company's Board of Directors or officers and the Company.

### 3.1.3 Other corporate offices

#### 3.1.3.1 Other corporate offices currently held by the directors

Name	Office held	Company
<b>Mr. Gérard Soula</b>	Director	Glowbl
<b>Mr. Olivier Soula</b>	Chairman of the board of directors	Glowbl
<b>Mr. Olivier Martinez</b>	Permanent representative of Bpifrance Investissement Board observer	POXEL
	Permanent representative of Bpifrance Investissement Director	HalioDx
	Board observer	Innate Pharma
	Board observer	Cerenis Therapeutics
<b>Mr. Laurent Arthaud</b>	Member of the supervisory board	Kurma Partners
	Director	Collectis SA
	Chairman of the board of directors	Sparingvision SA
	Director	Aledia SA
	Director	Calyxt Inc.
	Director	Ribogenics Inc.
<b>Ms. Dominique Takizawa</b>	Director, permanent representative and member of the audit committee	Transgène (*)
	Director and chair of the audit committee	Mérieux Nutrisciences (USA) (*)
	Director, chair of the audit committee and member of the investment committee	April Group
	Director and member of the audit committee	ABL Inc. (USA) (*)
	Representative director and President	ElsaLys (*)
	Director and vice-chairman	Lyon Place Financière
	Director	Lyon Pôle Bourse
	Director and member of the audit committee	Theradiag
<b>Ms. Ekaterina Smirnyagina</b>	Employee director	Institut Mérieux
	Director	Istar Medical SA (Belgique)
	Director	ConfoTherapeutics NV (Belgique)
	Director	InvestEurope (Belgique)
	Director	HalioDx (France)

(\*) Institut Mérieux group

In line with recommendation no. 1 of the MiddleNext Code, executive directors do not hold more than two other offices, including in foreign companies.

### 3.1.3.2 Other corporate offices, now expired, held by the directors during the last five fiscal years

Name	Office held	Company
<b>Mr. Gérard Soula</b>	Director	Life Cycle Pharma A/S
	Director	Cerenis Therapeutics
<b>Mr. Olivier Martinez</b>	Permanent representative of Bpifrance Investissement, Director	Alize Pharma
	Permanent representative of Bpifrance Investissement, Director	Poxel
	Permanent representative of Bpifrance Investissement, Member of the supervisory board	Genticel
	Permanent representative of Bpifrance Investissement, Member of the executive committee	Fab Pharma
	Member of the supervisory board	Cytheris
<b>Mr. Laurent Arthaud</b>	Board observer	Millendo Therapeutics Inc.
	Director	Scynexis Inc.
	Member of the supervisory board	Emertec gestion SA
<b>Ms. Ekaterina Smirnyagina</b>	Board observer	TxCell
	Director	Nexstim plc (FINLANDE)

### 3.1.4 Biographies of the directors

**Gérard Soula** PhD, 74 years old, holds a doctorate in organic chemistry and is a graduate of IAE (Aix Marseille).

He founded Flamel Technologies (1990), a company listed on NASDAQ that specializes in drug delivery. He held the positions of chairman and chief executive officer and research director in the Company until June 2005. When he left Flamel Technologies, the Company employed 250 persons and had a market valuation of \$500 million. Flamel Technologies' success was largely due to the performances of its Micropump and Medusa platforms.

Gérard Soula has lengthy experience in negotiating licensing agreements for technological innovations with major biopharmaceutical groups (Novo Nordisk, Bristol Myers Squibb, GlaxoSmithKline, etc.).

**Olivier Soula** PhD, 49 years old, holds a doctorate in polymer physical chemistry, and is a graduate of ENSIC Mulhouse. He also obtained an MBA from IAE in Lyon.

He began his career with Flamel Technologies, where he stayed for eight years and was *inter alia* nanotechnologies research manager. He directed the development of Medusa, a therapeutic protein sustained release platform, and successfully conducted clinical studies for three such projects. He is co-holder of nearly 40 patents.

**Olivier Martinez**, 48 years old, Senior Investment Director within the Innovation Division of Investment Bpifrance.

Olivier Martinez started his career with CapGemini Consulting where he worked on transformation projects in the pharmaceutical and health sectors. In 2000, he joined Bioam, a management company that invests in life science start-ups, as project manager; he was subsequently appointed investment manager and member of the management board. In 2010, Bioam was taken over by Bpifrance Investissement (previously known as CDC Entreprises). At Bpifrance, Olivier is in charge of investments in companies in the life sciences sector (start-ups, venture capital, listed companies). Olivier is an alumnus of the Ecole Normale Supérieure (Ulm) in Paris, holds a PhD in Cell Biology from the University of Paris XI, and an MBA from College des Ingénieurs.

**Laurent Arthaud**, 56 years old, is a graduate of the Ecole Polytechnique and the National Statistics and Economic Administration School (ENSAE).

He started his career in 1986 with INSEE, and then joined the economic forecasts division of the Economy and Finance Ministry. In 1993, he was appointed technical advisor to the Labor Ministry and, in 1995, technical advisor to Prime Minister Alain Juppé, in charge of employment issues. He created the system of personal services vouchers (*chèque emploi service*). In 1997, Laurent Arthaud joined Rhône-Poulenc as secretary general of the group's scientific division, in charge *inter alia* of external collaborations. In 1999, he created Aventis Capital within the Aventis group, the group's venture capital structure, and then created the Genavent venture capital fund in partnership with Société Générale. In 2004, Laurent Arthaud became the chairman of PharmaVent Partners, a newly created venture capital fund management company. In 2006, he joined CDC Entreprises as deputy chief executive officer for new developments. In 2009, he took over all CDC Entreprises life sciences activities and the InnoBio investment fund. He is currently in charge of Bpifrance's investments in life sciences, environmentally friendly technologies and French Tech.

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**Dominique Takizawa**, 62 years old, has held the office of Secretary General of Institut Mérieux since 2006. She joined Merieux Group in 2001 and has been involved in its strategic development, especially in merger and acquisition transactions and relationships with other shareholders and investors. She also managed the IPO of bioMérieux. Previously, she was the Chief Financial Officer of a number of companies: Pasteur Merieux Connaught (since renamed Sanofi Pasteur), Rhône Merieux/Mérial etc.

Dominique Takizawa is a graduate of the HEC Business School and holds a degree in Accounting and Financial Studies (DECF).

**Ekaterina Smirnyagina**, 52 years old, holds a doctorate in cellular and molecular biology.

After having completed her training by obtaining a master's degree in biochemistry and attending Stanford Medical School, she began her career with the Biotechnology Business Development Council. She then worked for Alta Partners, an investment fund company in San Francisco that specializes in the health field, from 2002 to 2012. Since then, she has held the position of manager with the Capricorn Venture Partners investment fund in Belgium.

### 3.1.5 Operation of the governing and management bodies

#### 3.1.5.1 Conditions for the preparation and organization of the work of the Board

The Board of Directors has its own Rules of Procedure, in line with the MiddleNext Code's recommendation no. 7. This document was approved by the Board of Directors at its meeting of October 24, 2011 and amended by the Board of Directors at its meeting of March 7, 2017. It is available on the Company's website.

In line with recommendation no. 2, the article of the Rules of Procedure on the prevention of conflicts of interest entitled "Disclosure Obligation" requires Directors to inform the other Board members whenever they are in a conflict-of-interest situation, so that it can be ascertained whether the Director should refrain from voting and/or may take part in deliberations.

In addition, the Rules of Procedure explain the regulations in force concerning the disclosure and use of privileged information, and state that the directors must refrain from carrying out transactions in the Company's shares if they hold privileged information. Each Board of Directors member is required to report to the Company and to the AMF any transactions in the Company's shares that they carry out directly or indirectly.

Prior to each meeting of the Board of Directors, and in accordance with the Rules of Procedure, the agenda for the meeting and the preparatory documents are sent to the Board members in a timely manner, informing them of the agenda and the matters which the Board will be asked to consider. In line with recommendation no. 4 of the MiddleNext Code, Directors will regularly receive key information concerning the Company that may have an impact on its commitments and financial situation, outside of scheduled Board meetings and whenever justified by events



affecting the Company. They may request explanations or additional information and, more generally, request access to any information they consider relevant.

### 3.1.5.2 Operation of the Board of Directors

The Board of Directors operates (notices of meetings, meetings, quorum, information for Directors) in compliance with the applicable laws and the Company's Articles of Incorporation and Bylaws, as set out in its Rules of Procedure.

The Board of Directors is responsible for determining the Company's business strategy and overseeing its implementation. Subject to the powers expressly granted to shareholders' meetings and within the limit of the corporate purpose, it considers all issues relating to the Company's operations and makes decisions on matters affecting the Company. It also appoints the Chairman of the Board, the Chief Executive Officer and the Deputy General Managers, and determines their compensation. Its duties also include closing of the financial statements and consolidated financial statements, convening shareholders' meetings, and determining the agenda of any meeting and the wording of the resolutions. Lastly, it carries out those checks and controls it considers appropriate and authorizes agreements falling within the scope of Article L. 225-38 *et seq.* of the French Commercial Code (*Code de commerce*).

During the past fiscal year, the Company's Board of Directors held nine meetings (in line with recommendation no. 5 of the MiddleNext Code), on February 8, March 5, March 17, July 18, September 25 and December 5, 2018. The Chairman of the Board chaired all 6 meetings, and the attendance rate was 97%.

The following main points were addressed at the meetings:

- Updates on Company financing;
- Advisability of raising capital;
- Arbitration against Eli Lilly;
- Current negotiations with potential partners;
- Progress reports on projects and main results;
- Renovation of the building
- Financial matters: quarterly reviews, 2019-2021 three-year plan, examination and closure of 2017 corporate financial statements and consolidated financial statements, presentation and approval of 2019 budget;
- Matters relating to compensation: Approval of compensation for the fiscal year, award of BSPCE founders' warrants, award of bonus shares, award of stock options, record of acquisition of vested bonus shares, determination of directors' fees;
- Convocation of the General Shareholders' Meeting: agenda and wording of resolutions.

In line with recommendation no. 14 of the MiddleNext Code, most of these matters are dealt with at Board meetings. However, the possibility of the Company CEO suffering an accident, or his sudden unavailability and the related issues were not discussed during fiscal year 2018, and will be put on the agenda of a forthcoming Board meeting.

Documents were sent to the directors prior to each meeting, to enable them to prepare for the meeting. Minutes are drawn up summarizing the deliberations at each Board meeting.

In line with recommendation no. 11 of the MiddleNext Code, it is being precised that, in fiscal year 2017, the Board carried out a self-assessment of its composition, organization and operating procedures. A questionnaire was sent to the Board members, and the results were commented upon. No self-assment was done in 2018.

Lastly, recommendation no. 12 advises managers to give minority shareholders an opportunity to meet with them and discuss the Company's affairs during 2018. They were given this opportunity on two separate occasions: at the Agora Biotech on June 19, 2018, at the General Shareholders' Meetings held in Lyon on May 17, 2018, and on November 9, 2018 and at the Actionaria exhibition in November 2018.

### 3.1.5.3 Organization of committees

In line with recommendation no. 6 of the MiddleNext Code, the Board of Directors decided:

- to set up two specialized committees: the Audit Committee and the Compensation Committee
- that the Chairman of the audit Committee is entrusted to an independent director. If the Company were to appoint a new independent director to the Board of Directors, based on its specific expertise, it could appoint the Chairman of the Compensation Committee.

#### ▪ Audit Committee

The Board of Directors of the Company, in its previous form as a *société par actions*, set up an Audit Committee. The Board of Directors of the Company, in its new form as a *société anonyme*, decided at its meeting of October 24, 2011 to maintain the existing Audit Committee.

The Audit Committee, which is independent from the Company's executive management team, is responsible for assisting the Board of Directors and verifying the fairness of the financial statements, the quality of internal control, the relevance of the information provided and the proper performance by the auditors of their duties.

The Audit Committee is composed of at least two members appointed by the Board of Directors. The term of office of the Audit Committee members is concurrent with their term of office as members of the Board of Directors. Members of the Audit Committee are chosen from among the members of the Board of Directors and, to the extent possible, two-thirds are independent members, including one with specific financial or accounting expertise; all members have a minimum level of expertise in finance and accounting.

As of the date of this report, the members of the Audit Committee are:

- Ms. Dominique Takizawa, independent member with financial and accounting expertise, and
- Mr. Olivier Martinez, Director.

Ms. Dominique Takizawa chairs this committee. Ms. Takizawa is the member of the Board with "specific financial or accounting expertise," due to her nearly 25 years of experience in the pharmaceutical industry and the positions she held at Sanofi Pasteur, Biomérieux and Institut Mérieux as financial director and company secretary.

The Audit Committee met two times in 2018, on March 1<sup>st</sup> and on July 17, 2018.

The Audit Committee's duties include:

- monitoring the process for preparing financial information;
- ensuring the effectiveness of the internal control and risk management systems;
- ensuring that the statutory auditors perform their duties with respect to the legal certification of the annual financial statements and, if applicable, the consolidated financial statements;
- making recommendations on the statutory auditors proposed for appointment to general shareholders' meetings, and reviewing the terms of their compensation;
- ensuring the independence of the statutory auditors;
- examining the conditions under which derivatives are used;
- regularly reviewing the status of major disputes; and
- in general, providing advice and making appropriate recommendations in connection with the above matters.

The Audit Committee's rules of procedure, which were adopted on October 24, 2011 after having been approved by the Board of Directors, describe the duties of the Audit Committee and its operating procedures, in particular the minimum number of meetings per year. These rules of procedure also state that the committee may interview any member of the Company's Board of Directors and conduct any internal or external audits on any matter it deems

to come within the scope of its duties. If it does so, the Audit Committee chair must give prior notice to the Board of Directors. In particular, the Audit Committee may interview any person involved in preparing or verifying the financial statements (the Chief Financial Officer, the Administrative and Financial Manager and the principal financial managers). The committee has the right to directly, independently and confidentially consult with the statutory auditors.

### ▪ Compensation Committee

The Board of Directors of the Company, in its previous form as a *société par actions simplifiée*, set up a Compensation Committee in June 2008. The Board of Directors of the Company, in its new form as a *société anonyme*, decided at its meeting of October 24, 2011 to maintain the existing Committee.

The Compensation Committee is responsible *inter alia* for examining the compensation policy proposed by Executive Management for the Company's executive corporate officers and employees. It presents its recommendations and proposals concerning said (fixed, variable, and exceptional) compensation to the Board of Directors. It validates the targets set for the award of long-term incentives (bonus shares, BSPCE founders' warrants, stock options, and BSA stock warrants) and assesses performance at year-end.

The Compensation Committee is composed of at least two members appointed by the Board of Directors; no member of the Board of Directors serving in a management capacity within the Company may be a member of this committee. The term of office of each Compensation Committee member is concurrent with his/her term of office as a member of the Board of Directors.

As of the date of this report, the members of the Compensation Committee are:

- Ms. Ekaterina Smirnyagina, independent member, and
- Mr. Laurent Arthaud, director.

Mr. Laurent Arthaud chairs this committee.

The Committee met two times in 2018: on September 21<sup>st</sup> and November 27<sup>th</sup>, 2018.

The Compensation Committee's duties include:

- reviewing the main objectives proposed by executive management with respect to compensation of Company managers who are not corporate officers, including bonus share plans and stock subscription or purchase options;
- reviewing the compensation of Company managers who are not corporate officers, including bonus share plans and stock subscription or purchase options, retirement and insurance plans and non-cash benefits;
- submitting recommendations and proposals to the Board of Directors concerning:
  - the compensation, retirement and insurance plans, non-cash benefits, and other financial rights, including severance pay, of members of the Board of Directors. The committee proposes compensation amounts and structures, in particular the rules for calculating the variable component of compensation, taking into account the Company's strategies, objectives and performance, as well as market practices, and bonus share plans, stock subscription or purchase options, and any other similar incentive plan, in particular benefits granted to specific members of the Board of Directors;
- reviewing the total amount of directors' fees and the method for distributing them among the members of the Board of Directors, as well as the requirements for obtaining reimbursement of expenses that Board members may incur,
- preparing and submitting to the Board of Directors any reports that may be required by the Rules of Procedure; and
- preparing any other compensation-related recommendations that may be requested by the Board of Directors.

In general, the Compensation Committee provides advice and makes appropriate recommendations in connection with the above matters.

The Compensation Committee meets at least twice a year, in accordance with a schedule set by the chair, pursuant to an agenda prepared by its chair and sent to the Compensation Committee members at least seven days before the date of the meeting. The committee may also meet at the request of its chair, two of its members, or the Board of Directors.

Non-executive Board of Directors members, who are not Compensation Committee members may attend the committee's meetings without restriction.

The chairman of the Company's Board of Directors, if he is not a committee member, may be invited to attend committee meetings. The committee may request that the chairman submit proposals to it. The chairman is not entitled to vote and may not be present during discussions concerning his personal situation.

The Compensation Committee may request the chairman of the Board of Directors to provide it with the assistance of any senior manager of the Company whose expertise may facilitate dealing with a matter of business on the agenda. The Compensation Committee chair or the meeting chair informs all persons who attend meetings that they are bound by a duty of confidentiality.

The Compensation Committee chair ensures that the reports on its work that it presents to the Board of Directors provide complete information to the board, thus facilitating its decision-making process.

The annual report includes a presentation of the committee's work during the past fiscal year.

In particular, the Compensation Committee reviews the draft Company report on executive compensation.

### 3.1.6 Conflicts of interest at the level of the governing and management bodies

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The Chairman and the directors are direct or indirect shareholders of the Company (see Chapter 5.4 "Major Shareholders").

There are no related-party agreements.

To the Company's knowledge, none of the Company's directors or officers was appointed pursuant to any contract or agreement with shareholders, customers, suppliers or other parties.

To the Company's knowledge, as of the filing date of this reference document, none of the persons listed in section 3.1.2 "Members of the Board of Directors" of this reference document has agreed to any restriction on the disposal of their equity interest in the Company, other than the collective undertaking to keep their Company securities (known as a "Dutreil" agreement), concluded by Gérard Soula, Olivier Soula, Rémi Soula and Laure Soula pursuant to Article 787 B of the French Tax Code (*Code général des impôts*).

To the Company's knowledge, there is no actual or potential conflict of interest between the obligations towards the Company and the private interests and/or other obligations of the persons who are members of the Company's governance and management bodies or members of the executive management team, as listed in section 3.1.2 "Members of the Board of Directors" above.

### 3.1.7 Report by the Board of Directors on corporate governance

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As required by Article 222-9 I of the AMF's General Regulation, and in accordance with Article L. 225-37 of the French Commercial Code, this reference document includes the report by the Board of Directors on corporate governance, which *inter alia* contains information on the composition of the Board, the conditions under which the Board prepares and organizes its work, and the internal control and risk management procedures set up by the Company in connection with the preparation and processing of accounting and financial information.

In the course of its expansion, with respect to internal control, the Company follows the risk management and internal control systems implementation guide for small-caps and midcaps published by the AMF on July 22, 2010.

### 3.1.8 Information that is likely to have an impact in the event of a public offering

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#### 3.1.8.1 Shareholder structure of the Company

See Chapter 5 of this reference document.

#### 3.1.8.2 Restrictions imposed by the Articles of Incorporation and Bylaws on exercising voting rights and share transfers or similar clauses of which the Company is aware, as required by Article L. 233-11 of the French Commercial Code

None.

#### 3.1.8.3 Direct or indirect equity stakes in the Company of which the Company is aware, as required by Articles L. 233-7 and L. 233-12 of the French Commercial Code

See Chapter 5 of this reference document.

#### 3.1.8.4 List of holders of any securities with special control rights and a description of such rights

The Company is not aware of the existence of any special control rights.

#### 3.1.8.5 Control mechanisms included in any employee share plan in which the control rights are not exercised by the employees

The Company has not set up any employee share plan that may contain control mechanisms in which the control rights are not exercised by the employees.

#### 3.1.8.6 Shareholder agreements of which the Company is aware that may impose restrictions on share transfers and exercising voting rights

None.

#### 3.1.8.7 Rules governing the appointment and replacement of Board of Directors members and amendments to the Articles of Incorporation and Bylaws

The rules governing these matters are set out in the Articles of Incorporation and Bylaws and are in compliance with the law.

### 3.1.8.8 Powers of the Board of Directors, in particular the power to issue or redeem shares

The general shareholders' meeting held on May 17, 2017 renewed the authority granted to the Board of Directors to carry out, for a period of 18 months as of the date of the meeting, a share buy-back program, in accordance with the provisions of Article L. 225-209 *et seq.* of the French Commercial Code and market practices accepted by the AMF (see sections 5.4.1, 5.4.2 and 5.1.4 of this reference document).

### 3.1.8.9 Agreements entered into by the Company that will be amended or terminated in the event of a change of control of the Company

None.

### 3.1.8.10 Agreements that provide for compensation to members of the Board of Directors or employees if they resign or are terminated without just cause or if their employment ends due to a takeover bid

None.

## 3.1.9 Compliance to MiddleNext recommendations

The Company aims at progressively comply to every MiddleNext Code recommendation. The chart below lists these MiddleNext code recommendations and indicates whether the Company complies to them or not.

Recommendations of MiddleNext Code	Compliance
<b>Supervisory Control</b>	
R1 - Ethics of the Board members	Yes (3.1.2.5)
R2 - Conflicts of interest	Yes (3.1.5.1)
R3 - Board composition – Presence of independant members	Yes (3.1.2.3)
R4 - Communication to Board members	Yes (3.1.5.1)
R5 - Organization of Board and committees' meetings	Yes (3.1.5.2)
R6 - Implementation of committees	Yes (3.1.5.3)
R7 - Implementation of Board rules of procedures	Yes (3.1.5.1)
R8 - Selection of each Board member	Yes (3.1.2.6)
R9 - Board members duration of office	Yes (3.1.2.4)
R10 - Board members remuneration	Yes
R11 - Implementation of the assessment of the work of the Board	Yes (3.1.5.2)
R12 - Relationship with the shareholders	Yes (3.1.5.2)
<b>Executive</b>	
R13 - Definition and transparency of the executive directors' remuneration	Yes
R14 - Preparation of the executives' succession	Yes, although the scenario of the accident or sudden unavailability of the executive has not been addressed in 2018. It will be at the agenda of an upcoming Board meeting.
R15 - Employment contract and corporate office concurrency	Yes, given the size of the Company, its desire to attract and retain highly experienced staff and the specific expertise of each member of the Executive Board, the Board of Directors has authorized the accumulation of the employment contract Olivier Soula with his mandate as Deputy Chief Executive Officer

Recommendations of MiddleNext Code	Compliance
R16 - Severance pay	N/A, no severance pay planned
R17 - Supplementary pension plan	N/A, no supplementary pension plan in place
R18 - Stock-options and bonus shares	Yes
R19 - Review of the critical points	Yes (3.1.1)

## 3.2 Compensation and benefits received by officers and directors

### 3.2.1 Compensation paid to corporate officers

All tables referred to in MiddleNext Code.AMF Positions. Templates mentioned in appendix 2 of the AMF Recommendations n° 2014-14 are presented below.

#### 3.2.1.1 Breakdown of compensation, stock options and bonus shares granted to each corporate officer

<i>In € thousands IFRS</i>	FY 2018	FY 2017
<b>Gérard Soula</b> - Chairman and chief executive officer		
Compensation due in respect of the year	583 387	358 387
Value of the BSPCE founders' warrants granted during the year	none	289 406
Value of the bonus shares granted during the year	none	none
<b>TOTAL</b>	<b>583 387</b>	<b>647 793</b>

<i>In € thousands IFRS</i>	FY 2018	FY 2017
<b>Olivier Soula</b> - Deputy chief executive officer		
Compensation due in respect of the year	401 157	284 186
Value of the share subscription or purchase options granted during the year	none	289 406
Value of the bonus shares granted during the year	3 000	none
<b>TOTAL</b>	<b>404 157</b>	<b>573 592</b>

#### 3.2.1.2 Breakdown of compensation paid to each corporate officer

The tables below show the compensation owed to the executive corporate officers for the fiscal years ended December 31, 2017 and December 31, 2018, as well as the compensation such persons received during those same fiscal years.

<i>In € thousands IFRS</i>	FY 2018		FY 2017	
	Amounts owed (1)	Amounts paid (2)	Amounts owed (1)	Amounts paid (2)
<b>Gérard Soula</b> - Chairman and chief executive officer				
Fixed compensation	349 999	349 999	349 999	349 999
Variable compensation *	225 000	225 000	none	225 000
Extraordinary compensation *	none	none	none	none
Directors' fees	none	none	none	none
Non-cash benefits *	8 388	8 388	8 388	8 388
<b>TOTAL</b>	<b>583 387</b>	<b>583 387</b>	<b>358 387</b>	<b>583 387</b>

<i>In € thousands IFRS</i>	FY 2018		FY 2017	
	Amounts owed (1)	Amounts paid (2)	Amounts owed (1)	Amounts paid (2)
<b>Olivier Soula</b> - Deputy chief executive officer				
Fixed compensation (including paid vacation)	270 157	270 157	281 286	281 286
Variable compensation *	130 000	130 000	none	130 000
Extraordinary compensation *	none	none	none	none
Invention premium	1 000	1 000	2 900	2 900
Directors' fees	none	none	none	none
Non-cash benefits *	none	none	none	none
<b>TOTAL</b>	<b>401 157</b>	<b>401 157</b>	<b>284 186</b>	<b>414 186</b>

(1) Amounts owed for the fiscal year (2) Amounts paid during the fiscal year

(\*) The compensation of each corporate officer is determined by the Board of Directors upon the recommendation of the Compensation Committee. It includes a fixed component, a variable component and an extraordinary component:

- The fixed component is the officer's reference compensation. It compensates his/her responsibilities, experience and technical and managerial skills.
- The variable component is tied to performance. It is based on the fixed salary and achievement of all the predetermined qualitative objectives, which may relate to signing license agreements, developing partnerships, launching clinical trials, signing feasibility contracts, cash levels and, more generally, the development and the growth of the Company.
- The extraordinary component rewards exceptional achievements that have a significant positive impact on the Company's development.

It is being specified that all the elements of remuneration paid to Mr. Olivier Soula are under the terms of his employment contract and as R&D director.

### 3.2.1.3 Directors' fees and other compensation awarded to non-executive corporate officers

<i>Non-executive corporate officers</i>	Amounts paid during fiscal year 2018	Amounts paid during fiscal year 2017
<b>Mr. Olivier Martinez</b> - Director		
Directors' fees (*)	-	-
Other compensation	-	-



<i>Non-executive corporate officers</i>	<b>Amounts paid during fiscal year 2018</b>	<b>Amounts paid during fiscal year 2017</b>
<b>BPI France Investissement, represented by Mr. Laurent Arthaud - Director</b>		
Directors' fees (*)	-	-
Other compensation	-	-
<b>Ms. Dominique Takizawa - Director</b>		
Directors' fees (*)	37 000	44 000
Other compensation	-	-
<b>Ms. Ekaterina Smirnyagina - Director</b>		
Directors' fees (*)	28 000	36 000
Other compensation	-	-
<b>TOTAL</b>	<b>65 000</b>	<b>80 000</b>

(\*) Only Ms. Dominique Takizawa and Ms. Ekaterina Smirnyagina received attendance fees to the extent that the Board of Directors of the Company decided to grant attendance fees only to the independent directors, based on their attendance at the Board meetings and on their participation in specialized committees



### 3.2.1.4 BSPCE founders' warrants granted to each executive corporate officer during the fiscal year

None.

### 3.2.1.5 Share subscription or purchase options exercised by each executive corporate officer during the fiscal year

None.

### 3.2.1.6 Bonus shares granted to each executive corporate officer during the fiscal year

Executive corporate officer name	Plan date and number	Value of bonus shares according to the method used for consolidated financial statements	Number of bonus shares granted during the fiscal year	Vesting date	Earliest selling date	Performance conditions
Olivier SOULA	2018 Plan n°2.2	3 000	150	05/17/2020	05/17/2020	None

### 3.2.1.7 Bonus shares that have become available to each corporate officer

Executive corporate officer name	Plan date and number	Number of shares vested during the year	Performance conditions	Vesting date
Olivier SOULA	2016 Plan corporate officers	2 000	No	03/15/2018
Olivier SOULA	2016 Plan corporate officers Board of Directors' meeting of 3/15/2016	4 000	Yes	03/15/2018

## 3.2.1.8 History of BSA stock warrants awarded to each corporate officer

	<b>BSA 12-2013 stock warrants</b>	<b>BSA 12-2013 stock warrants</b>
Date of shareholders' meeting	06/18/2013	06/18/2013
Date of board of directors' meeting	12/13/2013	12/13/2013
Number of BSA stock warrants authorized	10 000	10 000
Number of BSA stock warrants issued	10 000	10 000
Total number of shares that may be subscribed	10 000	10 000
Name of corporate officer beneficiaries	Dominique Takizawa	Ekaterina Smirnyagina
Earliest exercise date	01/01/2014	01/01/2014
Expiration date	12/13/2023	12/13/2023
Issue price	0.588	0.588
Exercise price	5.88	5.88
Exercise conditions	In full from 01/01/2014	Vesting over 3 years starting from 01/01/2014
Number of shares subscribed as of the filing date of this registration document	0	0
Total number of lapsed or canceled share subscription warrants as of the filing date of this registration document	0	0
BSA stock warrants remaining as of the filing date of this registration document	10 000	10 000
Total number of shares that may be subscribed on the filing date of this registration document	10 000	10 000

## 3.2.1.9 History of BSPCE founders' warrants awarded to each corporate officer

	<b>BSPCE corporate officers 2014</b>	<b>BSPCE corporate officers 2015</b>	<b>BSPCE corporate officers 2016</b>	<b>BSPCE corporate officers 2017</b>
Date of shareholders' meeting	06/24/2014	11/12/2015	11/12/2015	11/12/2015
Date of board of directors' meeting	09/25/2014	12/16/2015	03/15/2016	09/08/2017
Number of BSPCE founders' warrants authorized	65 000	40 000	40 000	150 000
Number of BSPCE founders' warrants issued	65 000	40 000	40 000	150 000
Total number of shares that may be subscribed (1)	65 000	40 000	40 000	150 000
<i>Of which, number that may be subscribed by Gérard Soula</i>	<i>65 000</i>	<i>40 000</i>	<i>40 000</i>	<i>75 000</i>
<i>Of which, number that may be subscribed by Olivier Soula</i>	<i>-</i>	<i>-</i>	<i>-</i>	<i>75 000</i>
Earliest exercise date	Immediate vesting upon fulfillment of relevant performance criteria, approved by the Board of Directors on 12/23/2014	Immediate vesting upon fulfillment of relevant performance criteria, approved by the Board of Directors on 12/16/2015	Immediate vesting upon fulfillment of relevant performance criteria, approved by the Board of Directors on 12/13/2016	Immediate vesting upon fulfillment of relevant performance criteria, defined for 3 years
Expiration date	09/24/2024	12/16/2025	03/15/2026	09/08/2027
Issue price	free	free	free	free
Exercise price (euros)	34.99	74.60	61.73	16.00
Exercise conditions	Immediate vesting from fulfillment of relevant performance criteria	Immediate vesting from fulfillment of relevant performance criteria	Immediate vesting from fulfillment of relevant performance criteria	Immediate vesting from fulfillment of relevant performance criteria

	BSPCE corporate officers 2014	BSPCE corporate officers 2015	BSPCE corporate officers 2016	BSPCE corporate officers 2017
Number of shares subscribed as of the filing date of this registration document	0	0	0	0
Total number of lapsed or canceled BSPCE founders' warrants as of the filing date of this registration document	0	0	16 000	0
BSPCE founders' warrants remaining as of the filing date of this registration document	65 000	40 000	24 000	150 000
Total number of shares that may be subscribed as of the filing date of this registration document	65 000	40 000	24 000	150 000

### 3.2.1.10 Share subscription or purchase options granted to, allocated to and exercised by the top ten non-corporate officer employees

Stock subscription or purchase options granted to the top ten non-corporate officer employees and options exercised by them	Total number of options granted/shares subscribed or purchased	Weighted average price (euros)	2015 SO Plan No. 1	2015 SO Plan No. 2	2017 SO Plan No. 1	2017 SO Plan No. 2	2018 SO
Total number of share subscription options at the beginning of the year	77 000	31.1	20 000	4 000	13 000	40 000	0
Share subscription options granted during the year	23 000	17.0					23 000
Share subscription options exercised during the year	91		none	none	none	91	
Share subscription options cancelled during the year	63 909		20 000	4 000		39 909	
Total number of share subscription options at the end of the year	36 000	17.4	0	0	13 000	0	23 000



### 3.2.1.11 History of bonus shares granted to executive and non-executive corporate officers

	2015 Plan corporate officers	2016 Plan corporate officers		2018 Plan No.2.2
Date of board of directors' decision	12/16/2015	03/15/2016		05/17/2018
Total number of bonus shares granted	5 000	8 000	12 000	150
Beneficiary	Olivier Soula	Olivier Soula	Olivier Soula	Olivier Soula
Vesting date of shares	12/16/2016	2 000 : 03/15/2017 2 000 : 03/15/2018 2 000 : 03/15/2019 2 000 : 03/15/2020	03/15/2018 upon fulfillment of relevant performance criteria	05/17/2020
Lock-in period end date	12/16/2017	2 000 : 03/15/2018 2 000 : 03/15/2019 2 000 : 03/15/2020 2 000 : 03/15/2021	03/15/2018	05/17/2020
Number of shares subscribed at the end of the year	5 000	4 000	4 000	
Total number of shares cancelled or lapsed	none	none	8 000	
Bonus shares remaining at the end of the fiscal year	0	4 000	0	150

### 3.2.1.12 History of compensation and other benefits awarded to executive corporate officers

Executive corporate officers	Employment contract		Supplemental retirement plan		Severance pay or benefits that will or may be due in the event the officer's position is terminated or changed		Payments in consideration for a covenant not to compete	
	Yes	No	Yes	No	Yes	No	Yes	No
<b>Gérard Soula</b> Chairman and chief executive officer		X		X		X		X
Term of office starting date	First appointment by the board of directors' meeting of October 24, 2011, renewed by the combined general meeting of June 24, 2014 and of June 27, 2017							
Term of office end date	Ordinary general shareholders' meeting convened to vote on the financial statements for the fiscal year ending December 31, 2019							
<b>Olivier Soula</b> Deputy chief executive officer	X			X		X		X
Term of office starting date	First appointment by the board of directors' meeting of December 19, 2012, renewed by the combined general meeting of June 24, 2014 and of June 27, 2017							
Term of office end date	Ordinary general shareholders' meeting convened to vote on the financial statements for the fiscal year ending December 31, 2018							

### 3.2.2 Amounts that the Company has provisioned for payment of pensions, retirement allowances and other benefits to corporate officers

As of December 31, 2018, the Company recognized provisions of €107,083 for the payment of retirement benefits to Olivier Soula.

The Company has not granted Mr. Soula any hiring or termination bonuses.

### 3.2.3 Summary of transactions in the Company's securities during the past fiscal year by managers and the persons referred to in Article L. 621-18-2 of the French Monetary and Financial Code (*Code monétaire et financier*)

None.

### 3.2.4 Matters submitted to shareholders in accordance with Article L225-37-2 of the French Commercial Code

#### 3.2.4.1 Principles and criteria to be applied in determining, allocating and awarding the fixed, variable and extraordinary components of total compensation and the benefits of all types that may be awarded to the Chairman and the Deputy General Manager for the 2018 fiscal year

In accordance with Article L225-37-2 of the French Commercial Code, the Board of Directors will submit for approval by the shareholders' meeting called to vote on the financial statements for the 2018 fiscal year the principles and

criteria to be applied in determining, allocating and awarding the fixed, variable and extraordinary components of total compensation and the benefits of all types that may be awarded to the Chairman and the Deputy General Manager for the performance of their duties in the 2018 fiscal year, and which makeup the compensation policy applicable to them.

These principles and criteria, which were determined by the Board of Directors on the basis of recommendations by the Compensation Committee, are set out below:

▪ For Mr. Gérard Soula, Chairman and Chief Executive Officer:

Compensation components	Principles	Determination criteria
Fixed compensation	The chairman and chief executive officer receives fixed compensation.	The annual gross amount of this fixed compensation is set at €356,993.
Variable compensation	The chairman and chief executive officer receives variable compensation that may equal 75% of his fixed compensation.	This variable compensation is based on defined qualitative objectives, which may be tied to signing licensing agreements, developing collaborations, launching clinical trials, signing feasibility contracts, cash levels and, more generally, the development and growth of the Company. Whether these objectives are met will be determined by the board of directors.
Extraordinary compensation	The chairman and chief executive officer may be awarded extraordinary compensation.	This extraordinary compensation is intended to compensate a specific performance that has a major impact on the Company's development.
Non-cash benefits	The chairman and chief executive officer is provided with a company car.	The annual value of this non-cash benefit is €8,388.
Supplemental retirement plan	None	None

The Chairman and Chief Executive Officer may also receive BSPCE founders' warrants, stock options and/or bonus shares, subject to continued employment and performance conditions.

▪ For Mr. Olivia Soula, Deputy General Manager:

It is being specified that all the elements of remuneration paid to Mr. Olivier Soula are under the terms of his employment contract and as R&D director

Compensation components	Principles	Determination criteria
Fixed compensation	The deputy chief executive officer receives fixed compensation.	The annual gross amount of this fixed compensation is set at €272,350 (impact of paid vacation excluded).
Variable compensation	The deputy chief executive officer receives variable compensation that may equal 60% of his fixed compensation.	This variable compensation is based on defined qualitative objectives, which may be tied to signing licensing agreements, developing collaborations, launching clinical trials, signing feasibility contracts, cash levels and, more generally, the development and growth of the Company. Whether these objectives are met will be determined by the board of directors.
Extraordinary compensation	The deputy chief executive officer may be awarded extraordinary compensation.	This extraordinary compensation is intended to compensate a specific performance that has a major impact on the Company's development.
Non-cash benefits	None	None
Supplemental retirement plan	None	None
Patent bonus	The deputy chief executive officer may be awarded patent bonus	Contribution to innovation and nomination as inventor

The Deputy General Manager may also receive BSPCE founders' warrants, stock options and/or bonus shares, subject to continued employment and/or performance conditions.

In accordance with Article L225-100 of the French Commercial Code, the shareholders will be asked to approve the amounts obtained by implementing the above principles and criteria at the shareholders' meeting called to vote on the financial statements for the 2018 fiscal year.

### 3.2.4.2 Resolutions submitted for an initial vote

We propose that you approve the principles and criteria as presented above, and the corresponding resolutions, reproduced below:

#### **Tenth resolution**

*Approval of principles and criteria to be applied in determining, allocating and awarding the fixed, variable and extraordinary components of total compensation and the benefits of all types that may be awarded to Mr. Gérard Soula as a Chief Executive Officer*

The shareholders, voting pursuant to the quorum and majority requirements for annual shareholders' meetings, having deliberated and reviewed the special report referred to in Articles L. 225-37-2 of the French Commercial Code included in the reference document for 2018,

**approve** the principles and criteria to be applied in determining, allocating and awarding the fixed, variable and extraordinary components of total compensation and the benefits of all types as presented in the report established and mentioned hereabove for the 2019 year that may awarded to Mr. Gérard Soula as a Chief Executive Officer, as detailed in the 2018 Reference Document, chapter 3 "Corporate Governance", section 3.2, sub-section 3.2.4 "Matters submitted to the shareholders in accordance with Article L225-37-2 of the French Commercial Code".

#### **Eleventh resolution**

*Approval of principles and criteria to be applied in determining, allocating and awarding the fixed, variable and extraordinary components of total compensation and the benefits of all types that may be awarded to Mr. Olivier Soula, Deputy Chief Executive Officer.*

The shareholders, voting pursuant to the quorum and majority requirements for annual shareholders' meetings, having deliberated and reviewed the special report referred to in Articles L. 225-37-2 of the French Commercial Code included in the reference document for 2018,

**approve** the principles and criteria to be applied in determining, allocating and awarding the fixed, variable and extraordinary components of total compensation and the benefits of all types as presented in the report established and mentioned hereabove for the 2019 year that may awarded to Mr. Olivier Soula Deputy Chief Executive Officer, as detailed in the 2018 Reference Document, chapter 3 "Corporate Governance", section 3.2, sub-section 3.2.4 "Matters submitted to the shareholders in accordance with Article L225-37-2 of the French Commercial Code".

### 3.2.4.3 Approval of compensation owed or awarded to the Chairman and Chief Executive Officer and the Deputy General Manager for the 2018 fiscal year

In accordance with Article L225-100, sub-section II of the French Commercial Code, at the general shareholders' meeting called to vote on the financial statements for the 2018 fiscal year, the shareholders will be asked to approve the fixed, variable and extraordinary compensation awarded or to be awarded for the 2018 fiscal year to the Chairman and Chief Executive Officer and the Deputy General Manager in connection with said offices, as determined by the Board of Directors in accordance with the principles and criteria approved by the shareholders at the Company shareholders' meeting of May 17, 2018 in the seventh and eighth resolutions, described in detail in section 3.2.1 above, will be submitted to the approval of the shareholders' meeting that will be held on May 16, 2019 in order to validate the financial statements for the fiscal year 2018.

In addition, during the 2018 fiscal year, the Board of Directors granted variable compensation to the Chief Executive Officer and the Chief Operating Officer of the Company due to a particular performance with a major impact on the development of the Company. This variable compensation was approved by the shareholders' meeting held on November 9, 2018.

## 3.3 Risk management and internal control procedures implemented by the Company

When preparing this part of the report, the Company followed the guide on implementation of the reference framework on internal control adapted for midcaps and small-caps published by the AMF on July 22, 2010.

### 3.3.1 General risk management principles

#### 3.3.1.1 Definition

Adocia continues to formalize its risk management system. The Company's work initially focused on management of the financial risks, with the creation of a number of official written procedures and the introduction of key control points.

The Company aims to extend this process to all risks and risk factors that may impact on the Company's activities and processes, via a documented risk mapping process, and to subsequently formalize its risk control procedures.

#### 3.3.1.2 Goals of risk management

Adocia has adopted the definition of risk management proposed by the French financial regulator, the AMF<sup>37</sup>, which states that risk management is a management tool of the Company that helps:

- create and protect the Company's value, assets and reputation;
- secure decision-making and the Company's processes to attain its objectives;
- achieve consistency between the Company's actions and its values; and
- ensure that the Company's employees have a shared vision of the main risks.

#### 3.3.1.3 Components of the risk management system

The risk factors the Company has identified to date are detailed in section 1.5 of the reference document.

### 3.3.2 Coordination of risk management with internal control

Risk management aims to identify and analyze the main risks and risk factors that could affect the Company's activities, processes and objectives and define the resources to be used to keep these risks at an acceptable level, in particular by implementing the preventive measures and controls that are part of the internal control system.

At the same time, the internal control system relies on risk management to identify the main risks that need to be controlled. The Company has always had an internal control system, which it has continued to develop, while the formalization of the risk management system is more recent. The Company is now committed to an initiative to coordinate the two systems, which aims to identify the control procedures to be addressed in the key processes of the Company that are likely to be affected by risks qualified as "major".

<sup>37</sup> Implementation guide for the reference framework on internal control adapted for midcaps and small-caps and updated on July 22, 2010

## 3.3.3 General principles of internal control

### 3.3.3.1 Definition

Adocia has adopted the definition of internal control proposed by the AMF<sup>38</sup>, which states that internal control is a system that the Company implements in order to ensure:

- compliance with laws and regulations;
- implementation of the instructions and directions given by Executive Management;
- proper functioning of the Company's internal processes;
- reliability of financial information; and
- in general that helps it to control its activities, improve the efficiency of its operations and use its resources efficiently.

The internal control system helps to prevent and control risks that the objectives set by the Company are not achieved, and therefore plays a key role in the conduct and management of its business activities.

Over the course of the fiscal year, Adocia continued to implement an internal control process aimed at "internally ensuring the relevance and reliability of the information used in and disseminated in the course of the Company's activities".

### 3.3.3.2 Components of internal control and stakeholders

#### ▪ Organization

The internal control system is based on a clear organization of responsibilities, standards, resources, and procedures implemented. In addition, the Company has always had a quality assurance system. The processes for all business segments are described in procedures (*Standard Operating Procedures, or SOPs*), work instructions, notices and forms. These written documents describe the conduct of business, define the resources and responsibilities of the stakeholders, specify the Company's know-how and provide specific instructions on how to carry out a particular operation.

All of the Company's stakeholders are involved in the internal control system.

#### ▪ Project management and business monitoring procedures.

The Company has set up a specific organization to monitor projects and ensure that the objectives set by Executive Management are met within the specified time frames and budgets. For each project it develops, the Company names a project leader who reports to the R&D director and who may seek out the expertise of the different departments within the Company, in order to complete the work defined by Executive Management. He or she is responsible for defining the research programs, validating the objectives with Executive Management, ensuring they are achieved on schedule and coordinating with any partners.

#### ▪ Operational process procedures

All documentation relating to the quality system is saved to a dedicated intranet in order to maximize access to the documents and their ongoing adaptation to changes in the business (document lifecycle management). The objective is the continual improvement in the quality of the Company's or the group's business processes, for operational, management, and support processes alike.

The quality assurance system covers the following areas:

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<sup>38</sup> Implementation guide for the reference framework on internal control adapted for midcaps and small-caps and updated on July 22, 2010



## Corporate Governance

- quality assurance, health and safety, operational risk management;
- administrative, legal, social, and financial matters, including internal control. The intention is to also include communications and rules relating to the Company's listing on Euronext;
- pharmaceutical, pre-clinical and clinical research and development.

With respect to information systems, procedures that have been incorporated into the quality system define the rules relating to access to and the protection and storage of information. An IT Charter has also been put in place.

### 3.3.3.3 Financial reporting procedures

The Company has set up the following organization to limit its financial management risks:

- The Company's Executive Management and, more specifically, the employees of the Finance Department are tasked with improving internal control and incorporating the recommendations of the external auditors and the Audit Committee;
- The Company maintains an internal separation between the production and oversight of the financial statements and brings in independent experts to value complex accounting items;
- If necessary, a chartered accountant is asked to verify the half-yearly and annual work for the corporate financial statements and the financial statements presented under IFRS;
- Payroll management is outsourced to an independent specialized firm.

#### ▪ Oversight of internal control, regular reviews

The Company's Executive Management has put in place specific internal control procedures that consist of regular reviews of key information for each activity. For each of the areas listed below, information deemed material for the corresponding activities has been identified and selected. It must reflect the reality of the activity and be used to track this activity both quantitatively and qualitatively, including compliance with the standards that govern it. This key information must be verifiable and documented. It should be updated every month by the people who conduct the work. This system covers the following areas:

- information about Research and Development projects (pre-clinical, clinical, pharmaceutical);
- financial reporting and transactions involving the capital;
- the Company's legal aspects, regulatory aspects and intellectual property;
- communication of accounting and financial information, as well as scientific and corporate information;
- quality and information systems;
- human resources and payroll.

These reviews are first conducted by the Company's Management Committee, which is composed of the Chairman and Chief Executive Officer, the R&D director, the Chief Financial Officer, and the Business Development director. This committee meets at least once a week. If needed, it reviews data using the "Weekly Flash" report. The purpose of these reviews is to ensure that information on each of the separate areas truly and fairly reflects the Group's activities and situation.

The Operations Committee (COMOP) also reviews the key information for each activity. It meets every month and is made up of the members of the Management Committee and all of the Company's department heads.

In general, all of the Company's accounting options are defined by the Chief Financial Officer, discussed with Executive Management and the Statutory Auditors and then presented to the Audit Committee and discussed. This ensures that the Company's practices are fully compliant with French and international (IFRS) standards and that the financial statements are presented in a consistent manner.

At the end of each year, the Chief Financial Officer prepares a detailed budget for the following fiscal year, which is then approved by Executive Management. This budget is presented to the Board of Directors. At the end of each quarter, the accounting teams prepare the closing of the Group companies' individual financial statements.

The budget reviews conducted with all operational managers ensure an analytical validation of the entries and a review of all expenditures, and the Chief Financial Officer prepares a report for Executive Management and the directors. This report is presented and discussed periodically at the meetings of the Board of Directors.

However, it should be noted that the internal control system implemented by the Company cannot provide an absolute guarantee that its objectives will be met.

- **Internal control stakeholders**

All of the Company's stakeholders, governance bodies and employees are involved in the internal control system.

Since the Company's creation, Executive Management has played a leading role in defining and implementing the internal control system and subsequently in risk management.

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### 3.3.4 Limitations on risk management and internal control and areas of improvement

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In 2018, the Company will continue to move forward with its risk management system and to improve its monitoring of the identified action plans. At the same time, the Company will work to update its internal control system in order to reflect changes in its internal organization and its business, and the closer coordination with the risk management process.





**4**  
**ANNUAL**  
**FINANCIAL**  
**STATEMENTS**  
**AT DECEMBER 31,**  
**2018**



## Chapter 4

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## 4 ANNUAL FINANCIAL STATEMENTS AT DECEMBER 31, 2018

### 4.1 Consolidated Financial Statements

#### 4.1.1 Consolidated Balance Sheet, IFRS

##### 4.1.1.1 Assets, IFRS

<i>In (€) thousands</i>	Notes	<b>FY 2018 (12 months)</b>	<b>FY 2017 (12 months)</b>
<b>Current assets</b>		<b>60 984</b>	<b>44 692</b>
Inventories	5	131	99
Trade and similar receivables	6	3	30
Other current assets	7	21 009	9 785
Cash and cash equivalents	8	39 841	34 778
<b>Non-current assets</b>		<b>9 058</b>	<b>9 069</b>
Other intangible assets	1	115	65
Land	2	2 032	2 032
Land development	2	157	169
Buildings and constructions	2	3 725	3 939
Laboratory equipment	2	942	1 253
Other property, plant and equipment	2	1 870	1 582
Non-current financial assets	3	217	28
<b>TOTAL ASSETS</b>		<b>70 043</b>	<b>53 761</b>

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## 4.1.2 Liabilities and Equity, IFRS

<i>In (€) thousands</i>	Notes	<b>FY 2018 (12 months)</b>	<b>FY 2017 (12 months)</b>
<b>Current liabilities</b>		<b>14 854</b>	<b>8 882</b>
Short-term financial debt	10	2 224	1 791
Trade and similar payables	12	7 546	4 931
Other current liabilities	12	5 084	2 160
<b>Non-current liabilities</b>		<b>9 340</b>	<b>8 022</b>
Long-term financial debt	10	4 892	5 781
Long-term provisions	11	2 756	2 241
Other non-current liabilities	13	1 692	0
<b>Equity</b>	<b>9</b>	<b>45 848</b>	<b>36 857</b>
Share capital		693	691
Share premium		78 849	78 868
Group translation gains and losses		(2)	(14)
Group reserves		(41 306)	(34 138)
Group net profit/loss		7 615	(8 550)
<b>TOTAL LIABILITIES</b>		<b>70 043</b>	<b>53 761</b>

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## 4.1.3 Consolidated Income Statement, IFRS

<i>In (€) thousands</i>	Notes	<b>FY 2018 (12 months)</b>	<b>FY 2017 (12 months)</b>
<b>Operating revenue</b>		<b>53 930</b>	<b>27 177</b>
Revenue	15	47 389	19 469
Grants, research tax credits and others	16	6 541	7 708
<b>Operating expenses excluding additions and reversals</b>	<b>14</b>	<b>(43 179)</b>	<b>(34 345)</b>
<b>Additions to and reversals of depreciation, amortization and provisions</b>	<b>19</b>	<b>(1 044)</b>	<b>(1 013)</b>
<b>PROFIT (LOSS) FROM ORDINARY OPERATING ACTIVITIES</b>	<b>14</b>	<b>9 707</b>	<b>(8 180)</b>
Financial income		2 388	78
Financial expense		(338)	(413)
<b>FINANCIAL INCOME (LOSS)</b>	<b>20</b>	<b>2 051</b>	<b>(335)</b>
<b>PROFIT (LOSS) BEFORE TAX</b>		<b>11 758</b>	<b>(8 516)</b>
Tax expense	21	(4 144)	(35)
<b>NET PROFIT (LOSS)</b>		<b>7 615</b>	<b>(8 550)</b>
Base earnings per share (€)	22	1,1	(1,2)
Diluted earnings per share (€)	22	1,0	(1,2)
<b>GROUP NET PROFIT (LOSS)</b>		<b>7 615</b>	<b>(8 550)</b>
Actuarial adjustments on defined pension liabilities	11	(156)	(191)
<b>Unclassified elements in the Group net profit (loss)</b>		<b>(156)</b>	<b>(191)</b>
<b>TOTAL PROFIT (LOSS) FOR THE YEAR</b>		<b>7 458</b>	<b>(8 741)</b>

## 4.1.4 Statement of Changes in Equity, IFRS

<i>In (€) thousands</i>	Number of Shares	Amount	Paid-in capital	Reserve	Other comprehensive income (OCI)	Net profit (loss)	Total equity
<b>BALANCE AT 12/31/2017</b>	<b>6 910 753</b>	<b>691</b>	<b>78 868</b>	<b>(32 971)</b>	<b>(1 181)</b>	<b>(8 550)</b>	<b>36 857</b>
Profit for the year 2018						7 615	(7 615)
Gain (losses) on actuarial adjustments on defined pension liabilities					(156)		(156)
<b>Comprehensive income for the period</b>					<b>(156)</b>	<b>7 615</b>	<b>7 458</b>
Allocation of profit for the year 2015				(8 550)		8 550	
Exercise of equity instruments (warrants)	20 491	2	(0)	(0)			1
Share-based payment				1 587			1 587
Liquidity Contract - Elimination of treasury shares			(18)	(49)			(67)
Others				13			13
Total shareholder relations	20 491	2	(19)	(7 000)		8 550	1 534
<b>BALANCE AT 12/31/2018</b>	<b>6 931 244</b>	<b>693</b>	<b>78 849</b>	<b>(39 971)</b>	<b>(1 338)</b>	<b>7 615</b>	<b>45 848</b>



## 4.1.5 Cash Flow Statement, IFRS

<i>In (€) thousands</i>	<b>FY 2018 (12 months)</b>	<b>FY 2017 (12 months)</b>
Net profit	7 615	(8 550)
Net depreciation, amortization & provisions (excl. current assets)	1 044	1 013
Capital gains and losses on non-current assets	0	(4)
Calculated income and expenses	(528)	3 215
Tax paid	0	(49)
<b>Cash flow from operations before cost of net financial debt and tax</b>	<b>8 131</b>	<b>(4 376)</b>
Cost of gross financial debt	2 239	(33)
<b>Change in deferred revenues</b>	<b>4 007</b>	<b>(18 823)</b>
<b>Change in working capital requirement (including employee benefits)</b>	<b>(8 064)</b>	<b>1 005</b>
<b>NET CASH FLOW RELATED TO OPERATING ACTIVITIES</b>	<b>6 313</b>	<b>(22 227)</b>
Acquisitions of property, plant and equipment & intangible assets	(784)	(1 980)
Disposals of property, plant and equipment & intangible assets	0	295
Acquisitions of non-current financial assets	0	0
Disposals of non-current financial assets	0	0
Other cash flows related to investing activities	(250)	(0)
<b>NET CASH FLOW RELATED TO INVESTING ACTIVITIES</b>	<b>(1 034)</b>	<b>(1 685)</b>
Capital increase	2	40
New loans and reimbursable advances	1 310	1 102
Repayments of loans and reimbursable advances	(1 528)	(489)
Other cash flows related to financing activities	0	0
<b>NET CASH FLOW RELATED TO FINANCING ACTIVITIES</b>	<b>(216)</b>	<b>653</b>
	0	0
<b>CHANGE IN NET CASH AND EQUIVALENTS</b>	<b>5 063</b>	<b>(23 259)</b>
Opening cash	34 778	58 037
Closing cash	39 841	34 778

## 4.1.5.1 Detailed Analysis of WCR:

<i>In (€) thousands</i>	<b>Change 2018/ 2017</b>
Inventories	36
Trade and similar receivables	(27)
Other receivables and advances	10 827
Pre-paid expenses / other receivables	397
Trade and similar payables	(2 559)
Other debt	(609)
<b>CHANGE IN WORKING CAPITAL REQUIREMENT</b>	<b>8 064</b>

**Components of consolidated net cash and cash equivalents analyzed by type and reconciliation with the balance sheet:**

<i>In (€) thousands</i>	<b>FY 2018 (12 months)</b>	<b>FY 2017 (12 months)</b>
Short-term investment securities (due in < 3 months)	7 093	8 090
Cash on hand	32 748	26 687
<b>NET CASH AND CASH EQUIVALENTS</b>	<b>39 841</b>	<b>34 778</b>

## 4.1.6 Notes to the Consolidated Financial Statements

Unless specified otherwise, the amounts indicated in these notes are in thousands of euros.

### 4.1.6.1 Information about the company

Adocia is a biotechnology company specializing in the development of innovative formulations of pre-approved therapeutic proteins. It has a high level of expertise in the field of insulin. The proprietary technology platform, called BioChaperone®, aims to improve the efficacy of therapeutic proteins and their ease of use for patients.

Adocia is a limited company (société anonyme) under French law created on December 22, 2005.

The company has been listed on NYSE Euronext (compartment B) since February 20, 2012.

It has a wholly-owned subsidiary (Adocia Inc.) established in March 2015 which aims to represent the company in the US.

The financial statements under IFRS for the period from January 1 to December 31, 2017 are presented on a consolidated basis for Adocia and its subsidiary (Adocia Inc.), the whole being called "the Company". The financial statements were approved by the Board of Directors on March 5, 2018 and authorized for publication.

2018 was marked by the strategic alliance with Tonghua Dongbao Pharmaceuticals Co. Ltd (« THDB »), Chinese leader of the production and commercialisation of insulin. In April 2018, Adocia and THDB announced the set up of two licensing agreements for BioChaperone® Combo, BioChaperone® Lispro, in China and in other Asian and Middle-East territories. Under the terms of the Licensing Agreements, Tonghua Dongbao is responsible for the future development, manufacturing, and commercialization of BioChaperone Combo and BioChaperone Lispro in the covered territories. Adocia received a total upfront payment of \$50 million and is entitled to receive development milestone payments up to \$85 million and Adocia is also expected to receive double-digit royalties on the sale of both products in the territories. Since the signature, both companies worked on the transfer of the technology to enable the manufacturing of both products. THDB envisages to start a Phase 3 clinical study for BioChaperone Lispro in 2019 and a first clinical study for BioChaperone Combo late 2019.

In June 2018, the partnership with THDB was reinforced by two supply agreements in insulin glargine et lispro. Under the terms of the supply agreements, Tonghua Dongbao will manufacture and supply insulin lispro and insulin glargine APIs to Adocia, in accordance with Adocia's specifications and established quality standards worldwide, excluding China. These agreements enable Adocia to carry on the development of the BioChaperone Lispro et BioChaperone Combo projects and also open additional collaboration opportunities. Adocia prepares a bridging study in order to qualify the insulin lispro manufactured by THDB as equivalent source to Lilly's insulin lispro. This study should be the only one required by authoritative agencies to enable the start in phase 3 of BioChaperone Lispro.

From a clinical perspective, Adocia realized in 2018 the first clinical study of BioChaperone® Pramlintide Insulin in people with type 1 diabetes. This study, whose positive topline results were announced in September showed a

significant 97% decrease in blood glucose excursion over the first two hours after the meal compared to Humalog®. The product was well tolerated. Adocia plans to start a second repeated administration trial during Q2 2019.

The development of our varied portfolio products to date revealed unique properties of the BioChaperone technology, which notably enables to significantly improve single agents and to combine multiple therapeutic proteins. In order to expand the use of this technology, Adocia announced early in 2018 that BioChaperone® would now be deployed in a selected range of injectable therapeutics across numerous therapeutic areas. Initial programs added to the portfolio include a ready-to-inject version of teduglutide for the treatment of short bowel syndrome and a fixed dose combination of glucagon and exenatide for the treatment of obesity, both in preclinical stage.

Lastly, regarding legal proceedings, the first phase of the arbitration procedure initiated by Adocia against Lilly concluded in favor of Adocia. The Arbitration Tribunal awarded Adocia \$ 11.6 million, as well as interests.

Adocia's additional claims against Lilly for a revalued amount of \$1.3 billion and the counterclaims of Lilly for an amount of \$188 million, remain pending, with a decision of the court expected in the third quarter of 2019.

Finally, in October 2018, Lilly filed a civil complaint against Adocia in the United States District Court of the Southern District of Indiana to seek a declaratory judgment for two of its US patents regarding ultra-rapid insulin formulation (Lilly's United States Patent Nos. 9,901,623 and 9,993,555 entitled "Rapid-acting insulin compositions"). Lilly contends in its complaint that it filed the action because Adocia has asserted that Lilly's patents reflect Adocia's inventive contribution. Adocia does not expect the matter to be resolved during this fiscal year.

#### 4.1.6.2 Accounting methods and principles used to draw up the financial statements

##### ▪ Accounting standards

In accordance with EU Regulation 1606/2002 of July 19, 2002 on international standards, the company's consolidated financial statements for the period ended December 31, 2017 were prepared according to the standards and interpretations published by the International Accounting Standards Board (IASB) and adopted by the European Union as of the reporting date.

These standards are available on the European Commission website at the following address:

[http://ec.europa.eu/internal\\_market/accounting/ias\\_fr.htm](http://ec.europa.eu/internal_market/accounting/ias_fr.htm)

They include the international accounting standards (IAS and IFRS) and the interpretations of the Standing Interpretations Committee (SIC) and the International Financial Interpretations Committee (IFRIC).

The accounting principles and methods used by the company for the consolidated financial statements are the same as those used for the financial statements for the year ended December 31, 2017.

In addition, the new mandatory texts applicable to fiscal years beginning on or after January 1, 2018 are as follows:

##### Standards, amendments to standards and interpretations applicable as of January 1, 2018:

- IFRS 9 - Financial Instruments
- IFRS 15 - Revenue from Contracts with Customers and amendments to the effective date of the IFRS 15 standard
- *Regarding the absence of material impact of the implementation of this standard, the Company has chosen to apply the partial retrospective method. Refer to the following section "Application of the IFRS 15 standard from January 1, 2018" for more information.*
- Clarifications to the IFRS 15 standard
- IFRIC 22
- Amendments to IFRS 2 - Classification and Measurement of Share-based Payment Transactions

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- Amendments to IFRS 4 - Applying IFRS 9 with IFRS 4
- Amendments to IAS 40 - Transfers of Investment Property
- Amendments to IAS 28 – Exemption in the application of the equity method: measure the fair value of associates and joint ventures
- Improvement to IFRS (2014-2016 cycle)

### Standards, amendments to standards and interpretations adopted by the European Union but not yet mandatory for 2018 annual financial statements:

- IFRS 16 – Leases
- Amendments to IFRS 9 – Prepayment features with negative compensation

### Standards and interpretations published by the IASB and not yet adopted by the European Union as of December 31, 2018:

- IFRS 17 - Insurance Contracts
- Amendments to IAS 28 – Long-term interests in associates and joint ventures
- Amendments to IAS 19 – Change, reduction or liquidation of the plan
- Amendments to IFRS 3 – Definition of a business
- Amendments to IAS 1 and IAS 8 – Definition of material
- Improvement to IFRS (2015-2017 cycle)

The Company assessed the impacts of the first application of these new standards and does not expect a material impact on its financial statements, including for IFRS 9 and IFRS 16 standards.

#### ▪ Application of the IFRS 15 standard from January 1, 2018

Starting from January 1, 2018, the Company adopts the IFRS 15 standard « Revenue from contracts with customers». The IFRS 15 standard replaces the IAS 11 standard « Construction contracts » and the IAS 18 standard « Revenue from ordinary activities », as well as the corresponding interpretations (IFRIC 13, IFRIC 15, IFRIC 18 et SIC 31).

The application of this new standard required no accounting restatement at January 1, 2018 as there were no ongoing contract at that date.

The Company's revenue primarily originates from the sale of licences and of research and development services.

The licences sold by the Company correspond to rights of use. As a consequence, the revenue generated from these licences is recognized immediately from the date the customer can start using the licence.

When the payment of a licence is a milestone payment depending on the achievement of a development, regulatory or commercial objective, the corresponding revenue is recognized when the objective achievement becomes highly probable.

When the payment of a licence is royalties calculated on sales made by the customer, the Company applies the exception to the general principle provided by the IFRS 15 standard on variable payments. Royalties are recognized as revenue when the customer sales occur.

The Company provides research and development services to customers as part of development projects which final objective is the grant of a marketing authorization. The revenue from these services is recognized according to the percentage of completion of the project, as the customer benefits from the services progressively. The percentage of completion is calculated from costs.

If the licence and the services are sold together, the contract price is allocated to the different elements of the contract proportionally to their fair value.

If the costs of one of the contract elements are not completely offset by the revenue calculated from fair values, the Company applies the residual method.

### ▪ Basis for preparation of the financial statements

Since the creation of the Adocia Inc. subsidiary in March 2015, the company has published consolidated financial statements. The methods used for consolidation and translation of the financial statements are specified below (Consolidation methods).

The company's financial statements were prepared based on the historical cost principle, with the exception of certain categories of assets and liabilities according to the rules set out in the IFRS. The relevant categories are indicated in the following notes.

The company supports the development of the projects licensed to Tonghua Dongbao and pursues its research and development activities while nevertheless focusing its expenses on projects and priority activities. The recovery of damages awarded under the first part of the arbitration proceeding against Lilly (\$ 11.6 million plus interest) is expected in 2019, following the conclusion of the second part of the arbitration. Pending the cash receipt of this amount, the possibility of an advanced payment of the research tax credit allows the Company to finance the defined operational plan and thus to meet its financial commitments for at least the next 12 months. Therefore, the going concern assumption has been retained.

To prepare the financial statements in accordance with IFRS, certain estimates, judgments and assumptions have been made by the company's management, which may have affected the amounts shown for the assets, liabilities and contingent liabilities as of the date of preparation of the financial statements, and the amounts shown for income and expenses during the year.

These estimates are based on the going concern assumption and on the information available at the time they were made. They are assessed continuously based on past experience and various other factors deemed reasonable which form the basis of the estimates of the carrying amount of the assets and liabilities. The estimates may be revised if the circumstances on which they were based change or as a result of new information. Actual results may differ significantly from these estimates based on different assumptions or conditions.

In preparing its annual financial statements, the main judgments made by management and the main assumptions used are the same as those used to prepare the financial statements for the fiscal year ended December 31, 2017. These assumptions mainly relate to IFRS 2 ("Share-based Payment") and IFRS 15 ("Revenue from Contracts with Customers") and are explained in the following sections.

### ▪ Consolidation principles

The consolidated financial statements include the financial statements of all the fully consolidated subsidiaries that Adocia directly or indirectly controls. In accordance with IFRS 10, control is determined on the basis of three criteria: power, exposure to variable returns and the relationship between power and these returns.

In March 2015, the company created a wholly-owned subsidiary called Adocia Inc., which was fully consolidated at the end of December 2017.

The addition of the Adocia Inc. subsidiary to the scope of consolidation was effective on the date of creation. Income and expenses are recorded in the consolidated income statement from the date of creation.

All transactions between the Adocia Inc. subsidiary and the company and internal results within the consolidated group are eliminated.

The company's financial statements are prepared in euros, which is the presentation currency and functional currency of the parent company and its subsidiary.

The method used by the company is that of the closing rate. This method entails translating the balance sheet items at the closing rate and the income items at the average rate for the year; the translation differences, both on the opening balance sheet items and on the income statement, are included in equity under "Translation differences".

▪ **Current/non-current distinction**

The balance sheet presentation used by the company makes a distinction between current and non-current assets and liabilities.

This distinction is made based on the following rules:

- assets and liabilities that fall within the scope of the company's operating working capital requirement are classified as "current";
- assets and liabilities that are not part of the company's normal operations are presented as "current" or "non-current" based on whether their due date is more than or less than one year.

▪ **Intangible assets**

**Research and development**

In accordance with IAS 38, internal research costs are recognized as expenses as soon as they are incurred. Development costs are capitalized if and only if the following criteria are met:

- technical feasibility needed to complete the development project is established,
- the company intends to complete the project,
- the company is able to use the intangible asset,
- the company is able to demonstrate the probability that the asset will generate future economic benefits,
- the company has the technical, financial and other resources to complete the project, and
- the development costs are measured reliably.

**Patents**

The costs incurred prior to filing and obtaining patents are capitalized by the company under the same conditions as those applicable to capitalizing development costs.

**Other intangible assets**

Intangible assets acquired separately by the company are recognized at historical cost and those acquired through a business combination are recognized at fair value.

Concessions, licenses and software are amortized over the expected useful life (three to five years depending on the type of software).

▪ **Property, plant and equipment**

Property, plant and equipment are recognized at their original cost. They are then measured at cost less any accumulated depreciation and impairment.

Depreciation is calculated on a straight-line basis according to the estimated useful life of the assets and, if applicable, the residual values:

Type of asset	Useful life
Land development	10 years
Buildings	20 years
Fixtures and facilities	3 à 10 years
Laboratory equipment	3 à 5 years
Furniture, office equipment	5 years

Land is not depreciated.



An item of property, plant and equipment is derecognized when it is disposed of or when no future economic benefits are expected from its use or disposal. Any gain or loss resulting from the derecognition of an asset (difference between the net proceeds and carrying amount of the asset) is included in the income statement for the year in which derecognition occurs.

The residual values, useful lives and depreciation methods of assets are reviewed and, if necessary, adjusted at each year-end closing. Such adjustments are treated as changes in estimate.

The depreciation of property, plant and equipment is recognized in profit or loss under depreciation and amortization.

- **Leasing (including lease financing)**

Where applicable, an asset held under a finance lease (which substantially transfers all the risks and rewards of ownership of the asset to the company) is recorded as an asset and a liability (in the same amount) on the balance sheet at the lower of the fair value of the asset and the sum of the discounted payments.

These assets are depreciated according to the same methods and rules described above in the previous section. The corresponding liabilities are recorded on the balance sheet and repaid in an amount equal to the theoretical amortization of loans whose characteristics are comparable to those of the lease agreements.

Operating lease agreements are recorded as expenses on a straight-line basis over the term of the agreement until its expiration.

- **Borrowing costs**

Borrowing costs directly attributable to the acquisition, construction or production of an asset that takes a substantial amount of time to prepare for its intended use or sale are included in the cost of the asset. All other borrowing costs are recorded as financial expenses for the fiscal year in which they are incurred. Borrowing costs include interest and other costs that an entity incurs to borrow funds.

- **Recoverable amount of non-current assets**

Assets with an indefinite useful life are not depreciated and are subject to an annual impairment test. Depreciated assets are subject to an impairment test whenever there is an internal or external indicator that an asset may be impaired.

Impairment testing entails comparing the net carrying amount of the tested asset to its recoverable amount. The test is performed at the cash generating unit level, which is the smallest group of assets that includes the asset and whose continuous use generates cash inflows that are largely independent of those generated by other assets or groups of assets.

Impairment is recorded in the amount by which the carrying amount of an asset exceeds its recoverable amount. The recoverable amount of an asset is the higher of its fair value less costs of disposal and its value in use.

Fair value less costs of disposal is the amount that can be obtained from the sale of an asset in an arm's length transaction between well-informed, consenting parties, less costs of disposal.

Value in use is the present value of the estimated future cash flows expected to be derived from the continuous use of an asset and from its disposal at the end of its useful life. Value in use is determined according to cash flow projections generally made on the basis of five-year budgets or forecasts. For periods after five years, cash flows are extrapolated using a steady or declining growth rate and discounted at long-term after-tax market rates that reflect market estimates of the time value of money and the risks specific to the asset. The terminal value is determined based on the discounting to infinity of the last cash flow of the test.

As of December 31, 2018, there were no internal or external impairment indicators for any non-current assets.

## ▪ Basis of measurement of inventories

Inventories are recognized at the lower of cost and net realizable value. They may be impaired if the expiration date has passed and/or if the project to which they refer was discontinued by the company and considered a failure. The cost of inventories is determined using the first-in first-out method.

## ▪ Financial assets

Financial assets are classified into four categories based on their type and the intention of holding them:

- Held-to-maturity investments,
- Financial assets at fair value through profit or loss,
- Loans and receivables,
- Available-for-sale financial assets.

With the exception of assets at fair value through profit or loss, all financial assets are initially recognized at cost, which corresponds to the fair value of the price paid plus acquisition costs.

All regular way purchases and sales of financial assets are recognized on the settlement date.

### Held-to-maturity investments

Held-to-maturity investments are financial assets which the company intends and is able to hold to maturity. After their initial recognition, these assets are measured at amortized cost, using the effective interest method, less the amount of any impairment.

### Financial assets at fair value through profit or loss:

This category represents assets held for trading, i.e. assets acquired by the company for the purpose of selling them in the short term. They are measured at fair value and changes in fair value are recorded in profit or loss. Certain assets can also be voluntarily classified in this category.

### Loans and receivables:

Non-current financial assets include advances and guarantee deposits given to third parties. Advances and guarantee deposits are non-derivative financial assets with fixed or determinable payments that are not quoted in an active market. Such assets are recognized at amortized cost using the effective interest method. Gains and losses are recorded in profit or loss when the loans and receivables are derecognized or impaired.

### Available-for-sale financial assets:

This category includes all other financial assets. They are measured at fair value and changes in fair value are recorded in profit or loss until the asset is sold, cashed in or disposed of in any other way or until it is shown that the asset has been impaired in a prolonged and significant manner. In such cases, the profit or loss, recognized until then in equity, is transferred to profit or loss.

Available-for-sale financial assets are tested for impairment when impairment indicators exist.

When the available-for-sale financial asset is an equity instrument, impairment is final. Subsequent increases in fair value are recognized directly in equity.

When the available-for-sale financial asset is a debt instrument, any subsequent increase is recorded in profit or loss in an amount equal to the impairment loss previously recorded in profit or loss.

Purchases and sales of financial assets are generally recognized on the trade date.

The only financial assets measured at fair value are cash and cash equivalents, which include short-term investment securities (money market mutual funds in euros) quoted in an active market. They therefore constitute level 1 financial assets at fair value.



**Cash reserve of the liquidity agreement:**

The cash reserve related to the liquidity agreement for the buyback of the company's own shares is recorded as non-current financial assets.

- **Cash and cash equivalents**

Cash and short-term deposits recorded on the balance sheet include bank balances, cash on hand and short-term deposits with an initial maturity of less than three months.

Cash equivalents are held for trading purposes, readily convertible to a known cash amount and subject to an insignificant risk of change in value. They are measured at fair value and changes in value are recorded in financial income/expense.

For the purposes of the cash flow statement, net cash includes cash and cash equivalents as defined above, net of bank overdraft facilities. In the balance sheet, bank overdrafts are shown in Current financial liabilities.

- **Repayable advances**

The company receives a certain amount of government assistance in the form of repayable advances.

Government grants are recognized as assets when there is reasonable assurance that:

- The company will comply with the conditions attached to the grants; and
- The grants are received.

Repayable advances are recognized as "Long-term financial debt" or "Short-term financial debt" depending on their due date. In case of failure to repay the grant, the debt write-off is recognized in "Grants, government financing and tax credits".

These advances were recognized in accordance with IAS 39: as financial advances granted at interest rates below the market rates, the difference between the applied rate and the market rate is valued according to IAS 20, if the impacts are material.

- **Equity**

Classification in equity depends on the specific analysis of the characteristics of each instrument issued. Ordinary shares and preferred shares have therefore been classified as equity instruments.

The incidental costs directly attributable to the issue of shares or stock options are accounted for as a deduction from equity, net of tax.

Treasury shares held by the company under a liquidity agreement are recognized at their acquisition cost as a reduction in equity. The gain or loss on disposal of these treasury shares is also recognized directly in equity.

- **Share-based payments**

In accordance with IFRS 2, benefits granted to certain employees in the form of share-based payments are measured at the fair value of the instruments granted.

This payment can take the form of equity-settled instruments or cash-settled instruments.

The company has introduced several equity-settled payment plans.

For example, stock options are granted to senior managers, certain company employees and other private individuals.

The company uses the Black-Scholes model to measure the fair value of these options. This model takes into account the features of the plan (strike price, exercise period), market data on the grant date (risk-free interest rate, volatility,

expected dividends) and grantee behavior assumptions. Changes in value subsequent to the grant date have no impact on this initial measurement.

The value of the options is based on their expected term. This value is recorded as payroll expense or external charges as follows: the fair value of the options granted is determined on the grant date and recognized in profit or loss over the vesting period (period between the grant date and the plan maturity date).

For bonus shares, the fair value is also determined based on the features of the plan, market data on the grant date and an assumption of continued employment at the end of the vesting period. If the plan does not specify vesting conditions, the expense is recognized in full when the plan is granted; otherwise, the expense is recorded over the vesting period based on the conditions being met.

#### ▪ Provisions

Provisions are recorded when the company has a present obligation (legal or constructive) resulting from a past event, it is probable that an outflow of resources representing economic benefits will be needed to settle the obligation, and the amount of the obligation can be measured reliably. If the company expects the full or partial reimbursement of the provision (for example under an insurance policy), the reimbursement is recognized as a separate asset, but only if the reimbursement is virtually certain. The expense related to the provision is shown in the income statement net of any reimbursement. If the effect of the time value of money is material, provisions are discounted using a pre-tax rate that reflects, where appropriate, the risks specific to the liability. When discounting is used, the increase in the provision related to the passage of time is recognized as a borrowing cost.

Provisions correspond to risks and charges that are specifically identified. They are classified as non-current or current liabilities based on their nature, purpose and duration.

#### ▪ Social commitments

In accordance with IAS 19R, retirement plans, similar payments and other employee benefits that are considered defined benefit plans (plan in which the company agrees to guarantee a defined amount or benefit level) are recorded in the balance sheet based on an actuarial assessment of the obligations on the closing date, reduced by the fair value of the plan assets. These calculations mainly include:

- an assumption related to the benefit payment date;
- a financial discount rate;
- an inflation rate;
- assumptions related to salary increases, employee turnover rate and mortality rate.

The main actuarial assumptions made at December 31, 2018 are described in note 11 to the financial statements.

Actuarial gains and losses include the effects on the obligation of changes in the calculation assumptions and experience adjustments to the obligation. These gains and losses are recognized in other comprehensive income for post-employment benefits.

The provision shown on a specific line of the balance sheet represents the total obligation on the closing date, adjusted, where appropriate, for past service costs. Past service costs related to a plan change are recognized immediately in the income statement for the portion of rights already acquired, and are spread out over the average period remaining until the corresponding benefits are vested.

The expense for the year consists of the cost of services rendered, which represents an operating expense, and the accretion expense, which represents a financial expense.

#### ▪ Financial liabilities

Financial liabilities are classified into two categories and include:

- financial liabilities recognized at amortized cost, and

- financial liabilities recognized at fair value through profit or loss.

#### Financial liabilities recognized at amortized cost:

Loans and other financial liabilities, such as conditional advances, are generally recognized at amortized cost calculated using the effective interest rate.

Loans and conditional advances are initially recorded at the fair value of the amount received, less directly attributable transaction costs. After the initial recognition, interest-bearing loans are measured at amortized cost using the effective interest method.

The portion of debt due in less than one year is presented as a current liability.

#### Financial liabilities at fair value through profit or loss:

This category represents liabilities held for trading, i.e. liabilities that are intended to be sold in the short term. They are measured at fair value and changes in fair value are recorded in the income statement.

- **Receivables and liabilities denominated in foreign currencies**

Receivables and liabilities denominated in foreign currencies are recognized at the exchange rate at the time of the initial transaction. At the end of the fiscal year, the items corresponding to assets and liabilities are measured at the closing rate or at the hedging rate, where appropriate.

- **Current and deferred tax**

Current tax assets and liabilities for the fiscal year and previous fiscal years are measured at the amount expected to be collected from or paid to the tax authorities. The tax rates and tax laws used to determine these amounts are those enacted or substantively enacted as of the closing date.

Deferred taxes are recognized using the balance sheet liability method for all temporary differences existing as of the closing date between the tax base of the assets and liabilities and their carrying amount on the balance sheet, and for carryforward losses.

A deferred tax asset, generated by tax losses, is recognized when there is persuasive evidence that a sufficient taxable profit will be available.

- **Revenue**

Revenue corresponds to the fair value of the consideration received or receivable for goods and services sold in the normal course of the company's business. Revenue is shown net of value-added tax, returns of merchandise, rebates and discounts.

In the normal course of its business, the company may enter into commercial agreements with pharmaceutical groups. Payment under these agreements may generally be based on:

- The payment of a signing bonus (access fees or up-front payment)
- Payment for specific developments based on the attainment of technical milestones (milestone payments)
- Payment for research and development efforts (collaborative agreements)
- Future sales of products (royalties).

The company recognizes revenue when the amount can be measured reliably, it is probable that future economic benefits will flow to the company, and specific criteria are met for each of the company's activities.

With regard to licenses and feasibility studies, contracts are analyzed on a case by case basis in order to recognize revenue according to the IFRS 15 standard (cf. section 4.1.6.3)

## ▪ Other income

### Grants:

Due to its innovative nature, since its creation the company has received a certain amount of assistance and grants from the French government and public authorities to help finance its operation or recruit specific individuals.

These grants are recognized as income over the fiscal year in which the corresponding costs or expenses are recorded.

### Research tax credit:

The French government grants research tax credits to companies to encourage them to conduct technical and scientific research. Companies that can substantiate expenditures meeting the required criteria (research costs in France or, since January 1, 2005, within the European Community or in another State that is part of the Agreement on the European Economic Area and has signed a tax treaty with France containing an administrative assistance clause) are eligible for a tax credit that can be used to pay the corporation tax due for the fiscal year in which the expenses are incurred and the following three fiscal years or, where appropriate, be reimbursed for the excess share of such tax.

## ▪ Segment information

To date, the company has not identified distinct operating segments. For the most part, the company's operations involve regenerative medicine for the treatment of chronic diseases. All the assets and operating income presented are located in France.

## ▪ Presentation of the income statement

The company presents its income statement by nature.

The purpose of the expenses is provided in note 14 to the financial statements.

### Research and development costs:

Internal and external costs related to the research and development of new products.

### Administrative expenses:

Total costs of the support and central management functions.

### Other operating income and expenses:

Information appears in this item when a significant event occurring during the accounting period could give a distorted view of the company's performance.

Other operating income and expenses include income and expenses that are very limited in number and unusual given their frequency, nature or amount.

### Operating profit/loss:

Operating profit/loss includes all income and expenses directly related to the company's activities, whether such income and expenses are recurrent or result from one-time decisions or operations.

### Financial income/expense:

Financial income/expense includes all:

- Expenses related to financing the company: interest paid and accretion expense on repayable advances
- Income related to interest received.

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oreign-exchange gains and losses are also recognized in financial income/expense.

#### Taxes:

Income tax: This item includes tax recorded for the year on any taxable income (French GAAP).

Deferred taxes are recognized for all temporary differences arising from the difference between the tax basis and accounting basis of the assets and liabilities shown in the financial statements. The main temporary differences relate to carryforward tax losses. The statutory tax rate on the closing date is used to determine deferred taxes.

Deferred tax assets are recognized only to the extent that it is probable that future earnings will be sufficient to absorb carryforward losses. Given its stage of development, which does not allow sufficiently reliable income projections to be made, the company did not recognize deferred tax assets on the balance sheet for carryforward losses.

#### ▪ Earnings per share

Basic earnings per share is calculated by dividing the profit or loss attributable to holders of the company's shares by the weighted average number of ordinary shares outstanding during the period.

Diluted earnings per share is determined by adjusting the profit or loss attributable to holders of ordinary shares and the weighted average number of ordinary shares outstanding for the effects of all dilutive potential ordinary shares.

#### ▪ Fair value of financial instruments

Fair value measurements are detailed by level according to the following fair value hierarchy:

- the instrument is quoted in an active market (level 1);
- measurement uses valuation techniques based on observable inputs, either directly (price) or indirectly (price derivatives) (level 2);
- at least one material component of fair value is based on unobservable inputs (level 3).

Fair value of financial instruments traded in active markets is based on quoted prices on the balance sheet date. A market is considered active if quoted prices are easily and regularly available from an exchange, trading officers, brokers, an appraiser or a regulatory agency and such prices are based on regular trades. These instruments are classified as level 1.

Fair value of financial instruments that are not quoted in an active market (for example, over-the-counter derivatives) is determined based on valuation techniques. These methods maximize the use of observable market inputs, if available, and, for the most part, are not based on the company's own estimates. If all the elements required to calculate the fair value of the instrument are observable, this instrument is classified as level 2.

If one or more of the main calculation elements are not based on observable market inputs, the instrument is classified as level 3.

### 4.1.6.3 Notes to the financial statements

#### Summary of notes

NOTE 1	Intangible assets
NOTE 2	Property, plant and equipment
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NOTE 23	Related parties and compensation of the corporate officers
NOTE 24	Financial risk management objectives and policies
NOTE 25	Off-balance sheet commitments
NOTE 26	Events subsequent to year end

**NOTE 1 Intangible assets**

<i>In (€) thousands</i>	12/31/2017	Acquisitions / Additions	Disposals / reversals	12/31/2018
Gross amount	137	70	0	207
Depreciation and impairment	72	20	0	92
<b>NET AMOUNT</b>	<b>65</b>	<b>50</b>	<b>0</b>	<b>115</b>

Given the risks and uncertainties related to regulatory authorizations and the R&D process, the six criteria for recognition of intangible assets are not considered as being met for any of the pending development projects. As a result, all costs incurred by the company are recognized as expenses. The treatment is the same for costs related to patents (see note 14).

**NOTE 2 Property, plant and equipment**

<i>In (€) thousands</i>	12/31/2017	Acquisitions / Additions	Disposals / reversals	12/31/2018
Lands	2 032	0	0	2 032
Land development	170	5	0	175
Buildings	4 276	0	0	4 276
Laboratory equipment	3 514	157	(13)	3 658
Fixtures and facilities	1 970	440	0	2 410
Furniture, office equipment	1 202	167	0	1 369
<b>GROSS AMOUNT</b>	<b>13 164</b>	<b>769</b>	<b>(13)</b>	<b>13 920</b>
Lands	0	0	0	0
Land development	1	17	0	18
Buildings	336	214	0	550
Laboratory equipment	2 262	467	(13)	2 716
Fixtures and facilities	781	143	0	924
Furniture, office equipment	804	177	0	981
<b>DEPRECIATION AND IMPAIRMENT</b>	<b>4 184</b>	<b>1 018</b>	<b>(13)</b>	<b>5 189</b>
Lands	2 032	0	0	2 032
Land development	169	(12)	0	157
Buildings	3 939	(214)	0	3 725
Laboratory equipment	1 253	(311)	0	942
Fixtures and facilities	1 187	297	0	1 484
Furniture, office equipment	396	(9)	0	386
<b>NET AMOUNT</b>	<b>8 975</b>	<b>(249)</b>	<b>0</b>	<b>8 727</b>

Net property, plant and equipment decreased by €0.2 million between 2017 and 2018, due mainly to the ongoing restructuring works on the building for €0.4 million and the purchase of laboratory and office equipment, offset by the depreciation recorded for 2018 for €1 million.

**NOTE 3 Non-current financial assets**

The company's non-current financial assets were as follows:

## Annual financial statements at December 31, 2018

<i>In (€) thousands</i>	12/31/2017	Acquisitions / Additions	Disposals / reversals	12/31/2018
Gross amount	28	250	(62)	217
Amortization and impairment				
<b>NET AMOUNT</b>	<b>28</b>	<b>250</b>	<b>0</b>	<b>217</b>

Non-current financial assets consist mainly of guarantee deposits paid under operating lease agreements and the cash reserve related to the liquidity agreement (refer to section "Capital management" in note 9).

### NOTE 4 Additional information regarding deferred taxes

The company cannot determine with sufficient reliability when it will be able to absorb its accumulated tax loss. Therefore, no deferred tax asset related to these losses was recognized.

Prior carryforward losses that may give rise to deferred tax assets totaled €95.9 million at December 31, 2017 and €115.5 million at December 31, 2018.

### NOTE 5 Inventories

<i>In (€) thousands</i>	12/31/2018	12/31/2017
Raw materials	131	99
Semi-finished products		
Finished products		
<b>TOTAL NET VALUE</b>	<b>131</b>	<b>99</b>

The net value of inventories was €99,000 at December 31, 2017 and €131,000 at December 31, 2018.

Impairment was recorded for the inventories, mainly for products related to a project which the company recognized as a failure.

### NOTE 6 Trade receivables

<i>In (€) thousands</i>	12/31/2018	12/31/2017
Gross amount	3	30
Impairment		
<b>TOTAL NET VALUE</b>	<b>3</b>	<b>30</b>

At the end of 2018, trade receivables included only rent on properties and related occupancy expenses.

### NOTE 7 Other current assets

<i>In (€) thousands</i>	12/31/2018	12/31/2017
Research tax credit	6 368	7 535
Accrued income - Eli Lilly arbitration	11 915	0
VAT claims	1 001	861
Receivables from suppliers	247	298
Pre-paid expenses	1 046	649
Carry-back	333	333
Miscellaneous	100	108



<b>TOTAL NET VALUE</b>	<b>21 009</b>	<b>9 785</b>
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All other current assets have a maturity of less than one year.

Since its inception, the company has been entitled to a research tax credit (CIR). At the end of each period, it therefore recognizes as a receivable the amount of the tax credit calculated for the eligible expenses during the year. In 2017 and 2018, the company cannot apply its CIR and its tax credit for competitiveness and employment (CICE) to any tax liability. It therefore requested immediate reimbursement of the CIR (because of its status as a European SME) and recognized the amounts of €7.5 million and €6.4 million, respectively, under current assets.

The first phase the arbitration proceedings initiated by Adocia against Lilly outcome favorably for the Company. The Arbitration Tribunal ordered Lilly to pay the disputed milestone payment of \$11.6 million, or €10.3 million, plus interests (accrued end of December for \$1.6 million). The payment of this total receivable of €11.9 million at the end of December 2018 is expected in 2019, after the conclusion of the second phase of the arbitration.

Prepaid expenses relate to current expenses.

In addition to social security claims and other creditors, the miscellaneous item includes grants receivable.

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#### NOTE 8 Classification and fair value of financial assets

The only financial assets measured at fair value are cash and cash equivalents, which include mutual funds, time accounts quoted in an active market and interest-bearing accounts. They therefore constitute level 1 financial assets at fair value.

<i>In (€) thousands</i>	12/31/2018 Balance sheet value	Value on the balance sheet under IAS 39				12/31/2018 Fair value
		Assets at fair value through profit or loss	Held-to-maturity investments	Loans and receivables	Available-for-sale financial assets	
Cash on hand	32 748	32 748				32 748
Cash equivalents (UCITS)	7 093	7 093				7 093
<b>TOTAL ASSETS</b>	<b>39 841</b>	<b>39 841</b>				<b>39 841</b>

#### NOTE 9 Equity

For easier cross-reference between the periods, the number of shares in fiscal year 2011 has been restated to reflect the decision by the shareholders' meeting on October 24, 2011 to approve a 10-for-1 stock split and to grant 10 shares, each with a par value of €0.10, for a previously held share with a par value of €1.

Annual financial statements at December 31, 2018

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	Number of shares (*)	Ordinary shares	Preferred shares - cat. A	Preferred shares - cat. B	Nominal amount (euros)
<b>AT JANUARY 1, 2007</b>	<b>140 000</b>			<b>140 000</b>	<b>1 400 000</b>
10/19/2007 - Capital increase	93 339		93 339		933 390
12/20/2007 - Capital increase	46 668		46 668		466 680
10/22/2009 - Reduction of par value					(2 520 063)
10/22/2009 - Capital increase	119 007		119 007		119 007
01/20/2010 - Grant of bonus shares	1 050	1 050			1 050
04/06/2010 - Capital increase	5 424		5 424		5 424
06/06/2010 - Grant of bonus shares	140	140			140
06/18/2010 - Capital increase	1 283		1 283		1 283
12/10/2010 - Capital increase	37 630		37 630		37 630
03/04/2011 - Grant of bonus shares	1 050	1 050			1 050
06/17/2011 - Grant of bonus shares	140	140			140
10/24/2011 - Reduction of par value and increase of number of shares	4 011 579	21 420	2 730 159	1 260 000	0
12/15/2011 - Grant of bonus shares	1 400	1 400			140
02/14/2012 - Issue of IPO shares	1 592 798	1 592 798			159 280
02/14/2012 - Conversion of preferred shares to ordinary shares		4 433 510	(3 033 510)	(1 400 000)	0
03/07/2012 - Grant of bonus shares	10 500	10 500			1 050
03/17/2012 - Issue of IPO shares	130 268	130 268			13 027
06/15/2012 - Grant of bonus shares	2 800	2 800			280
12/19/2012 - Grant of bonus shares	2 800	2 800			280
03/26/2013 - Grant of bonus shares	8 400	8 400			840
06/18/2013 - Grant of bonus shares	2 800	2 800			280
12/13/2013 - Grant of bonus shares	2 800	2 800			280
12/13/2013 - Grant of bonus shares	1 400	1 400			140
12/07/2014 - Grant of bonus shares	1 400	1 400			140
12/15/2014 - Grant of bonus shares	1 400	1 400			140
02/12/2015 - Grant of BSA	700	700			70
03/03/2015 - Exercice of BSPCE	700	700			70
03/27/2015 - Exercice of BSPCE	1 400	1 400			140
03/31/2015 - Issue of IPO Shares by private placement	621 887	621 887			62 189
03/31/2015 - Grant of bonus shares	1 400	1 400			140
07/28/2015 - Exercice of BSPCE	2 800	2 800			280
12/16/2015 - Grant of bonus shares	1 400	1 400			140
06/21/2016 - Exercice of BSPCE	700	700			70
12/13/2016 - Grant of bonus shares	12 700	12 700			1 270
06/27/2017 - Grant of bonus shares	2 000	2 000			200
12/10/2017 - Grant of bonus shares	36 290	36 290			3 629
12/13/2017 - Grant of bonus shares	10 000	10 000			1 000
12/16/2017 - Grant of bonus shares	2 700	2 700			270
03/15/2018 - Grant of bonus shares	6 000	6 000			600
04/06/2018 - Exercice of bonus shares	91	91			9
12/13/2018 - Grant of bonus shares	9 325	9 325			933
12/14/2018 - Grant of bonus shares	2 375	2 375			238
12/16/2018 - Grant of bonus shares	2 700	2 700			270
<b>AT DECEMBER 31, 2018</b>	<b>6 931 244</b>	<b>6 931 244</b>	<b>0</b>	<b>0</b>	<b>693 124</b>

## Share capital

The company was created on December 22, 2005. All the shares issued are fully paid-up.

The company owns treasury shares under its liquidity agreement.

Following the initial public offering, preferred shares were converted into ordinary shares and the Ratchet stock warrants became null and void.

## Stock warrants

Stock options were granted to (i) certain employees in the form of start-up company stock warrants ("BSPCE") and stock options ("SO"), (ii) two independent directors on the Board of Directors in the form of ordinary stock warrants ("BSA") and (iii) scientific consultants in the form of ordinary stock warrants ("BSA").

The main characteristics of these share-based compensation plans are described in detail in section 5.1.5 of this registration document.

Operating expenses related to the stock option plans are calculated on the basis of a Black-Scholes model. The following parameters are used:

- volatility takes into account both the historical volatility observed in the stock market over a five-year period and implied volatility as measured by the options exchange. Periods of abnormal volatility are excluded from the observations;
- the risk-free interest rate used is the long-term government borrowing rate.

The cost of services rendered is recognized as an expense over the vesting period. This expense amounted to €0.6 million in 2018 compared to €0.5 million in 2017.

The following table shows the main characteristics of the payment plans giving a right to stock options:

Plan date and number	Recipients	Performance conditions	Vesting period	Strike price (euros)
BSPCE 2013 N°1	Employees	No	Until 01/01/2018	5.76
BSPCE 2013 N°2	Employees	No	Until 01/01/2018	5.76
BSA 2013	Independent directors	No	Until 01/01/2016	5.88
BSPCE 2014 N°1	Employees	No	Until 01/01/2018	34.99
BSPCE 2014 N°2	Employees	No	Until 01/01/2019	34.99
BSPCE 2014	Employees et corporate officers	Yes	Immediate vesting upon fulfillment of relevant performance criteria	34.99
SO 2015 N°1	Employees	No	Until 01/01/2019	55.64
SO 2015 N°2	Employees	No	Until 01/01/2020	71.12
BSPCE 2015	Corporate officer	Yes	Immediate vesting upon fulfillment of relevant performance criteria	74.6
BSPCE 2016	Corporate officer	Yes	Immediate vesting upon fulfillment of relevant performance criteria	61.73
BSA 2017	Consultant	Yes	Immediate vesting upon fulfillment of relevant performance criteria	20.65
SO 2017 N°1	Employee	No	Until 01/01/2020	18.00
SO 2017 N°2	Employee	No	Until 01/01/2021	18.00
BSPCE 2017	Corporate officer	Yes	Immediate vesting upon fulfillment of relevant performance criteria	16.00
SO 2018	Employees	No	Until 05/02/2022	17.00

The number of options granted are presented in the following table:

Plan date and number	Number of granted warrants	Number of cancelled warrants	Number of exercised warrants	Number of vested warrants	Warrants not yet vested	Initial value (in € thousands)
BSPCE 2013 N°1	28 000		4 900	23 100		107
BSPCE 2013 N°2	22 400		700	21 700		85
BSA 2013	20 000			20 000		69
BSPCE 2014 N°1	14 000	2 800		11 200		429
BSPCE 2014 N°2	5 600	5 600				172
BSPCE 2014	100 000			100 000		3 063
SO 2015 N°1	20 000	20 000				732
SO 2015 N°2	4 000	4 000				201
BSPCE 2015	40 000			40 000		2 220
BSPCE 2016	40 000	16 000		24 000		1 238
BSA 2017	40 000			15 000	25 000	307
SO 2017 N°1	13 000			9 750	3 250	375
SO 2017 N°2	40 000	39 909	91			375
BSPCE 2017	150 000			50 000	100 000	579
SO 2018	23 000			5 500	17 500	217
<b>TOTAL</b>	<b>560 000</b>	<b>88 309</b>	<b>5 691</b>	<b>320 250</b>	<b>145 750</b>	<b>10 168</b>

#### Bonus shares

Bonus shares have been granted to certain employees and managers of the company since 2008. The number of shares granted are presented in the following table:

Plan date and number	Number of shares initially granted	Number of cancelled shares	Number of vested shares	Number of shares with ongoing vesting
2008 Plan N°1	42 000	2 100	39 900	
2008 Plan N°2	5 600		5 600	
2009 Plan	5 600		5 600	
2010 Plan N°1	5 600		5 600	
2010 Plan N°2	5 600		5 600	
2015 Plan N°1 - 10 years	39 150	2 860	36 290	
2015 Plan N°2.1	5 000		5 000	
2015 Plan N°2.2	12 600	1 800	8 100	2 700
2015 Plan Corporate officers	5 000		5 000	
2016 Plan Corporate officers	20 000	8 000	8 000	4 000
2016 Plan N°2	40 000	2 025	19 325	18 650
2017 Plan	9 500		2 375	7 125
2018 Plan N°1	2 700			2 700
2018 Plan N°2	19 050	1 330		17 720
2018 Plan N°3	5 600			5 600
2018 Plan N°4	5 600			5 600
2018 Plan N°5	11 600			11 600
<b>TOTAL</b>	<b>240 200</b>	<b>18 115</b>	<b>146 390</b>	<b>75 695</b>

Movements in bonus shares are as follows:

<i>Number of shares</i>	<b>FY 2018</b>	<b>FY 2017</b>
Number of shares with ongoing vesting at the beginning of the year	62 900	105 755
Shares granted during the year	44 550	9 500
Shares vested during the year	20 400	50 990
Shares cancelled during the year	11 355	1 365
<b>NUMBER OF SHARES WITH ONGOING VESTING AT THE END OF THE YEAR</b>	<b>75 695</b>	<b>62 900</b>

The cost of services rendered is recognized as a payroll expense over the vesting period. This expense amounted to €0.9 million in 2018 compared to €2.6 million in 2017.

### Dividends

The company has not paid out any dividends over the last three years.

### Capital management

The group's policy is to maintain a solid capital base in order to safeguard investor and creditor confidence and support future business development.

On May 19, 2014, Adocia signed a liquidity agreement with Kepler Capital Market following the termination of a previous agreement with DSF Markets. Adocia allocated 15,026 Adocia shares and €300,000 in cash to this new agreement.

Under the terms of the liquidity agreement, on February 10, 2015 the company decided to reduce the resources allocated to this agreement by €700,000. On September 10, 2015, the resources made available under the liquidity agreement with Kepler Capital Markets S.A. were increased by €200,000.

Over the course of 2018, the share buyback program was used only in connection with the liquidity agreement to meet the objective of making a market in the company's shares and increasing their liquidity.

On February 12, 2018, the resources made available under the liquidity agreement with Kepler Capital Markets S.A. were increased by €250,000.

As of December 31, 2018, the company had 10,555 shares and €214,471 allocated to the liquidity account under this agreement.

### NOTE 10 Long-term financial debt

Long-term financial debt includes bank loans and repayable advances. The repayable advances were classified, in 2017 reference document, in other financial liabilities for the short-term part, which amounted to €0.2 million.

Bank loans in the amount of €5.5 million were obtained in 2016 to finance the purchase of the building in which the company's research center and head office are located. An additional amount of €0.3 million was released in 2017. At end-December 2018, the amount of financial debt related to these loans was €4.9 million, €4.4 million of which was long-term.

At the end of 2018, the classification as current and non-current was as follows:

<i>In (€) thousands</i>	<b>Current</b>	<b>Non-current</b>	<b>Total</b>	<b>Bank overdrafts</b>
Reimbursable advances	194	302	496	0
Bank Loans	1 783	4 391	6 174	0
Other financial debts	247	200	447	0
<b>TOTAL FINANCIAL DEBT</b>	<b>2 224</b>	<b>4 892</b>	<b>7 117</b>	<b>0</b>

Details about advances granted and repaid in 2018:

<i>In (€) thousands</i>	Amount	Historical cost
<b>VALUE AT DECEMBER 31, 2017</b>	<b>717</b>	<b>761</b>
Long term portion	481	
Short term portion	236	
Grant during the year		
Repayment during the year	(241)	(241)
Discount on grant during the year		
Financial expenses	20	
<b>VALUE AT DECEMBER 31, 2018</b>	<b>496</b>	<b>520 (*)</b>
Long term portion	302	
Short term portion	194	

<i>(*) in € thousands</i>	12/31/2018	Less than 1 year	1 to 5 years	More than 5 years
Avance Insuline (2012)	520	200	320	-
<b>TOTAL</b>	<b>520</b>	<b>200</b>	<b>320</b>	<b>,</b>

<i>In (€) thousands</i>	12/31/2017	New debt	Repayment	Currency fluctuation	12/31/2018
Reimbursable advances	717	0	(221)	0	496
Bank Loans	6 151	1 310	(1 287)	0	6 174
Other financial debts	704	0	(257)	0	447
<b>TOTAL FINANCIAL DEBT</b>	<b>7 571</b>	<b>1 310</b>	<b>(1 764)</b>	<b>0</b>	<b>7 117</b>

<i>In (€) thousands</i>	12/31/2018		
	Balance sheet value	Fair value	Breakdown by category of instrument Fair value through the income statement    Debt at amortized cost
Reimbursable advances	496	496	496
Other financial debts	6 621	6 621	6 621
<b>TOTAL FINANCIAL DEBT</b>	<b>7 117</b>	<b>7 117</b>	<b>7 117</b>

**NOTE 11 Provisions**

<i>In (€) thousands</i>	Employee benefits	Other long-term provisions	Provisions for risks and charges - less than one year	TOTAL
<b>VALUE AT DECEMBER 31, 2017</b>	<b>2 241</b>	<b>0</b>	<b>0</b>	<b>2 241</b>
Additions	514			514
Reversal of used provisions				0
Reversal of unused provisions				0
<b>VALUE AT DECEMBER 31, 2018</b>	<b>2 756</b>	<b>0</b>	<b>0</b>	<b>2 756</b>

Provisions consist mainly of the provision for retirement benefits. This provision was estimated based on the terms of the applicable collective agreement, i.e. collective agreement 176.

Regarding Adocia arbitration claims against Eli Lilly & Company arising out of Lilly's misappropriation and improper use of Adocia's confidential information and discoveries as well as Lilly's breaches of several collaboration and confidentiality agreements, Adocia is seeking monetary damages in excess of \$1.3 billion (before taking into account the interests pre-and post judgement) as well as others specific relief.

The Company is pursuing vigorously its legal action to assert its rights. It considers that Lilly's counter-claims of \$ 188 million are unfounded.

The decision of the Arbitral Tribunal is expected in the third quarter of 2019.

The main actuarial assumptions used to value retirement benefits are as follows:

<i>In (€) thousands</i>	12/31/2018	12/31/2017
<b>Economic assumptions</b>		
Discount rate	1.55%	1.30%
Rate of annual salary increase	5%	between 5 and 6%
<b>Demographic assumptions</b>		
Retirement age	between 62 and 67 years	between 62 and 67 years
Type of retirement	Initiated by employee	Initiated by employee
Mortality table	INSEE 11-13	INSEE 10-12
Rate of tax and social security charges	44.50%	44.50%
Annual mobility	Average or High depending on category	Average or High depending on category
Present value of obligations	2 756	2 241
Payments to a fund		
<b>Provision recorded on the balance sheet</b>	<b>2 756</b>	<b>2 241</b>
Past service costs for the period	324	286
Financial expense	33	26
Actuarial gains and losses	(156)	(191)
Annual expense	358	313

#### NOTE 12 Trade payables and other current liabilities

The company's current liabilities are as follows:

<i>In (€) thousands</i>	12/31/2018	12/31/2017
<b>Trade payables</b>	<b>7 546</b>	<b>4 931</b>
Subsidiary accounts	3 657	1 617
Notes payable		
Invoices pending	3 889	3 314
<b>Other current liabilities</b>	<b>5 084</b>	<b>2 160</b>
Customer credit balances		
Tax and social security liabilities	2 750	2 122
Other debt	20	39
Unearned income	2 314	0
<b>TOTAL CURRENT OPERATING LIABILITIES</b>	<b>12 630</b>	<b>7 091</b>

## Annual financial statements at December 31, 2018

Trade payables reached €7.5 million as of December 31, 2018 compared to €4.9 million as of December 31, 2017 which reflects the intense activity at the end of 2018 with, mainly, the Arbitration Tribunal hearings that held in December 2018 as part of the arbitration procedure launched against Eli Lilly.

Unearned income accounted for at the end of 2018, for €2.3 million, corresponds to the short-term part of the not-yet recognized revenue from Tonhua Dongbao's upfront payment.

All trade payables and other current liabilities have a maturity of less than one year.

Tax and staff cost liabilities are as follows:

<i>In (€) thousands</i>	<b>12/31/2018</b>	<b>12/31/2017</b>
Compensation owed	959	752
Debt owed to social welfare agencies	1 311	1 197
Other tax and social security liabilities	480	173
<b>TOTAL TAX AND SOCIAL DEBTS</b>	<b>2 750</b>	<b>2 122</b>

Compensation owed as of December 31, 2018 increased compared to last year because of the increase of the accrual for paid holiday.

Other tax and staff cost liabilities at December 31, 2018 included an accrual for the value-added contribution tax (CVAE) for €0.3 million, compared to none at the end of 2017.

<i>In (€) thousands</i>	<b>12/31/2018</b>	<b>31/12/2017</b>
Advances and payments on account		
Other	20	39
<b>TOTAL OTHER DEBTS</b>	<b>20</b>	<b>39</b>

### NOTE 13 Other non-current liabilities

Other non-current liabilities amounted to €1.7 million at December 31, 2018 and include the long-term part of the unearned revenue from Tonghua Dongbao's upfront payment in April 2018.

### NOTE 14 Operating profit/loss

<i>In (€) thousands</i>	Notes	<b>FY 2018 (12 months)</b>	<b>FY 2017 (12 months)</b>
<b>Operating revenue</b>		<b>53 930</b>	<b>27 177</b>
Revenue	15	47 389	19 469
Grants, research tax credits and others	16	6 541	7 708
<b>Operating expenses</b>		<b>(44 223)</b>	<b>(35 358)</b>
Purchases used in operations		(2 188)	(1 740)
Payroll expense	18	(14 807)	(13 368)
External expenses	17	(25 630)	(19 019)
Taxes and contributions		(553)	(217)
Dotation aux amortissements et provisions	19	(1 044)	(1 013)
Other current operating income and expenses		0	(0)
<b>PROFIT (LOSS) FROM ORDINARY OPERATING ACTIVITIES</b>		<b>9 707</b>	<b>(8 180)</b>



Breakdown of expenses by function:

<i>In (€) thousands</i>	<b>FY 2018 (12 months)</b>	<b>FY 2017 (12 months)</b>
Research and development expenses	(25 760)	(27 074)
General and administrative expenses	(18 463)	(8 284)
<b>OPERATING EXPENSES</b>	<b>(44 223)</b>	<b>(35 358)</b>

General and administrative expenses amounted to €18.5 million in 2018 compared to €8.3 million in 2017. This increase of €10.2 million is mainly due, for an amount of €8.3 million, to the legal expenses related to the current litigation proceedings and, for an amount of €1.5 million, to the increase in staff expenses, notably following the payment of performance bonuses to employees, as a result of the signature of the partnership with THDB.

Research and development costs were as follows:

<i>In (€) thousands</i>	<b>FY 2018 (12 months)</b>	<b>FY 2017 (12 months)</b>
Purchases used in operations	(2 188)	(1 740)
Payroll expense	(9 142)	(8 121)
Share-based payments	(722)	(1 634)
External expenses	(12 567)	(14 638)
Taxes and contributions	(339)	(131)
Depreciation, amortization & provisions	(801)	(809)
<b>OPERATING EXPENSES</b>	<b>(25 760)</b>	<b>(27 074)</b>

#### NOTE 15 Revenue

<i>In (€) thousands</i>	<b>FY 2018 (12 months)</b>	<b>FY 2017 (12 months)</b>
Research and collaborative agreements	0	650
Licencing revenues	47 389	18 819
<b>REVENUE</b>	<b>47 389</b>	<b>19 469</b>

Revenue of €47.4 million in 2018 resulted up to €37.1 million from the partnership and licensing agreement signed with Tonghua Dongbao Pharmaceuticals Co. Ltd (THDB) in April 2018. It reflects the rights thus granted to THDB to develop, manufacture, and commercialize BioChaperone® Lispro and BioChaperone® Combo in China and other territories in Asia and the Middle-East.

By the end of December 2018, licensing revenues also included an amount of \$11.6 million (€10.3 million) corresponding to a contractual milestone payment contested by Lilly, for which Adocia obtained a favorable arbitration judgement in August 2018. The payment is expected to be received in 2019 after the conclusion of the second phase of the arbitration.

These contracts concern projects, with independant developments, considered as distincts.

According to them, the Company:

- receives upfront payments amounting to 40 million dollars (BC Combo) and 10 million dollars (BC Lispro), paying for licenses and exclusive rights granted to Tonghua Dongbao as well as the transfer of know-how and related services,
- could benefit from the reimbursement of specific research and development expenses initiated at the request of Tonghua Dongbao,

- is entitled to receive development milestone payments up to 50 million dollars for BC Combo and 35 million dollars for BC Lispro,
- is expected to receive royalties on the sale of both products in the territories.

The Company analyzes the licence and the transfer of know-how as two distinct performance obligations:

The licences granted by the Company are rights of use. Indeed, as soon as the contract signature, Tonghua Dongbao can assimilate the production process of both combinations, adapt it to its productive equipment and lead the clinical development of BC Combo and BC Lispro.

As static licences, the performance obligation is satisfied immediately. As a consequence, the revenue from licences is recognized immediately from the date the customer can start using the licence.

The transfer of know-how and the related services aim at facilitating the progress of the project by allowing Tonghua Dongbao to benefit from the Company's expertise by providing a technical and regulatory support.

The expected services:

- will not impact the granted patents
- could be done by Tonghua Dongbao independantly of the Company. However, Adocia's experience and skills enable an optimum efficiency in the development of the projects with shorter deadlines.

This performance obligation is satisfied progressively during the services execution.

The revenue from these services is recognized according to a percentage of completion, calculated by comparison between the costs incurred and the total estimated budget for the contract period.

The price of each contract corresponds to the upfront payment only. Milestone payments will be included to the price of the contract when they become highly probable.

Regarding the royalties calculated on sales made by Tonghua Dongbao, the Company applies the exception to the general principle provided by the IFRS 15 standard on variable payments. Royalties will be recognized as revenue when the Tonghua Dongbao's sales occur.

Each performance obligation fair value was estimated by an NPV calculation for licences and by an expenses budget for the services provided by the Company. However, in the context of the contracts signed with Tonghua Dongbao, an allocation of the contract price, for which the variable payments were excluded, to each performance obligation proportionally to their fair value does not allow to completely offset the costs of services provided by the Company to Tonghua Dongbao. As a consequence, in the half-year financial statements, the Company applies the residual method to allocate the upfront payment to both performance obligations.

The Company's revenue for the fiscal year 2018 amounted to €47.4 million, of which €37.1 million were due to the two products licensed to Tonghua Dongbao.

The outstanding amount of the \$50 million, or €41.1 million, that reached €4 million will be recognized according to the percentage of completion of the research and development services provided by the Company as part of the products transfer and development.

#### NOTE 16 Other income

<i>In (€) thousands</i>	<b>FY 2018 (12 months)</b>	<b>FY 2017 (12 months)</b>
Research tax credit	6 368	7 535
Other	173	173
<b>OTHER INCOME</b>	<b>6 541</b>	<b>7 708</b>

The Research Tax Credit amounted to €6.4 million at December 31, 2018 compared to €7.5 million at December 31, 2017. This slight decrease is in line with the smaller amount of research and development costs recorded for the year and eligible to the tax credit.

A portion of the premises owned by Adocia is leased to companies, resulting in €0.2 million of lease income shown on the "other income" line.

#### NOTE 17 Other purchases and external charges

Purchases and external charges mainly consist of the company's in-vivo studies, preclinical and clinical studies, subcontracting and all its operating expenses, including the expenses for claim procedures against Eli Lilly.

#### NOTE 18 Payroll expense

Payroll expense was as follows:

<i>In (€) thousands</i>	<b>FY 2018 (12 months)</b>	<b>FY 2017 (12 months)</b>
Wages and salaries	9 473	8 015
Social contributions	3 854	2 829
Share-based payment	1 480	2 525
<b>PAYROLL EXPENSE</b>	<b>14 807</b>	<b>13 368</b>
	<b>31/12/2018</b>	<b>31/12/2017</b>
Technicians	58	59
Management personnel	74	70
<b>STAFF</b>	<b>132</b>	<b>129</b>

At December 31, 2018, the company had 52 postdoctoral researchers. Nearly 80% of employees are directly assigned to research and development activities.

#### NOTE 19 Depreciation, amortization and impairment

Net depreciation, amortization and provisions were as follows:

<i>In (€) thousands</i>	<b>FY 2018 (12 months)</b>	<b>FY 2017 (12 months)</b>
<b>Depreciation, amortization and provisions for fixed assets</b>	<b>1 038</b>	<b>1 008</b>
Depreciation of property, plant and equipment	768	756
Amortization of intangible assets	20	12
Depreciation of leased assets	250	239
<b>Depreciation, amortization and provisions for fixed assets</b>	<b>6</b>	<b>5</b>
Provisions for current assets (additions)	6	5
<b>DEPRECIATION, AMOTIZATION AND IMPAIRMENT</b>	<b>1 044</b>	<b>1 013</b>

#### NOTE 20 Financial income/expense

The cost of net financial debt was as follows:

<i>In (€) thousands</i>	<b>FY 2018 (12 months)</b>	<b>FY 2017 (12 months)</b>
<b>Cost of net financial debt</b>	<b>1 510</b>	<b>(35)</b>
Cash and cash equivalents income	1 659	76
Interest on conditional advances	(149)	(110)
<b>Foreign exchange gains and losses</b>	<b>574</b>	<b>(256)</b>
<b>Other financial income and expenses</b>	<b>(33)</b>	<b>(45)</b>
<b>FINANCIAL INCOME (LOSS)</b>	<b>2 051</b>	<b>(335)</b>

The financial income of €2.1 million is mainly due to the accrued interests awarded by the Arbitration Tribunal in the first phase of the arbitration procedure initiated by Adocia against Lilly. They amounted to €1.6 million at December 31, 2018.

Exchange rates had a positive impact of €0.6 million. Currency fluctuations were classified, in 2017 reference document, as other financial income and expenses.

#### NOTE 21 Corporation tax

In 2018, Adocia SA had a tax profit subject to reduced tax rate of 15%. This tax profit generated corporation tax for €4.1 million, which will be fully paid by a tax credit related to the withholding tax applied, in China, on Tonghua Dongbao's upfront payment.

The amount of carryforward tax losses amounted to €115.5 million. This carryforward loss is not limited in time. Since the company cannot determine with sufficient reliability when it will be able to absorb its accumulated tax loss, it did not recognize a deferred tax asset for this loss.

The difference between pre-tax profit/loss and the actual tax expense in the consolidated financial statements under IFRS is shown below:

<i>In (€) thousands</i>	<b>FY 2018 (12 months)</b>	<b>FY 2017 (12 months)</b>
<b>PROFIT (LOSS) BEFORE TAX</b>	<b>11 758</b>	<b>(8 516)</b>
National tax at the period standard rate	(4 048)	2 932
Permanent differences	11 512	1 717
Uncapitalized tax loss adjusted for deferred tax	(11 607)	(4 684)
<b>ACTUAL TAX EXPENSE</b>	<b>(4 144)</b>	<b>(35)</b>
<i>Effective tax rate</i>	35%	0%

#### NOTE 22 Earnings per share

	<b>FY 2018 (12 months)</b>	<b>FY 2017 (12 months)</b>
<b>CONSOLIDATED NET PROFIT / LOSS (in euros thousands)</b>	<b>7 615</b>	<b>(8 550)</b>
Average number of shares	6 916 270	6 863 485
<b>NET EARNINGS (LOSS) PER SHARE (in euros)</b>	<b>1,1</b>	<b>(1,2)</b>
<b>NET EARNINGS (LOSS) PER SHARE FULLY DILUTED (in euros)</b>	<b>1,0</b>	<b>(1,2)</b>

#### NOTE 23 Related parties and compensation of the corporate officers

The main related parties are the key executives of the company and its directors.

Remuneration paid to related parties is described in the table below.

<i>In (€) thousands</i>	<b>FY 2018 (12 months)</b>	<b>FY 2017 (12 months)</b>
Short-term benefits	1 035	728
Posterior employment benefits	107	92
Share-based payment	517	290
<b>TOTAL COMPENSATION PAID TO CORPORATE OFFICERS</b>	<b>1 658</b>	<b>1 109</b>

## **NOTE 24 Financial risk management objectives and policies**

### Foreign exchange risk

Foreign exchange risk is the risk that the fair value or future cash flows of a financial instrument will fluctuate due to changes in foreign exchange rates. The company's strategy is to enter into agreements denominated in euros, because its expenditures are also largely denominated in euros.

However, as a result of the partnership and licensing agreement signed with Tonghua Dongbao Pharmaceuticals Co. Ltd (THDB) to develop, manufacture, and commercialize BioChaperone® Lispro and BioChaperone® Combo in China and other territories in Asia and the Middle-East, a major part of the company's revenues, in addition to the upfront payment received in connection with that agreement, were denominated in US dollars. As a result, the company was exposed to risk in relation to fluctuations in the euro-US dollar exchange rate, as it had been during the collaborative and licensing agreements with Eli Lilly, between December 2011 and July 2013 and between December 2014 and January 2017.

Significant growth in the company's business may create more exposure to foreign exchange risk. In that case, the company will consider adopting a new policy appropriate to hedging this risk, such as currency hedging transactions and the purchase of foreign exchange forward contracts.

### Credit risk

The receivables related to government grants and the research tax credit pose a credit risk that is considered immaterial in light of the company's history.

Credit risk related to cash, cash equivalents and current financial instruments is immaterial given the quality of the contracting financial institutions.

Regarding its customers, the company believes it is not very exposed to credit risk given the types of customers with whom it has partnership agreements (large global pharmaceutical companies). Furthermore, it has implemented policies that ensure that its customers have an appropriate level of credit risk.

### Liquidity risk

The company obtains financing under a policy implemented by the Finance Department.

The structure of the company's financing is based primarily on equity, the use of public financing (Bpifrance Financement – ex OSEO) and an initial public offering.

### Interest rate risk

In 2016, the company took out a loan from two banks to finance the acquisition of the building in which its research center and headquarters are located. These loan agreements were negotiated at a fixed rate for a 12-year term.

The company is exposed to changes in interest rates in the course of managing its cash and cash equivalents. The company's cash and cash equivalents totaled close to €35 million at December 31, 2017 and close to €40 million at December 31, 2018. This item includes term deposits, accounts that pay fixed interest and investments in money market mutual funds. The company's policy is to invest exclusively in liquid products with no capital risk.

## Annual financial statements at December 31, 2018

The company strives to reduce the credit risk to which its cash and cash equivalents are exposed by monitoring the quality of the financial institutions to which it entrusts its investments.

The company has no guarantee that it will obtain the same interest rates when it renews its time-deposit accounts at maturity.

### Equity risk

The company has no non-consolidated holdings or investment securities tradable on a regulated market.

### **NOTE 25 Off-balance sheet commitments**

When obtaining the loans used to purchase the building and parking spaces, the company provided the following guarantees:

- a lender's lien and subrogation in the seller's lien for the purchase amount of the building,
- a mortgage on the construction budget.

The company also made a term deposit of €1.5 million as security for a line of credit provided by a bank to finance part of the legal costs related to the applications for arbitration against Lilly.

### **NOTE 26 Events subsequent to year end**

None.

## 4.2 Statutory auditors' report on the consolidated financial statements

ODICEO  
115, boulevard de Stalingrad  
CS 52038  
69616 Villeurbanne cedex  
S.A. au capital de € 275.000  
430 130 393 R.C.S. Lyon

Commissaire aux Comptes  
Membre de la compagnie  
régionale de Lyon

ERNST & YOUNG et Autres  
Tour Oxygène  
10-12, boulevard Marius Vivier Merle  
69393 Lyon Cedex 03  
S.A.S. à capital variable  
438 476 913 R.C.S. Nanterre

Commissaire aux Comptes  
Membre de la compagnie  
régionale de Versailles

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### Adocia

Year ended December 31, 2018

#### Statutory auditors' report on the consolidated financial statements

To the Annual General Meeting of Adocia,

#### Opinion

In compliance with the engagement entrusted to us by your Annual General Meetings, we have audited the accompanying consolidated financial statements of Adocia for the year ended December 31, 2018.

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 December 31, 2018 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.

The audit opinion expressed above is consistent with our report to the Audit Committee.

#### Basis for Opinion

##### ■ Audit Framework

We conducted our audit in accordance with professional standards applicable in France. We believe that the audit evidence we have obtained is sufficient and appropriate to provide a basis for our opinion.

Our responsibilities under those standards are further described in the Statutory Auditors' Responsibilities for the Audit of the Consolidated Financial Statements section of our report.

##### ■ Independence

We conducted our audit engagement in compliance with independence rules applicable to us, for the period from January 1, 2018 to the date of our report and specifically we did not provide any prohibited non-audit services referred to in Article 5(1) of Regulation (EU) No 537/2014 or in the French Code of Ethics (Code de déontologie) for statutory auditors.

**Justification of Assessments - Key Audit Matters**

In accordance with the requirements of Articles L. 823-9 and R. 823-7 of the French Commercial Code (Code de commerce) relating to the justification of our assessments, we inform you of the key audit matters relating to risks of material misstatement that, in our professional judgment, were of most significance in our audit of the consolidated financial statements of the current period, as well as how we addressed those risks.

These matters were addressed in the context of our audit of the consolidated financial statements as a whole, and in forming our opinion thereon, and we do not provide a separate opinion on specific items of the consolidated financial statements.

■ Arbitration against Eli Lilly & Company



Risk identified	Our response
<p>In February 2018, your Company announced through a press release filing new applications for arbitration against Eli Lilly &amp; Company for the appropriation and misuse by Lilly &amp; Company of confidential information and discoveries belonging to your company, as well as for the violation by Eli Lilly &amp; Company of several collaboration and confidentiality agreements. Your Company is claiming for these damages amounting to approximately USD 1.3 billion. As part of this second phase of the arbitration, Eli Lilly &amp; Company filed a counterclaim against your Company for an amount of approximately MUSD 188.</p> <p>Besides this action, and as mentioned in paragraph 4.1.6.1 and note 11 of the appendices of the consolidated financial statements, on October 9, 2018, Eli Lilly &amp; Company launched a civil action against your Company before the District Court of the Southern District of Indiana, United States, in order to obtain a declaratory judgment relating to inventors' designations for two of its U.S. patents on ultra-fast insulin formulations (US patent [Lilly] Nos. 9,901,623 and 9,993,555).</p> <p>As described in Note 11 to the consolidated financial statements, your company considered that Eli Lilly &amp; Company's applications are groundless and, as such, no provision has been recorded as at December 31, 2018.</p> <p>We considered this arbitration to be a key audit matter because of the importance of the compensation claimed by each of the two parties and of the level of judgement required to assess the arguments supporting the lack of provision relating to this arbitration and the relevance of information regarding this dispute provided in the Note to the consolidated financial statements.</p>	<p>In the context of our audit of the consolidated financial statements, our work mainly consisted in:</p> <ul style="list-style-type: none"> <li>▶ acknowledging the risk analysis carried out by your Company, the relevant documentation and examining, if necessary, the written consultations of the external councils;</li> <li>▶ making a request for confirmation from the lawyers in charge of this dispute;</li> <li>▶ assessing with the assistance of our experts, who spoke with the lawyers of the company, the risks presented by this arbitration and the assumptions adopted by Management to justify the absence of provision at the closing;</li> <li>▶ examining the appropriateness of the information relating to this risk presented in the Notes to the consolidated statements.</li> </ul>



■ Going concern

Risk identified	Our response
<p>Fiscal year 2017 ended with a loss of MEUR 8.6 and a cash burn amounted to MEUR 23.3 over the year. At 2018 year-end, your Group had negative reserves of MEUR 41.3 but a profit of MEUR 7.6 and an increase of its cash position of MEUR 5.1 (closing cash amounted to MEUR 39.8).</p> <p>Fiscal year 2018 was marked in particular by the establishment of a strategic alliance with Tonghua Dongbao Pharma Co for which your Company received a total upfront payment of M\$ 50. Moreover, while your Company's arbitration proceedings against Eli Lilly &amp; Company, the first part of that procedure was in favor of your Company, the Court ordered Eli Lilly &amp; Company to pay the disputed step worth of MUS\$ 11.6. The collection of the damages thus granted (amount of MUS\$ 11.6 plus interest) is expected in 2019, after the conclusion of the second part of the arbitration, as mentioned in the "Basis of preparation of the consolidated financial statements" section of Note 4.1.6.1 to the consolidated financial statements.</p> <p>As set out in the "Basis of preparation of the consolidated financial statements" section of Note 4.1.6.1 to the consolidated financial statements, the going concern assumption was applied at year-end given (i) the measures to select expenses relating to high-priority projects and activities for your Group and (ii) the ability to anticipate the collection of the research tax credit (credit d'impôt recherche).</p> <p>We considered the application of this principle to be a key audit matter as it is based on cash flow forecasts, which present a risk of not being achieved.</p>	<p>As part of our audit of the consolidated financial statements, we reviewed the financial statement forecasts presented to the Board of Directors and analyzed the detailed cash flow forecasts prepared by General Management for the period from January 1, 2019 to June 30, 2020. Our analyses consisted in:</p> <ul style="list-style-type: none"> <li>▶ assessing the consistency of the forecasts with the historical data;</li> <li>▶ evaluating the assumptions used by Management;</li> <li>▶ for a selection of planned outflows in respect of external expenditures for which your Group had made contractual commitments, reconciling the amounts applied with the agreements concerned;</li> <li>▶ for a selection of outflows relating to external expenses on studies for which your Company has not yet entered into agreements with suppliers, comparing the amounts applied with the data underlying the budgets approved by your Board of Directors and with the historical data relating to studies of the same type, to assess the frequency of invoicing;</li> <li>▶ analyzing the main data and assumptions (personnel expenses, external and internal expenditures) on which your Company's calculation of the research tax credit is based, and the expected date on which it will be received.</li> <li>▶ Lastly, we assessed whether the information provided in the "Information about the Company" section of Note 4.1.6.1 and in the "Basis of preparation of the financial statements" section of Note 4.1.6.2 to the consolidated financial statements was representative of your Group's situation.</li> </ul>

■ Revenue recognition related to licensing contracts entered into with Tonghua Dongbao Pharma Co

Risk identified	Our response
<p>In April 2018, your Company and Tonghua Dongbao Pharma Co announced the establishment of two licensing contracts for BioChaperone Lispro and BioChaperone Combo for the Chinese market and other markets in Asia and the Middle East. Your Company received a total initial payment of USD 50 million, or approximately MEUR 41.1.</p> <p>The recognition method of revenues generated from these contracts, in accordance with IFRS 15, is described in Note 15 to the consolidated financial statements. Thus, the initial payment was assigned to two performance obligations. MEUR 37.1 of turnover were recognized on the fiscal year under these licensing contracts entered into with Tonghua Dongbao. The deferred income written off from 2018, which amounts to MEUR 4, will be recorded in revenue following the advancement of research and development services provided by your Company, in the context of the transfer and development of products.</p> <p>In June 2018, the partnership with Tonghua Dongbao was strengthened by the implementation of two contracts for the supply of glargine and lispro insulins.</p> <p>We considered this subject as a key audit matter because of the importance of the income generated from these contracts and the level of judgement required to determine the rate of recognition of such income in the financial income statement, in particular as regards the progress of the identified performance obligations.</p>	<p>As part of our audit of the consolidated financial statements, our work included:</p> <ul style="list-style-type: none"> <li>▶ reviewing the licensing contracts on products developed by your Company: BioChaperone lispro and BioChaperone combo, and the supply contracts entered into with Tonghua Dongbao Pharma co;</li> <li>▶ understanding the methodology implemented by the client to identify the different performance obligations and then allocating part of the contract price thereto;</li> <li>▶ assessing the total budgeted costs for each performance obligation;</li> <li>▶ for each performance obligation, assessing the period of recognition of the income and the degree of advancement defined by the Company, regarding to the costs incurred. Therefore, we tested in particular a sample of the expenses incurred during the fiscal year relating to each performance obligation used in the calculation of the progress and therefore in the calculation of the income to be recognized over the period;</li> <li>▶ examining the appropriateness of the information relating to this accounting treatment set out in the Notes to the consolidated financial statements.</li> </ul>

#### Specific verifications

We have also performed, in accordance with professional standards applicable in France, the specific verifications required by laws and regulations of the information pertaining to the Group presented in the Board of Directors' management report.

We have no matters to report as to its fair presentation and its consistency with the consolidated financial statements.

## Report on Other Legal and Regulatory Requirements

### ■ Appointment of the Statutory Auditors

We were appointed as statutory auditors of Adocia by Decision of the Sole Shareholder of December 10, 2011 for ODICEO and by your Annual General Meeting held on October 24, 2011 for ERNST & YOUNG et Autres.

As at December 31, 2018, ODICEO and ERNST & YOUNG et Autres were in the eighth year of total uninterrupted engagement, including seven years since securities of the Company were admitted to trading on a regulated market.

## Responsibilities of Management and Those Charged with Governance for the Consolidated Financial Statements

Management is responsible for the preparation and fair presentation of the consolidated financial statements in accordance with International Financial Reporting Standards as adopted by the European Union and for such internal control as management determines is necessary to enable the preparation of consolidated financial statements that are free from material misstatement, whether due to fraud or error.

In preparing the consolidated financial statements, management is responsible for assessing the Company's ability to continue as a going concern, disclosing, as applicable, matters related to going concern and using the going concern basis of accounting unless it is expected to liquidate the Company or to cease operations.

The Audit Committee is responsible for monitoring the financial reporting process and the effectiveness of internal control and risks management systems and where applicable, its internal audit, regarding the accounting and financial reporting procedures.

The consolidated financial statements were approved by the Board of Directors.

## Statutory Auditors' Responsibilities for the Audit of the Consolidated Financial Statements

### ■ Objectives and audit approach

Our role is to issue a report on the consolidated financial statements. Our objective is to obtain reasonable assurance about whether the consolidated financial statements as a whole are free from material misstatement. Reasonable assurance is a high level of assurance, but is not a guarantee that an audit conducted in accordance with professional standards will always detect a material misstatement when it exists. Misstatements can arise from fraud or error and are considered material if, individually or in the aggregate, they could reasonably be expected to influence the economic decisions of users taken on the basis of these consolidated financial statements.

As specified in Article L.823-10-1 of the French Commercial Code (Code de commerce), our statutory audit does not include assurance on the viability of the Company or the quality of management of the affairs of the Company.

As part of an audit conducted in accordance with professional standards applicable in France, the statutory auditor exercises professional judgment throughout the audit and furthermore:

- ▶ Identifies and assesses the risks of material misstatement of the consolidated financial statements, whether due to fraud or error, designs and performs audit procedures responsive to those risks, and obtains audit evidence considered to be sufficient and appropriate to provide a basis for his opinion. The risk of not detecting a material misstatement resulting from fraud is higher than for one resulting from error, as fraud may involve collusion, forgery, intentional omissions, misrepresentations, or the override of internal control.
- ▶ Obtains an understanding of internal control relevant to the audit in order to design audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the internal control.
- ▶ Evaluates the appropriateness of accounting policies used and the reasonableness of accounting estimates and related disclosures made by management in the consolidated financial statements.
- ▶ Assesses the appropriateness of management's use of the going concern basis of accounting and, based on the audit evidence obtained, whether a material uncertainty exists related to events or conditions that may cast significant doubt on the Company's ability to continue as a going concern. This assessment is based on the audit evidence obtained up to the date of his audit report. However, future events or conditions may cause the Company to cease to continue as a going concern. If the statutory auditor concludes that a material uncertainty exists, there is a requirement to draw attention in the audit report to the related disclosures in the consolidated financial statements or, if such disclosures are not provided or inadequate, to modify the opinion expressed therein.
- ▶ Evaluates the overall presentation of the consolidated financial statements and assesses whether these statements represent the underlying transactions and events in a manner that achieves fair presentation.
- ▶ Obtains sufficient appropriate audit evidence regarding the financial information of the entities or business activities within the Group to express an opinion on the consolidated financial statements. The statutory auditor is responsible for the direction, supervision and performance of the audit of the consolidated financial statements and for the opinion expressed on these consolidated financial statements.

■ Report to the Audit Committee

We submit to the Audit Committee a report which includes in particular a description of the scope of the audit and the audit program implemented, as well as the results of our audit. We also report, if any, significant deficiencies in internal control regarding the accounting and financial reporting procedures that we have identified.

Our report to the Audit Committee includes the risks of material misstatement that, in our professional judgment, were of most significance in the audit of the consolidated financial statements of the current period and which are therefore the key audit matters that we are required to describe in this report.

We also provide the Audit Committee with the declaration provided for in Article 6 of Regulation (EU) No. 537/2014, confirming our independence within the meaning of the rules applicable in France such as they are set in particular by Articles L. 822-10 to L. 822-14 of the French Commercial Code (Code de commerce) and in the French Code of Ethics (Code de déontologie) for statutory auditors. Where appropriate, we discuss with the Audit Committee the risks that may reasonably be thought to bear on our independence, and the related safeguards.

Villeurbanne and Lyon, April 11, 2019

The Statutory Auditors  
French original signed by

ODICEO

ERNST & YOUNG et Autres

Agnès Lamoine

Mohamed Mabrouk

## 4.2.1 Corporate annual financial statements

## 4.2.2 Balance sheet, French GAAP

<i>In € thousands French gaap</i>	<b>12/31/2018</b>	<b>12/31/2017</b>
Intangible assets - Gross amount	157	137
(Cumulated depreciation and amortization)	(92)	(72)
<b>Intangible assets - Net amount</b>	<b>65</b>	<b>65</b>
<b>Tangible fixed assets</b>		
Lands	2 207	2 202
Constructions	4 275	4 275
Fixtures & fittings, industrial equipment	2 545	2 401
Other tangible fixed assets	3 127	2 893
Construction work in progress	699	275
Total tangible fixed assets	12 853	12 047
(Cumulated depreciation and amortization)	(4 522)	(3 767)
<b>Total tangible fixed assets - Net amount</b>	<b>8 330</b>	<b>8 280</b>
<b>Fiancial assets - Net amount</b>	<b>344</b>	<b>137</b>
<b>Long term assets</b>	<b>8 739</b>	<b>8 482</b>
<b>Inventory and work in progress</b>	<b>131</b>	<b>99</b>
<b>Receivables</b>		
Advance payments made on orders	57	70
Trade and similar receivables	3	30
Other receivables	19 907	9 067
<b>Total receivables</b>	<b>19 966</b>	<b>9 167</b>
<b>Cash assets and miscellaneous</b>		
Short-term investment securities	7 057	8 059
Cash assets	32 725	26 678
Pre-paid expenses	952	573
<b>Total Cash assets and Miscellaneousm</b>	<b>40 734</b>	<b>35 311</b>
<b>Current assets</b>	<b>60 832</b>	<b>44 576</b>
Translation losses	31	28
<b>TOTAL ASSETS</b>	<b>69 602</b>	<b>53 086</b>

*In € thousands French gaap*

	12/31/2018	12/31/2017
Paid-up capital	693	691
Additional paid-in capital	79 624	79 625
Balance brought forward	(41 454)	(16 788)
Profit/loss for the year	9 423	(24 667)
<b>Equity</b>	<b>48 286</b>	<b>38 861</b>
<b>Conditional advances</b>	<b>520</b>	<b>761</b>
<b>Provisions for risks and charges</b>	<b>31</b>	<b>28</b>
Loans and debt with credit institutions	6 174	6 151
Misc.loans and financial debt	12	14
<b>Total financial debt</b>	<b>6 185</b>	<b>6 164</b>
Trade and similar payables	7 741	5 085
Tax and social security liabilities	2 729	2 119
Debt on fixed assets and similar accounts	79	23
Other debt	20	39
<b>Total miscellaneous debt</b>	<b>10 570</b>	<b>7 267</b>
<b>Unearned income</b>	<b>4 007</b>	<b>0</b>
<b>Translation gain</b>	<b>3</b>	<b>4</b>
<b>TOTAL LIABILITIES</b>	<b>69 602</b>	<b>53 086</b>

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### 4.2.3 Income statement, French GAAP

*In € thousands French gaap*

	FY 2018 (12 months)	FY 2017 (12 months)
Net revenue	47 562	938
Reversals of depr./amort.and prov., transfers of charges	204	87
Other income	261	63
<b>Operating income</b>	<b>48 028</b>	<b>1 088</b>
Purchase of raw materials ans other supplies (incl. change in inventory)	(2 188)	(1 746)
Other purchases and external charges	(26 724)	(19 767)
Taxes and similar payments	(553)	(217)
Wages and salaries	(8 682)	(7 372)
Social contributions	(3 740)	(2 760)
Depreciation and provisions for fixed assets	(788)	(773)
Provisions for current assets	(6)	(5)
Other operating expenses	(220)	(145)
<b>Operating expenses</b>	<b>(42 901)</b>	<b>(32 785)</b>
<b>Operating profit / loss</b>	<b>5 126</b>	<b>(31 697)</b>
<b>Financial profit / loss</b>	<b>2 104</b>	<b>(265)</b>
<b>Profit / loss from ordinary activities before tax</b>	<b>7 230</b>	<b>(31 963)</b>
<b>Extraordinary profit / loss</b>	<b>(49)</b>	<b>(239)</b>
Income tax	2 242	7 535
<b>PROFIT / LOSS</b>	<b>9 423</b>	<b>(24 667)</b>

## 4.2.4 Notes to the corporate annual financial statements

### 4.2.4.1 Accounting rules and methods

(Decree 83-1020 of 11/29/1983 – Articles 7, 21, 24 beginning, 24-1, 24-2 and 24-3)

The total balance sheet before allocation for the fiscal year ended December 31, 2018 was €69.6 million.

The net accounting profit was €9.4 million.

The following notes and tables form an integral part of the annual financial statements, which were approved by the Board of Directors on March 11, 2019.

The financial statements were prepared in accordance with:

- the 1999 General Chart of Accounts approved by the ministerial order of June 22, 1999
- Law 83 353 of April 30, 1983
- Decree 83 1020 of November 29, 1983
- accounting regulations:
  - 2000-06 and 2003-07 on liabilities
  - 2002-10 on depreciation, amortization and impairment of assets
  - 2004-06 on the definition, recognition and valuation of assets
  - 2015-05 on foreign exchange gains and losses.

General accounting conventions have been applied based on the principle of conservatism in accordance with the following basic assumptions:

- going concern,
- consistency of the accounting methods used from one year to the next,
- independence of fiscal years, and

in accordance with the general rules regarding the preparation and presentation of annual financial statements.

To prepare its financial statements, the company used the going concern assumption.

The company supports the development of the projects licensed to Tonghua Dongbao and pursues its research and development activities while nevertheless focusing its expenses on projects and priority activities. The recovery of damages awarded under the first part of the arbitration proceeding against Lilly (\$ 11.6 million plus interest) is expected in 2019, following the conclusion of the second part of the arbitration. Pending the cash receipt of this amount, the possibility of an advanced payment of the research tax credit allows the Company to finance the defined operational plan and thus to meet its financial commitments for at least the next 12 months.

The basic method used to determine the value of the items accounted for is the historical cost method.

#### ▪ Intangible assets

Start-up costs were capitalized and amortized over a three-year period.

Research and development costs are not capitalized and are recorded as expenses in the company's income statement.

#### ▪ Property, plant and equipment

Tangible fixed assets are recorded at their acquisition cost (purchase price and incidental expenses).



The company took advantage of the leeway offered and opted to depreciate assets that cannot be broken down into components based on their useful lives.

The company has no assets that can be broken down into components.

Depreciation is calculated on a straight-line basis according to the expected useful life:

Type of asset	Useful life
Software	3 to 5 years
Land development	10 years
Buildings	20 years
Technical installations	3 to 5 years (used – new)
Fixture and fittings	7 to 10 years
Office equipment	3 to 5 years
Furniture	5 years

Other purchases of property, plant and equipment correspond to the acquisition of land, for which no impairment was recorded.

#### ▪ Equity holdings and other long-term investments

As of the filing date of this registration document, the company had a subsidiary in the United States called Adocia Inc. which employs two people: a medical director and a marketing director.

The subsidiary's share capital is \$1 and is composed of 100 shares, all of which are owned by Adocia.

#### ▪ Short-term investment securities

The company invests its funds in short-term investment securities (money market mutual funds) measured at their acquisition cost. It has also invested a portion of its liquidity in short-term term deposits at a guaranteed fixed rate.

At the end of fiscal year 2018, the unrealized capital gain on these investments was €34,100.

#### ▪ Inventories

Inventories are measured using the "first-in first-out" method. They may be impaired if the expiration date has passed and/or if the project to which they refer was discontinued by the company and considered a failure.

#### ▪ Tax Credit for Employment Competitiveness

The Tax Credit for Employment Competitiveness was €0.1 million in 2018 and remained stable compared to 2017. This amount is recognized as a deduction from payroll expense.

#### ▪ Revenue

Revenue of €47.4 million in 2018 resulted up to €37.1 million from the partnership and licensing agreement signed with Tonghua Dongbao Pharmaceuticals Co. Ltd (THDB) in April 2018. It reflects the rights thus granted to THDB to develop, manufacture, and commercialize BioChaperone® Lispro and BioChaperone® Combo in China and other territories in Asia and the Middle-East.

By the end of December 2018, licensing revenues also included an amount of \$11.6 million (€10.3 million) corresponding to a contractual milestone payment contested by Lilly, for which Adocia obtained a favorable arbitration judgement in August 2018. The payment is expected to be received in 2019.

In 2018, the company also recorded €0.2 million in lease income on a portion of the premises owned by it compared to €0.3 million in 2017.

- **Change in methods**

None.

#### 4.2.4.2 Highlights of the fiscal year

2018 was marked by the strategic alliance with Tonghua Dongbao Pharmaceuticals Co. Ltd (« THDB »), Chinese leader of the production and commercialisation of insulin. In April 2018, Adocia and THDB announced the set up of two licensing agreements for BioChaperone® Combo, BioChaperone® Lispro, in China and in other Asian and Middle-East territories. Under the terms of the Licensing Agreements, Tonghua Dongbao is responsible for the future development, manufacturing, and commercialization of BioChaperone Combo and BioChaperone Lispro in the covered territories. Adocia received a total upfront payment of \$50 million and is entitled to receive development milestone payments up to \$85 million and Adocia is also expected to receive double-digit royalties on the sale of both products in the territories. Since the signature, both companies worked on the transfer of the technology to enable the manufacturing of both products. THDB envisages to start a Phase 3 clinical study for BioChaperone Lispro in 2019 and a first clinical study for BioChaperone Combo late 2019.

In June 2018, the partnership with THDB was reinforced by two supply agreements in insulin glargine et lispro. Under the terms of the supply agreements, Tonghua Dongbao will manufacture and supply insulin lispro and insulin glargine APIs to Adocia, in accordance with Adocia's specifications and established quality standards worldwide, excluding China. These agreements enable Adocia to carry on the development of the BioChaperone Lispro et BioChaperone Combo projects and also open additional collaboration opportunities. Adocia prepares a bridging study in order to qualify the insulin lispro manufactured by THDB as equivalent source to Lilly's insulin lispro. This study should be the only one required by authoritative agencies to enable the start in phase 3 of BioChaperone Lispro.

From a clinical perspective, Adocia realized in 2018 the first clinical study of BioChaperone® Pramlintide Insulin in people with type 1 diabetes. This study, whose positive topline results were announced in September showed a significant 97% decrease in blood glucose excursion over the first two hours after the meal compared to Humalog®. The product was well tolerated. Adocia plans to start a second repeated administration trial during Q2 2019.

The development of our varied portfolio products to date revealed unique properties of the BioChaperone technology, which notably enables to significantly improve single agents and to combine multiple therapeutic proteins. In order to expand the use of this technology, Adocia announced early in 2018 that BioChaperone® would now be deployed in a selected range of injectable therapeutics across numerous therapeutic areas. Initial programs added to the portfolio include a ready-to-inject version of teduglutide for the treatment of short bowel syndrome and a fixed dose combination of glucagon and exenatide for the treatment of obesity, both in preclinical stage.

Lastly, regarding legal proceedings, the first phase of the arbitration procedure initiated by Adocia against Lilly concluded in favor of Adocia. The Arbitration Tribunal awarded Adocia \$ 11.6 million, as well as interests.

Adocia's additional claims against Lilly for a revalued amount of \$1.3 billion and the counterclaims of Lilly for an amount of \$188 million, remain pending, with a decision of the court expected in the third quarter of 2019.

Finally, in October 2018, Lilly filed a civil complaint against Adocia in the United States District Court of the Southern District of Indiana to seek a declaratory judgment for two of its US patents regarding ultra-rapid insulin formulation (Lilly's United States Patent Nos. 9,901,623 and 9,993,555 entitled "Rapid-acting insulin compositions"). Lilly contends in its complaint that it filed the action because Adocia has asserted that Lilly's patents reflect Adocia's inventive contribution. Adocia do not expect the matter to be resolved during this fiscal year.

## 4.2.4.3 Notes to the financial statements, French GAAP

## Summary of notes

NOTE 1	Intangible assets
NOTE 2	Property, plant and equipment
NOTE 3	Receivables and debts
NOTE 4	Accrued expenses
NOTE 5	Revenue accruals
NOTE 6	Prepaid expenses and unearned income
NOTE 7	Share capital structure
NOTE 8	Workforce
NOTE 9	Repayable advances and Bpifrance grants
NOTE 10	Income statement
NOTE 11	Balance sheet

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## NOTE 1 Intangible assets

	12/31/2017	Acquisitions, contributions, creation, transfers	Decreases	12/31/2018
Start-up and development costs	11			11
Other intangible assets	126	20	0	146
<b>GROSS AMOUNT</b>	<b>137</b>	<b>20</b>	<b>0</b>	<b>157</b>
Start-up and development costs	(11)			(11)
Other intangible assets	(60)	(20)	0	(81)
<b>DEPRECIATION / AMORTIZATION</b>	<b>(72)</b>	<b>(20)</b>	<b>0</b>	<b>(92)</b>
Start-up and development costs	0			0
Other intangible assets	65	0		65
<b>NET AMOUNT</b>	<b>65</b>	<b>0</b>	<b>0</b>	<b>65</b>

**NOTE 2 Property, plant and equipment**

	12/31/2017	Acquisitions, contributions, creation, transfers	Decreases	12/31/2018
Lands	2 032	0	0	2 032
Land development	170	5	0	175
Buildings	4 275	0	0	4 275
Laboratory equipment	2 401	157	(13)	2 545
Fixtures and facilities	1 695	70	0	1 765
Furniture, office equipment	1 198	163	0	1 362
Advances and payment on account	275	424	0	698
<b>GROSS AMOUNT</b>	<b>12 047</b>	<b>819</b>	<b>(13)</b>	<b>12 853</b>
Lands	0	0	0	0
Land development	1	17	0	18
Buildings	336	214	0	550
Laboratory equipment	1 844	218	(13)	2 049
Fixtures and facilities	782	143	0	925
Furniture, office equipment	803	177	0	980
<b>DEPRECIATION / AMORTIZATION</b>	<b>3 767</b>	<b>768</b>	<b>(13)</b>	<b>4 522</b>
Lands	2 032	0	0	2 032
Land development	169	(12)	0	157
Buildings	3 939	(214)	0	3 725
Laboratory equipment	557	(61)	0	496
Fixtures and facilities	912	(73)	0	840
Furniture, office equipment	395	(13)	0	382
Advances and payment on account	275	424	0	698
<b>NET AMOUNT</b>	<b>8 280</b>	<b>51</b>	<b>0</b>	<b>8 331</b>

The classification of property, plant and equipment presented in the chart above differ from the one presented in 2017 reference document. In order to clarify the financial information, the classification has been aligned with the one presented in the notes to the consolidated financial statements.

**NOTE 3 Receivables and debts**

Receivables <i>In € thousands French gaap</i>	Gross amount	Up to 1 year	1 year or more
<b>Long-term financial assets</b>	<b>344</b>		<b>344</b>
Other trade receivables	3	3	
Social security and other social agencies	15	15	
Government - Income tax (including CICE et CIR)	6 786	6 453	333
Government - Value added tax	1 001	1 001	
Miscellaneous debtors	12 162	12 162	
<b>Current assets</b>	<b>19 966</b>	<b>19 633</b>	<b>333</b>
<b>Pre-paid expenses</b>	<b>952</b>	<b>952</b>	
<b>TOTAL</b>	<b>21 262</b>	<b>20 586</b>	<b>677</b>

<b>Debts</b> <i>In € thousands French gaap</i>	<b>Gross amount</b>	<b>Up to 1 year</b>	<b>1 year or more</b>
Loans and debt with credit institutions	6 174	1 783	4 390
Miscellaneous loans and financial debt	12		12
<b>Financial debts</b>	<b>6 185</b>	<b>1 783</b>	<b>4 402</b>
Trade and similar payables	7 458	7 458	
Staff and similar accounts	938	938	
Social security and other agencies	1 311	1 311	
Value added tax	0	0	
Other taxes and similar	479	479	
Debt on fixed assets and similar accounts*	79	79	
Group and partners	283	283	
Other debt	20	20	
<b>Miscellaneous debt</b>	<b>10 570</b>	<b>10 570</b>	
<b>Unearned income</b>	<b>4 007</b>	<b>2 314</b>	1 692
<b>TOTAL GENERAL</b>	<b>20 762</b>	<b>14 667</b>	<b>6 095</b>

**NOTE 4 Accrued expenses**

<i>In € thousands French gaap</i>	<b>12/31/2018</b>	<b>12/31/2017</b>
Trade and similar payables	3 889	3 314
Tax and social security liabilities	1 845	1 258
<b>TOTAL</b>	<b>5 734</b>	<b>4 572</b>

**NOTE 5 Revenue accruals**

<i>In € thousands French gaap</i>	<b>12/31/2018</b>	<b>12/31/2017</b>
Trade and similar receivables	3	23
Government	85	107
Other receivables	262	300
Cash assets	0	6
<b>TOTAL</b>	<b>350</b>	<b>436</b>

**NOTE 6 Prepaid expenses and unearned income**

<i>In € thousands French gaap</i>	<b>12/31/2018</b>	<b>12/31/2017</b>
Operating income or expense	(3 055)	573
Financial income or expense		
Extraordinary income or expense		
<b>TOTAL</b>	<b>(3 055)</b>	<b>573</b>

**NOTE 7 Share capital structure**

	As of January 1st, 2018	Capital increase (in euros)	As of December 31st, 2018	Share capital (in euros)
Common shares	6 910 753	20 491	6 931 244	693 124

**NOTE 8 Workforce**

	12/31/2018	12/31/2017
Technicians	58	59
Management personnel	72	68
<b>Total employees</b>	<b>130</b>	<b>127</b>

**NOTE 9 Repayable advances and Bpifrance grants****Bpifrance (ex-OSEO Innovation) agreement of April 25, 2012**

As part of the Insulin project, the company signed an agreement with Bpifrance Financement on April 25, 2012 under which it received a repayable advance totaling €0.8 million for the development of a fast-acting "human" insulin formulation and the Phase 2a clinical trial. After fulfilling all the technical and financial conditions, the company received the full amount of this repayable assistance on April 30, 2012.

In 2018, the company repaid €0.15 million, and all or part of the balance is repayable through 2020 (see section 1.3.7).

**Coface – International business development insurance agreement of October 1, 2012**

As part of its business development in new markets (India and China), the company signed a business development agreement with Coface (French insurance company for foreign trade) on October 26, 2012 in return for the payment of a premium equivalent to 2% of the annual budget.

Under the terms of the agreement, Coface guarantees the repayment of 75% of the expenses incurred during the four-year guarantee period, which runs from October 1, 2012 to September 30, 2016 and was extended for two years through 2018.

For the expenses incurred during the first insured period, i.e. from October 1, 2012 to September 30, 2013, the company received the sum of €0.91 million on December 17, 2013.

During the period between October 1, 2013 and September 30, 2014, since the company did not incur any business development expenses on the target markets, the contract was canceled. Therefore, the company began to amortize the amounts received up to then, i.e. €91,000, according to the terms specified in the agreement and described above.

In 2018, given the partnership signed with Tonghua Dongbao, the Company reimbursed fully the advance granted, ie €91,000, accordingly to the contract terms.

**NOTE 10 Income statement**

The Company's revenue of €47.6 million mostly results from:

- the contracts signed with Tonghua Dongbao in April 2018, for €37.1 million
- a contractual milestone payment contested by Lilly, for which Adocia obtained a favorable arbitration judgement in August 2018, for €10.3 million (\$11.6 million)

<i>In € thousands French gaap</i>	<b>FY 2018 (12 months)</b>	<b>FY 2017 (12 months)</b>
Net revenue	47 562	938
Reversals of depr./amort.and prov., transfers of charges	204	87
Other income	261	63
<b>Operating income</b>	<b>48 028</b>	<b>1 088</b>

Operating expenses totaled €42.9 million compared to €32.8 million in 2017 and included the following items:

<i>In € thousands French gaap</i>	<b>FY 2018 (12 months)</b>	<b>FY 2017 (12 months)</b>
Purchase of raw materials ans other supplies	(2 188)	(1 746)
Other purchases and external charges	(26 724)	(19 767)
Taxes and similar payments	(553)	(217)
Payroll expense	(12 422)	(10 132)
Depreciation and provisions	(795)	(778)
Other operating expenses	(220)	(145)
<b>Operating expenses</b>	<b>(42 901)</b>	<b>(32 785)</b>

There was an operating profit of €5.1 million versus a loss of €32.8 million the previous year.

A net financial profit of €2.1 million was recorded in 2018 compared to a loss of €0.3 million in income the previous year. It consisted mainly in the accrued interests awarded by the Arbitration Tribunal in the first phase of the arbitration procedure initiated by Adocia against Lilly. They amounted to €1.6 million at December 31, 2018. Exchange rates had a positive impact of €0.6 million. Foreign exchange fluctuations are also recognized for a net amount of € 0.6 million.

As a result, there was a pre-tax profit on ordinary activities of €7.2 million versus a loss of €32 million the previous year.

After taking into account the Research Tax Credit of €6.4 million and the tax expense of €4.1 million, fiscal year 2018 ended with a net profit after tax of €9.4 million compared to a loss of €24.7 million the previous year. It is stated that 2018 tax will be fully paid by a tax credit related to the withholding tax applied, in China, on Tonghua Dongbao's upfront payment.

#### **NOTE 11 Balance sheet**

##### **Assets**

**Non-current assets** amounted to €8.7 million at December 31, 2018 compared to €8.5 million at December 31, 2017. The net increase of €0.2 million resulted primarily from the restructuring works on two floors of 450 sqm each, mainly dedicated to the Analytical Department, for an amount of € 0.5 million at 31 December 2018.

**Current assets** totaled €60.8 million compared to €44.6 million a year earlier. They consisted of the following items:

- "Cash and cash equivalents" increased from €34.7 million at December 31, 2017 to €39.8 million at December 31, 2018. The €5 million in cash improvement during the year reflects the collection of Tonghua Dongbao's upfront payment for €37.2 million (\$45 million), net from Chinese withholding tax, as well as a similar level of expenses as the previous year, restated from the expenses for the claim procedures against Eli Lilly.
- The "other receivables" item amounted to €19.9 million at December 31, 2018 compared to €9.1 million a year earlier. It includes the receivable of €11.9 million due to the favorable outcome of the first phase the arbitration proceedings initiated by Adocia against Lilly. This receivable consists of €10.3 million for the

execution of the contractual term (\$11.6 million), plus accrued interests for €1.6 million awarded by the Arbitral Tribunal. The item 'other receivables' included also receivables from the government, such as the Research Tax Credit (CIR) for the year in the amount of €6.4 million, the carryback receivable for €0.3 million, the VAT credit and the Tax Credit for Employment Competitiveness (CICE).

In accordance with Article L. 441-6-1 of the French Commercial Code, invoices issued for which payment was in arrears on the balance sheet date were as follows:

<i>Receivables</i> in € thousands	Invoices received with passed due date but not paid at the end of the year				Total
	1 to 30 days	31 to 60 days	61 to 90 days	91 days and more	
<b>(A) Periods of payment delay</b>					
Number of concerned invoices	0	0	0	0	0
Total amount of concerned invoices, tax included	0	0	0	0	0
Percentage of the turnover of the year, tax included	0%	0%	0%	0%	0%
<b>(B) Invoices excluded from (A) due to contentious or unrecognized debts and receivables</b>					
Number of invoices excluded			0		
Total amount of invoices excluded, tax included			0		
<b>(C) Standard payment delay used</b>					
Payment term used to calculate the payment delay	Contract terms: upon invoice reception				

**Prepaid expenses** amounted to 1 million euros in 2018 compared to €0.6 million a year earlier.

#### Liabilities

The company's **equity** totaled €48.2 million compared to €38.9 million a year earlier. Share capital amounted to €693,124 at December 31, 2018 versus €691,075 at the end of the previous year. The share premium of €79.6 million at the end of 2018 was stable compared to 2017.

At the end of 2018, carryforward losses totaled €41.5 million compared to €16.8 million at the end of 2017, with the difference coming from the allocation of the €24.7 million loss of the fiscal year closed ed of 2017.

The conditional advances decreased by €0.2 million to €0.5 million at December 31, 2018 (see note 9 on repayable advances).

#### The company's debt position based on business volume and complexity

**Financial debt** totaled €6.2 million at end-December 2018 and was stable relative to the end of 2017.

**"Tax and staff cost liabilities"** amounted to €2.7 million, rising by €0.6 million compared to the previous year. This results from the increase of the accrual for paid holiday by €0.2 million and the accrual for the value-added contribution tax (CVAE) for €0.3 million at December 31, 2018.

**"Trade payables"** totaled €7.7 million compared to €5.1 million at end-December 2017, which reflects the intense activity at the end of 2018 with, mainly, the Arbitration Tribunal hearings that held in December 2018 as part of the arbitration procedure launched against Eli Lilly.

In accordance with Article L. 441-6-1 of the French Commercial Code, invoices received for which payment was in arrears on the balance sheet date were as follows:



<i>Debts in € thousands</i>	Invoices received with passed due date but not paid at the end of the year				Total
	1 to 30 days	31 to 60 days	61 to 90 days	91 days and more	
<b>(A) Periods of payment delay</b>					
Number of concerned invoices	41	5	2	3	51
Total amount of concerned invoices, tax included	1 548	9	6	36	1 598
Percentage of total purchases amount for the year, tax included	5%	0%	0%	0%	5%
<b>(B) Invoices excluded from (A) due to contentious or unrecognized debts and receivables</b>					
Number of invoices excluded			15		
Total amount of invoices excluded (tax included)			56		
<b>(C) Standard payment delay used</b>					
Payment term used to calculate the payment delay	Contract terms: depending on the supplier, upon invoice reception, within 30 days, within 45 days, etc.				

An invoice of €1.2 million has been received by the company at the end of December 2018, during annual closing. It explains the high level of unpaid invoices at the end of 2018.

#### 4.2.4.4 Proposed allocation of losses for fiscal year 2018

A proposal is made to allocate the profit for the fiscal year ended December 31, 2018 in the amount of €9.4 million to retained earnings.

As a reminder, the company did not paid out dividends over the last three years.

#### 4.2.4.5 Non-tax-deductible expenses

In accordance with Article 223 (4) of the French General Tax Code (Code Général des Impôts), the company did not incur any luxury expenditure and non-deductible expense referred to in Article 39-4 of this code for the fiscal year ended December 31, 2018.

#### 4.2.4.6 Off-balance sheet commitments

##### Retirement obligation

The company decided not to recognize a provision for its retirement obligations.

However, it chose to quantify these obligations in the financial statements prepared under IFRS in the amount of €2.8 million at December 31, 2018 compared to €2.2 million at December 31, 2017. (See note 11 to the consolidated financial statements prepared under IFRS in section 4.16 of this registration document).

##### Signing of financial leases

The company owns several assets financed through leasing. At the end of December 2017, it had four agreements. These agreements cover equipment for which the total acquisition cost is €1 million. Three of the agreements have a financing term of four years (€0.8 million) and the fourth has a financing term of three years (€0.1 million).

##### Guarantees provided

When obtaining the loans used to purchase the building and parking spaces, the company provided the following guarantees:

## Annual financial statements at December 31, 2018

- a lender's lien and subrogation in the seller's lien for the purchase amount of the building,
- a mortgage on the construction budget.

The company also made one term deposit of €1.5 million for a line of credit provided by one bank to finance a part of the legal costs related to the applications for arbitration against Lilly.

### Bonus shares, ordinary stock warrants and start-up company stock warrants

Information regarding grants of bonus shares, start-up company stock warrants, stock options and ordinary stock warrants is provided in section 5.1.5 of this registration document.

#### 4.2.4.7 Statutory auditors' fees

The table below shows the statutory auditors' fees paid by the company over the last two years:

<i>In € thousands French gaap</i>	Ernst & Young		Odicéo	
	12/31/2018	12/31/2017	12/31/2018	12/31/2017
Statutory auditor services, certification, review of individual and consolidated financial statements	43	41	43	42
Other services and due diligence directly related to the statutory audit assignement		3		3
<b>Subtotal audit services</b>	<b>43</b>	<b>44</b>	<b>43</b>	<b>42</b>
Tax services				
Other services				
<b>Subtotal other services</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>
<b>TOTAL</b>	<b>43</b>	<b>44</b>	<b>43</b>	<b>42</b>

#### 4.2.4.8 Events subsequent to year end

None.

## 4.2.4.9 Table showing results over the last five fiscal years

<i>In € thousands French gaap</i>	<b>12/31/2018</b>	<b>12/31/2017</b>	<b>12/31/2016</b>	<b>12/31/2015</b>	<b>12/31/2014</b>
<b>Capital during the fiscal year (in euros)</b>					
Share capital	693 124	691 075	685 976	684 636	621 608
Number of existing ordinary shares	6 931 244	6 910 753	6 859 763	6 846 363	6 216 076
Number of existing ordinary shares cum dividend	6 931 244	6 910 753	6 859 763	6 846 363	6 216 076
Maximum number of future shares to be created					
by bond conversion					
by exercise of subscription rights	75 695	62 900	105 755	61 750	2 800
<b>Transactions and results for the fiscal year</b>					
Pre-tax revenue	47 562	938	11 976	26 189	41 043
Profit/loss before tax, employee profit-sharing, depreciation, amortization and provisions	7 976	(31 424)	(21 096)	(2 131)	24 994
Income tax	(2 242)	(7 535)	(7 812)	(7 101)	617
Employee profit-sharing owed for the year					421
Profit/loss after tax, employee profit-sharing, depreciation, amortization and provisions	9 423	(24 667)	(13 993)	4 478	23 733
Distributed profit	0	0	0	0	0
<b>Earnings per share (in euros per share)</b>					
Profit/loss after tax and employee profit-sharing, but before depreciation, amortization and provisions	1	(3)	(2)	1	4
Profit/loss after tax, employee profit-sharing, depreciation, amortization and provisions	1	(4)	(2)	1	4
Dividend per share					
<b>Staff (in thousands of euros)</b>					
Average number of employees during the year	127	126	120	95	77
Total payroll for the year	(8 682)	(7 372)	(7 622)	6 410	4 982
Total employee benefits paid for the year (social security, social agencies, etc.)	3 732	3 593	3 502	2 953	2 329

## 4.3 Statutory auditors' report on the corporate financial statements

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C.S. 52038  
69616 Villeurbanne cedex  
S.A. au capital de € 275.000  
430 130 393 R.C.S. Lyon

Commissaire aux Comptes  
Membre de la compagnie  
regionale de Lyon

ERNST & YOUNG et Autres  
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Commissaire aux Comptes  
Membre de la compagnie  
regionale de Versailles

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### Adocia

Year ended December 31, 2018

#### Statutory auditors' report on the financial statements

To the Annual General Meeting of Adocia,

#### Opinion

In compliance with the engagement entrusted to us by your Annual General Meetings, we have audited the accompanying financial statements of Adocia for the year ended December 31, 2018.

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, 2018 and of the results of its operations for the year then ended in accordance with French accounting principles.

The audit opinion expressed above is consistent with our report to the Audit Committee.

#### Basis for Opinion

##### ■ Audit Framework

We conducted our audit in accordance with professional standards applicable in France. We believe that the audit evidence we have obtained is sufficient and appropriate to provide a basis for our opinion.

Our responsibilities under those standards are further described in the Statutory Auditors' Responsibilities for the Audit of the Financial Statements section of our report.

##### ■ Independence

We conducted our audit engagement in compliance with independence rules applicable to us, for the period from January 1, 2018 to the date of our report and specifically we did not provide any prohibited non-audit services referred to in Article 5(1) of Regulation (EU) No 537/2014 or in the French Code of Ethics (Code de déontologie) for Statutory Auditors.

## Justification of Assessments - Key Audit Matters

In accordance with the requirements of Articles L.823-9 and R.823-7 of the French Commercial Code (Code de commerce) relating to the justification of our assessments, we inform you of the key audit matters relating to risks of material misstatement that, in our professional judgment, were of most significance in our audit of the financial statements of the current period, as well as how we addressed those risks.

These matters were addressed in the context of our audit of the financial statements as a whole, and in forming our opinion thereon, and we do not provide a separate opinion on specific items of the financial statements.

### ■ Arbitration against Eli Lilly & Company

Risk identified	Our response
<p>In February 2018, your Company announced through a press release filing new applications for arbitration against Eli Lilly &amp; Company for the appropriation and misuse by Eli Lilly &amp; Company of confidential information and discoveries belonging to your Company, as well as for the violation by Eli Lilly &amp; Company of several collaboration and confidentiality agreements. Your Company is claiming damages amounting to approximately USD 1.3 billion. As part of this second phase of the arbitration, Eli Lilly &amp; Company filed a counterclaim against your Company for an amount of approximately MUSD 188.</p> <p>Besides this action, and as mentioned in paragraph 4.3.3.2 "Significant events", on October 9, 2018, Eli Lilly &amp; Company launched a civil action against your Company before the District Court of the Southern District of Indiana, United States, in order to obtain a declaratory judgment relating to inventors' designations for two of its U.S. patents on ultra-fast insulin formulations (US patent [Lilly] Nos. 9,901,623 and 9,993,555).</p> <p>As described in Note 11 to the financial statements, your Company considered that Eli Lilly &amp; company's applications are groundless and, as such, no provision has been recorded as at December 31, 2018.</p> <p>We considered this arbitration to be a key audit matter because of the importance of the compensation claimed by each of the two parties and of the level of judgement required to assess the arguments supporting the lack of provision relating to this arbitration and the relevance of information regarding this dispute provided in the Note to the financial statements.</p>	<p>In the context of our audit of the financial statements, our work mainly consisted in:</p> <ul style="list-style-type: none"> <li>▶ acknowledging the risk analysis carried out by your Company, the relevant documentation and examining, if necessary, the written consultations of the external councils;</li> <li>▶ making a request for confirmation from the lawyers in charge of this dispute;</li> <li>▶ assessing with the assistance of our experts, who spoke with the lawyers of the Company, the risks presented by this arbitration and the assumptions adopted by Management to justify the absence of provision at the closing;</li> <li>▶ examining the appropriateness of the information relating to this risk presented in the Notes to the financial statements.</li> </ul>

#### ■ Going concern

Risk identified	Our response
<p>Fiscal year 2017 ended with a loss of MEUR 8.6 and a cash burn amounted to M€ 23.3 over the year. At 2018 year-end, your Group had negative reserves of MEUR 41.3 but a profit of M€ 7.6 and an increase of its cash position of MEUR 5.1 (closing cash amounted to MEUR 39.8).</p> <p>Fiscal year 2018 was marked in particular by the establishment of a strategic alliance with Tonghua Dongbao Pharma Co for which your Company received a total upfront payment of MUSD 50. Moreover, while Adocia's arbitration proceedings against Eli Lilly, the first part of that procedure was in favor of your company, the Court ordered Eli Lilly &amp; Company to pay the disputed step worth of MUSD 11.6. The collection of the damages thus granted (amount of MUSD 11.6 plus interest) is expected in 2019, after the conclusion of the second part of the arbitration, as mentioned in the "Accounting rules and methods" section of Note 4.3.3.1 to the financial statements.</p> <p>As set out in the "Accounting rules and methods" sections of Note 4.3.3.1 to the financial statements, the going concern assumption was applied at year-end given (i) the measures to select expenses relating to high-priority projects and activities for your Group and (ii) the ability to anticipate the collection of the research tax credit (crédit d'impôt recherche).</p> <p>We considered the application of this principle to be a key audit matter as it is based on cash flow forecasts, which present a risk of not being achieved.</p>	<p>As part of our audit of the financial statements, we reviewed the financial statement forecasts presented to the Board of Directors and analyzed the detailed cash flow forecasts prepared by General Management for the period from January 1, 2019 to June 30, 2020. Our analyses consisted in:</p> <ul style="list-style-type: none"> <li>▶ assessing the consistency of the forecasts with the historical data;</li> <li>▶ evaluating the assumptions used by Management;</li> <li>▶ for a selection of planned outflows in respect of external expenditures for which your Group had made contractual commitments, reconciling the amounts applied with the agreements concerned;</li> <li>▶ for a selection of outflows relating to external expenses on studies for which your Company has not yet entered into agreements with suppliers, comparing the amounts applied with the data underlying the budgets approved by your Board of Directors and with the historical data relating to studies of the same type, to assess the frequency of invoicing;</li> <li>▶ analyzing the main data and assumptions (personnel expenses, external and internal expenditures) on which your Company's calculation of the research tax credit is based, and the expected date on which it will be received.</li> </ul> <p>Lastly, we assessed whether the information provided in the "Accounting rules and methods" section of Note 4.3.3.1 of the notes to the financial statements was representative of your Company's situation.</p>

#### Specific verifications

We have also performed, in accordance with professional standards applicable in France, the specific verifications required by laws and regulations.

- Information given in the Management Report and in the Other Documents with respect to the financial position and the financial statements provided to the Shareholders

We have no matters to report as to the fair presentation and the consistency with the financial statements of the information given in the Board of Directors' management report and in the other documents with respect to the financial position and the financial statements provided to the shareholders.

We attest that the information relating to payment terms referred to in article D. 441-4 of the French Commercial Code (Code de commerce) is fairly presented and consistent with the financial statements.

#### ■ Information relating to Corporate Governance

We attest that the corporate governance section of the Board of Directors' management report sets out the information required by Articles L. 225-37-3 and L. 225-37-4 of the French Commercial Code (Code de commerce).

Concerning the information given in accordance with the requirements of Article L. 225-37-3 of the French Commercial Code (Code de commerce) relating to remunerations and benefits received by the directors and any other commitments made in their favor, 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 controlling and controlled companies. Based on these procedures, we attest the accuracy and fair presentation of this information.

With respect to the information relating to items that your Company considered likely to have an impact in the event of a public purchase offer or exchange, provided pursuant to Article L. 225-37-5 of the French Commercial Code (Code de commerce), we have agreed these to the source documents communicated to us. Based on our work, we have no observations to make on this information.

#### ■ Other information

In accordance with French law, we have verified that the required information concerning the identity of the shareholders and holders of the voting rights has been properly disclosed in the management report.

### Report on Other Legal and Regulatory Requirements

#### ■ Appointment of the Statutory Auditors

We were appointed as statutory auditors of Adocia by Decision of the Sole Shareholder of December 10, 2011 for ODICEO and by your Annual General Meeting held on October 24, 2011 for ERNST & YOUNG et Autres.

As at December 31, 2018, our firms were in the eighth year of total uninterrupted engagement, including seven years since securities of the Company were admitted to trading on a regulated market.

### Responsibilities of Management and Those Charged with Governance for the Financial Statements

Management is responsible for the preparation and fair presentation of the financial statements in accordance with French accounting principles and for such internal control as management determines is necessary to enable the preparation of financial statements that are free from material misstatement, whether due to fraud or error.

In preparing the financial statements, management is responsible for assessing the Company's ability to continue as a going concern, disclosing, as applicable, matters related to going concern and using the going concern basis of accounting unless it is expected to liquidate the Company or to cease operations.

The Audit Committee is responsible for monitoring the financial reporting process and the effectiveness of internal control and risks management systems and where applicable, its internal audit, regarding the accounting and financial reporting procedures.

The financial statements were approved by the Board of Directors.

#### Statutory Auditors' Responsibilities for the Audit of the Financial Statements

##### ■ Objectives and audit approach

Our role is to issue a report on the financial statements. Our objective is to obtain reasonable assurance about whether the financial statements as a whole are free from material misstatement. Reasonable assurance is a high level of assurance, but is not a guarantee that an audit conducted in accordance with professional standards will always detect a material misstatement when it exists. Misstatements can arise from fraud or error and are considered material if, individually or in the aggregate, they could reasonably be expected to influence the economic decisions of users taken on the basis of these financial statements.

As specified in Article L. 823-10-1 of the French Commercial Code (Code de commerce), our statutory audit does not include assurance on the viability of the Company or the quality of management of the affairs of the Company.

As part of an audit conducted in accordance with professional standards applicable in France, the statutory auditor exercises professional judgment throughout the audit and furthermore:

- ▶ Identifies and assesses the risks of material misstatement of the financial statements, whether due to fraud or error, designs and performs audit procedures responsive to those risks, and obtains audit evidence considered to be sufficient and appropriate to provide a basis for his opinion. The risk of not detecting a material misstatement resulting from fraud is higher than for one resulting from error, as fraud may involve collusion, forgery, intentional omissions, misrepresentations, or the override of internal control.
- ▶ Obtains an understanding of internal control relevant to the audit in order to design audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the internal control.
- ▶ Evaluates the appropriateness of accounting policies used and the reasonableness of accounting estimates and related disclosures made by management in the financial statements.
- ▶ Assesses the appropriateness of management's use of the going concern basis of accounting and, based on the audit evidence obtained, whether a material uncertainty exists related to events or conditions that may cast significant doubt on the Company's ability to continue as a going concern. This assessment is based on the audit evidence obtained up to the date of his audit report. However, future events or conditions may cause the Company to cease to continue as a going concern. If the statutory auditor concludes that a material uncertainty exists, there is a



requirement to draw attention in the audit report to the related disclosures in the financial statements or, if such disclosures are not provided or inadequate, to modify the opinion expressed therein.

- ▶ Evaluates the overall presentation of the financial statements and assesses whether these statements represent the underlying transactions and events in a manner that achieves fair presentation.

■ Report to the Audit Committee

We submit to the Audit Committee a report which includes in particular a description of the scope of the audit and the audit program implemented, as well as the results of our audit. We also report, if any, significant deficiencies in internal control regarding the accounting and financial reporting procedures that we have identified.

Our report to the Audit Committee includes the risks of material misstatement that, in our professional judgment, were of most significance in the audit of the financial statements of the current period and which are therefore the key audit matters that we are required to describe in this report.

We also provide the Audit Committee with the declaration provided for in Article 6 of Regulation (EU) No. 537/2014, confirming our independence within the meaning of the rules applicable in France such as they are set in particular by Articles L. 822-10 to L. 822-14 of the French Commercial Code (Code de commerce) and in the French Code of Ethics (Code de déontologie) for statutory auditors. Where appropriate, we discuss with the Audit Committee the risks that may reasonably be thought to bear on our independence, and the related safeguards.

Villeurbanne and Lyon, April 11, 2019

The Statutory Auditors  
French original signed by

ODICEO

ERNST & YOUNG et Autres

Agnès Lamoine

Mohamed Mabrouk



**5**  
**INFORMATION**  
**ON THE COMPANY**  
**AND THE CORPORATE**  
**CAPITAL**



## Chapter 5

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## 5 INFORMATION ON THE COMPANY AND THE CORPORATE CAPITAL

### 5.1 Corporate capital

#### 5.1.1. Amount of corporate capital

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As of December 31, 2018, the Company's capital was €693,124.40, divided into 6,931,244 fully paid-in common shares, with a par value of €0.10 each.

#### 5.1.2. Shares not representing capital

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None.

#### 5.1.3. Company shares pledged as collateral, guarantees or security

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None.

#### 5.1.4. Acquisition by the Company of its own shares

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The combined general meeting of the Company's shareholders held on May 17, 2018 authorized the board of directors, for an 18-month period from the date of the meeting, to implement a share buyback program under Article L. 225-209 of the French Commercial Code (*Code de commerce*) and in accordance with the General Regulation of the *Autorité des marchés financiers* (AMF) under the conditions described below. This authorization supersedes the authorization granted on June 27, 2017 for the same purpose, under the same terms and conditions as those adopted on May 17, 2018.

**Maximum number of shares that may be purchased:** 10% of the corporate capital on the share buyback date. If the shares are acquired for the purpose of stimulating the market and increasing liquidity, the number of shares included in the calculation of the 10% limit specified above corresponds to the number of shares purchased, less the number of shares resold over the duration of the authorization.

**Objectives of the share buyback program:**

- To ensure the liquidity of the Company's shares under a liquidity agreement to be entered into with an investment services provider, in accordance with the code of conduct recognized by the AMF;
- To honor obligations under stock option, bonus share or employee savings plans or other allocations of shares to employees and managers of the Company or its affiliates;
- To deliver shares when the rights attached to marketable securities conferring equity rights are exercised;
- To purchase shares for the purpose of holding them for subsequent delivery as a means of exchange or payment for a potential acquisition; or
- To cancel all or some of the repurchased shares, in accordance of the reduction of the share capital.
- More, generally, operate for any purpose that may be authorized by law or any market practice that may be accepted by the market authorities, it being specified that, in such a case, the Company would inform its shareholders by press release

**Maximum purchase price:** €150 per share. This purchase price will be adjusted, if necessary, to reflect transactions involving the capital (including capitalization of reserves and bonus issues, grants of bonus shares, reverse stock splits or stock consolidations) that may have occurred during the authorization period;

The number of shares acquired by the Company for the purpose of holding them for subsequent delivery as a means of payment or exchange in a merger, demerger or contribution of assets may not exceed 5% of the Company's capital.

**Maximum amount of funds** that may be used for share buybacks: €5,000,000. The repurchased shares may be canceled.

As of the date of the current reference document, this stock option purchase program was exclusively used in the context of the Liquidity agreement with Kepler Cheuvreux - see below.

#### 5.1.4.1 Liquidity contract signed with Kepler Cheuvreux:

The aforementioned liquidity agreement entered into for a period of 12 months, renewable annually by tacit agreement, relates to the Company's shares listed on Compartment C of the regulated market of Euronext in Paris. At the signature of the liquidity agreement, the liquidity account was allocated [an amount of € 300,000 and a number of 15,026 shares.

#### 5.1.4.2 The grant of shares to the employees:

During the year ended December 31, 2018, the Company did not purchase any of its own shares for the purpose of allocating them to its employees under a stock option program, free allocation of shares, employee savings plans or other share allocations to employees and officers of the Company or its affiliates or associates thereof with the Liquidity agreement with Kepler Cheuvreux.

#### 5.1.4.3 Report on the liquidity contract with Kepler Cheuvreux

	FY 2018	FY 2017
Number of shares purchased	119 493	59 254
Average price of the purchases (euros)	16.00	22.59
Number of shares sold	116 454	51 498
Average price of the sales (euros)	15.89	19.71
Number of shares used during the year	none	none
Number of shares owned at year end and percentage of control	10 555	7 516
Value estimated at the average price of the purchases (euros)	0.15% of capital	0.10% of capital
Total trading fees (euros)	126 830.48	113 708.71
Total fees (euros)	22 500	22 500

As of December 31, 2018, in connection with this contract, the Company held 10,555 shares, ie 0.15% of its capital and € 214,471.18 in cash.

## 5.1.5. Potential capital

As of the date of this reference document, there were four types of shares conferring equity rights.

### 5.1.5.1. BSA stock warrants plan

	<b>BSA 06-2011</b>	<b>BSA 09-2011</b>	<b>BSA 12-2013</b>	<b>BSA 03-2017</b>
Date of shareholders' meeting	06/17/2011	06/17/2011	06/18/2013	11/12/2015
Date of board of directors' decision	06/17/2011	09/27/2011	12/13/2013	03/07/2017
Number of BSA stock warrants authorized	140	70	20 000	40 000
Number of BSA stock warrants issued	140	70	20 000	40 000
Total number of shares that may be subscribed <sup>(1)</sup>	1 400	700	20 000	40 000
Of which, number that may be subscribed by corporate officers	-	-	20 000	-
Earliest BSA stock warrant exercise date	06/17/2011	09/27/2011	01/01/2014	03/07/2017
BSA stock warrant expiration date	06/17/2021	09/27/2021	12/13/2023	03/07/2027
BSA stock warrant issue price (euros)	free	free	0.588	1
BSA stock warrant strike price (euros)	8.571 <sup>(1)</sup>	8.571 <sup>(1)</sup>	5.88	20.65
Exercise conditions	<sup>(2)</sup>	<sup>(2)</sup>	<sup>(3)</sup>	<sup>(4)</sup>
Number of subscribed shares at the filing date of this registration document	0	700	0	0
Number of lapsed or cancelled warrants at the filing date of this registration document	0	0	0	0
Remaining warrants at the filing date of this registration document	140	0	20 000	40 000
Total number of shares that may be subscribed at the filing date of this registration document	1 400	0	20 000	40 000

<sup>(1)</sup> The exercise conditions for the BSA stock warrants have been adjusted to reflect the 10-for-1 stock split approved by the general shareholders' meeting of October 24, 2011. The phrase "Total number of shares that could originally be subscribed" corresponds to figures after accounting for this split.

<sup>(2)</sup> In principle, the BSA stock warrants may be exercised at any time over a 10-year period from the date they are granted, provided the holder of the BSA stock warrants has served continuously, until the BSA stock warrants are exercised, as an external scientific advisor to the Company.

<sup>(3)</sup> All BSA12-2013 stock warrants may be exercised as of the date of this reference document and for a period of 10 years.

<sup>(4)</sup> 15,000 BSA 03-2017 stock warrants can be exercised at the date of the current document the remaining balance, ie 25,000 BSA will be, provided the terms and conditions and performance objectives set out in the "Warrants Agreement" and approved by the board of directors have been met.

As of the date of the present reference document, 61,400 BSA may be exercised, provided the terms and conditions and performance objectives, the full exercise of the BSA would result into the creation of 61,400 shares with a par value of € 0.10.

## 5.1.5.2 Bonus shares

	2008 Plans		2009 Plan	2010 Plans	
	managers		managers	managers	
Date of shareholders' meeting	01/23/2008	06/06/2008	12/15/2009	03/05/2010	12/07/2010
Recipients	Employees	Employees	Employees	Employees	Employees
Vesting date	01/23/2012 (1)	06/06/2012 (1)	12/15/2013 (1)	03/05/2015 (3)	12/07/2015 (3)
End of retention period	01/23/2014 (2)	06/06/2014 (2)	12/15/2015 (2)	03/05/2017 (2)	12/07/2017 (2)
Total number of bonus shares	42 000	5 600	5 600	5 600	5 600
Number of cancelled bonus shares at the end of the year	2 100	0	0	0	0
Number of shares with ongoing vesting at the end of the year	0	0	0	0	0

	2015 Plans			
	n°1 10 years	n°2.1 managers	n°2.2 employees	corporate officer
Date of shareholders' meeting	12/10/2015	12/16/2015	12/16/2015	12/16/2015
Recipients	Employees	Employees	Employees	Olivier Soula
Vesting date	12/10/2017 (4)	12/16/2016 (5)	12/16/2019 (1)	12/16/2016 (5)
End of retention period	12/10/2017 (4)	12/16/2017 (5)	12/16/2020 (6)	12/16/2017 (5)
Total number of bonus shares	39 150	5 000	12 600	5 000
Number of cancelled bonus shares at the end of the year	2 860	0	1 800	0
Number of shares with ongoing vesting at the end of the year	0	0	2 700	0

	2016 Plans			2017 Plan
	corporate officers	corporate officers	employees	managers
Date of shareholders' meeting	03/15/2016	03/15/2016	12/15/2016	12/14/2017
Recipients	Olivier Soula	Olivier Soula	Employees	Employees
Vesting date	03/15/2020 (1)	03/15/2018 (7)	12/15/2020 (1)	12/15/2021 (1)
End of retention period	03/15/2021 (6)	03/15/2018 (7)	12/15/2021 (6)	12/15/2022 (2)
Total number of bonus shares	8 000	12 000	40 000	9 500
Number of cancelled bonus shares at the end of the year	0	8000	2025	0
Number of shares with ongoing vesting at the end of the year	4 000	0	18 650	7 125

## Information on the Company and the corporate capital

	2018 Plans						
	n°1 employees	n°2.1 employees	n°2.2 employees	n°2.2 corporate officers	n°3 employees	n°4 employees	n°5 employees
Date of shareholders' meeting	02/08/2018	05/17/2018	05/17/2018	05/17/2018	17/05/2018	25/09/2018	05/12/2018
Recipients	employees	employees	employees	Olivier Soula	employees	employees	employees
Vesting date	02/08/2022 <sup>(1)</sup>	05/17/2019 <sup>(8)</sup>	05/17/2020 <sup>(4)</sup>	05/17/2020 <sup>(4)</sup>	05/17/2022 <sup>(1)</sup>	09/25/2022 <sup>(1)</sup>	12/05/2022 <sup>(1)</sup>
End of retention period	02/08/2023 <sup>(6)</sup>	05/17/2020 <sup>(6)</sup>	05/17/2020 <sup>(4)</sup>	05/17/2020 <sup>(4)</sup>	02/08/2023 <sup>(6)</sup>	09/25/2023 <sup>(6)</sup>	12/05/2023 <sup>(6)</sup>
Total number of bonus shares	2 700	4 000	14 900	150	5 600	5 600	11 600
Number of cancelled bonus shares at the end of the year	0	0	1 330	0	0	0	0
Number of shares with ongoing vesting at the end of the year	2 700	4 000	13 570	150	5 600	5 600	11 600

(1) The vesting period is four years, with a block of one-quarter vesting on each anniversary date. The date stated is the latest date for the last one-quarter block.

(2) The retention period is two years from the vesting date.

(3) The vesting period is five years, with a block of one-quarter vesting on each anniversary date starting from the second anniversary. The date stated is the latest date for the last one-quarter block.

(4) The vesting period is two years, without retention period (ten-year plan only).

(5) Vesting is conditioned on meeting the performance objectives set for the year. The vesting date is the date the board of directors validates these objectives. Thereafter, a one-year retention period ensues.

(6) The retention period is one year from the vesting date.

(7) Vesting is conditioned on meeting the performance objectives set for a two-year period. The vesting date is the date the board of directors validates these objectives. There is no retention period.

(8) the vesting period is 1 year starting with the board of directors validation date of these objectives.

As of the date of this reference document, 75,695 bonus shares were in the process of being acquired, which may result in the creation of 75,695 shares with a par value of €0.10.



## 5.1.5.3 BSPCE founders' warrants

	2013 Plans		2014 Plans		
	n°1 managers	n°2 managers	n°1 managers	n°2 managers	corporate officers
Date of shareholders' meeting	06/18/2013	06/18/2013	06/24/2014	06/24/2014	06/24/2014
Date of board of directors' decision	12/13/2013	12/13/2013	09/25/2014	09/25/2014	09/25/2014
Number of BSPCE stock warrants authorized	28 000	22 400	14 000	5 600	100 000
Number of BSPCE stock warrants issued	28 000	22 400	14 000	5 600	100 000
Total number of shares that may be subscribed	28 000	22 400	14 000	5 600	100 000
<i>Of which by Gérard Soula</i>	-	-	-	-	20 000
<i>Of which by Olivier Soula</i>	-	-	-	-	45 000
Earliest BSPCE stock warrant exercise date	12/13/2014 (1)	12/13/2015 (1)	06/24/2015 (1)	06/24/2015 (1)	Fulfillment of performance criterias approved by the Board of directors meeting of 12/23/2014
BSPCE stock warrant expiration date	12/13/2023	12/13/2023	09/25/2024	09/25/2024	09/24/2024
BSPCE stock warrant issue price (euros)	free	free	free	free	free
BSPCE stock warrant strike price (euros)	5.76	5.76	34.99	34.99	34.99
Exercise conditions	(1)	(1)	(1)	(1)	Immediate vesting upon fulfillment of relevant performance criteria
Number of subscribed shares at the end of the year	4 900	700	0	0	0
Number of lapsed or cancelled warrants at the end of the year	0	0	2 800	5 600	0
Remaining warrants at the end of the year	23 100	21 700	11 200	0	100 000

	<b>BSPCE Corporate officers 2015</b>	<b>BSPCE Corporate officers 2016</b>	<b>BSPCE Corporate officers 2017</b>
Date of shareholders' meeting	12/11/2015	11/12/2015	11/12/2015
Date of board of directors' decision	12/16/2015	03/15/2016	09/08/2017
Number of BSPCE stock warrants authorized	40 000	40 000	150 000
Number of BSPCE stock warrants issued	40 000	40 000	150 000
Total number of shares that may be subscribed	40 000	40 000	150 000
<i>Of which by Gérard Soula</i>	40 000	40 000	75 000
<i>Of which by Olivier Soula</i>	-	-	75 000
Earliest BSPCE stock warrant exercise date	Fulfillment of performance criterias approved by the Board of directors meeting of 12/16/2015	Fulfillment of performance criterias approved by the Board of directors meeting of 12/13/2016	Dès la réalisation de critères de performance définis pour 3 ans (1)
BSPCE stock warrant expiration date	12/16/2025	03/15/2026	09/08/2027
BSPCE stock warrant issue price (euros)	free	free	free
BSPCE stock warrant strike price (euros)	74.60	61.73	16.00
Exercise conditions	Immediate vesting upon fulfillment of relevant performance criteria	Immediate vesting upon fulfillment of relevant performance criteria	Immediate vesting upon fulfillment of relevant performance criteria

## Information on the Company and the corporate capital

	<b>BSPCE Corporate officers 2015</b>	<b>BSPCE Corporate officers 2016</b>	<b>BSPCE Corporate officers 2017</b>
Number of subscribed shares at the filing date of this registration document	0	0	0
Number of lapsed or cancelled warrants at the filing date of this registration document	0	16 000	0
Remaining warrants at the end of the year	40 000	24 000	150 000

(1) These performance criteria were validated by the Board of Directors on May 17, 2018, concerning 20,000 BSPCE, the latter being exercisable on the date of this Registration Document.

As of the date of this reference document, 370,000 BSPCE founders' warrants are exercisable (provided the performance objectives are met), and the exercise of all of these BSPCE founders' warrants would lead to the creation of 370,000 shares of 0.10 par value.

5

### 5.1.5.4 Stock options

	<b>2015 SO Plan n°1</b>	<b>2015 SO Plan n°2</b>	<b>2017 SO Plan n°1</b>	<b>2017 SO Plan n°2</b>	<b>2018 SO Plan</b>
Date of shareholders' meeting	06/18/2013	11/12/2015	11/12/2015	11/12/2015	05/17/2018
Date of board of directors' decision	03/31/2015	12/16/2015	04/14/2017	07/19/2017	05/17/2018
Number of stock options authorized	20 000	4 000	13 000	40 000	23 000
<i>Of which corporate officers</i>	-	-	-	-	-
Earliest stock option exercise date			04/14/2017	07/19/2017	17/05/2018
Stock option expiration date			04/14/2027	07/19/2027	17/05/2028
Stock option strike price (euros)	55.64	71.12	18.00	19.00	17.00
Number of subscribed shares at the end of the year				91	
Number of lapsed or cancelled stock options at the end of the year	20 000	4 000		39 909	
Remaining stock options at the end of the year	0	0	13 000	0	23 000

(1) the 20,000 BSA granted on May 17, 2018 to an employee can be exercised by their beneficiary according to the following exercising agenda:

- 20% of the BSA starting August 3<sup>rd</sup>, 2018;
- 20% of the BSA starting May 2<sup>nd</sup>, 2019;
- 20% of the BSA starting May 2<sup>nd</sup>, 2020;
- 20% of the BSA starting May 2<sup>nd</sup>, 2021; and
- The remaining balance, ie 20% of the BSA starting May 2<sup>nd</sup>, 2022.

Therefore, as of the date of the present reference document, 20% of the BSA can be exercised.

(2) Half of the 3,000 BSA granted to an employee can be exercised as of the date of the present reference document, the remaining balance, ie 1,500 BSA, can be exercised on May 17<sup>th</sup>, 2019.

As of the filing date of this reference document, 36,000 stock options are exercisable, which, if fully exercised, would result in the creation of 36,000 shares with a par value of €0.10.

### 5.1.5.5 Synthèse des instruments dilutifs

At the date of this Reference Document, the total number of ordinary shares that may be created by full exercise of all rights giving access to the Company's share capital amounts to 543,095 shares, ie a maximum dilution of 7.3% based on fully diluted capital. Dilution in voting rights is identical and stands at 5.35% on the basis of fully diluted voting rights.

## 5.2 Authorized capital

### 5.2.1 Delegations of authority in effect and uses thereof

Type of delegation or authorization	Period of validity/Expiration	Ceiling (par value)	Procedures for setting the price	Date and conditions of use by the board of directors
<b>General shareholders' meeting of November 12, 2015</b>				
Authorization to the board to grant options to subscribe or purchase shares of the Company	38 months January 12, 2019	200,000 shares (1)	(2)	The board used this authorization by awarding: 4,000 options on 12/16/2015 13,000 options on 04/14/2017 40,000 options on 07/19/2017
Authorization granted to the Board to award bonus shares in existence or to be issued	38 months January 12, 2019	200,000 shares up to a maximum of 10% of the capital at the time of the grant (1)	n/a	The board used this authorization by awarding: 39,150 shares on 12/10/2015 22,600 shares on 12/16/2015 20,000 shares on 03/15/2016 40,000 shares on 12/13/2016 9,500 shares on 12/14/2017 2,700 shares on 02/08/ 2018 24,650 shares on 05/17/ 2018 5,600 shares on 09/25/ 2018 11,600 shares on 12/05/2018
<b>General shareholders' meeting of June 27, 2017</b>				
Authorization granted to the board of directors to issue, maintaining preemptive subscription rights, shares and/or securities conferring immediate and/or future equity rights in the Company	26 months August 26, 2019	€210,000 (3)	n/a	The board did not use this authorization
Authorization granted to the board of directors to issue, cancelling preemptive subscription rights, by a public offering, shares and/or securities conferring immediate and/or future equity rights in the Company, and the right to confer priority rights	26 months August 26, 2019	€137,000 (3)	(4)	The board did not use this authorization
Delegation of authority to the board to increase the number of shares to be issued in the event of a capital increase with or without preemptive subscription rights	26 months August 26, 2019	15% of the original issue (3) (7)	Same price as the original issue price	The board did not use this authorization
Authorization granted to the board, in the event of an issue of shares or any securities conferring equity rights cancelling shareholders' preemptive subscription rights, to set the issue price, up to 10% of the capital and in accordance with the limitations set by the general shareholders' meeting	26 months August 26, 2019	up to 10% of the capital (3)	(5)	The board did not use this authorization
Delegation of authority to the board to issue ordinary shares or securities conferring equity rights to pay for contributions of securities pursuant to a public offer with an exchange component initiated by the Company	26 months August 26, 2019	€68,000 (3)	n/a	The board did not use this authorization
Delegation of authority to the board to increase capital up to 10% of the capital to pay for non-cash contributions of equity securities or securities conferring equity rights in third-party companies not in connection with an exchange offer	26 months August 26, 2019	€68,000 up to 10% of the capital per year (3)	n/a	The board did not use this authorization
Delegation of authority to the board to increase capital by capitalizing premiums, reserves, profits or other funds	26 months August 26, 2019	€100,000	n/a	The board did not use this authorization

## Information on the Company and the corporate capital

Type of delegation or authorization	Period of validity/Expiration	Ceiling (par value)	Procedures for setting the price	Date and conditions of use by the board of directors
<b>General shareholders' meeting of May 17, 2018</b>				
Authorization granted to the board of directors to carry out a capital increase, immediately or in the future, by issuing ordinary shares or any securities conferring equity rights, cancelling shareholder's preemptive subscription rights, by making an offer to qualified investors or a limited circle of investors within the meaning of Article L. 411-2, paragraph II, of the French monetary and financial code (private placement)	26 months July 16, 2020	€138,000 (6)	(4)	The board did not use this authorization
Delegation to the Board to increase the number of securities to be issued in the event of a capital increase without a preemptive subscription right	26 months July 16, 2020	15% of the original issue (6) (7)	Same price as the original issue price	The board did not use this authorization
If shares or any equity securities without a preemptive subscription right for shareholders are issued, authorization to be granted to the Board to determine the issue price for up to 10% of stated capital and up to the limits specified by the shareholders	26 months July 16, 2020	up to 10% of the capital (6)	(5)	The board did not use this authorization (5)
Authorization granted to the board of directors to carry out a capital increase by issuing ordinary shares or any securities convertible into shares, cancelling preemptive subscription rights for the benefit of a class of persons, in connection with an equity financing line	18 months November 16, 2019	€68,000 (6)	(8)	The board did not use this authorization
Authorization granted to the board of directors to issue BSA stock warrants to (i) the members of the Company's board of directors in office on the date the warrants are awarded and who are not employees or officers of the Company or any of its subsidiaries, (ii) persons who have entered into a services or consulting contract with the Company, or (iii) members of any committee the board of directors may set up, and who are not employees or officers of the Company or any of its subsidiaries	18 months November 16, 2019	100,000 BSA conferring the right to 100,000 shares (1)	(9)	The board did not use this authorization
Authorization given to the Board of Directors to grant options to subscribe or purchase shares of the Company	38 months July 16, 2021	200,000 shares (1)	(2)	The board used this authorization by attributing 23,000 shares on May 17, 2018
Delegation of authority to the Board of Directors to grant free shares of existing or future shares	38 months July 16, 2021	200,000 shares up to 10% of the capital at the moment of the attribution (1)	n/a	The board did not use this authorization

1) The sum of (i) the shares that may be issued or acquired by exercising options granted, (ii) the shares that may be awarded free of charge, (iii) the shares that may be issued upon the exercise of the BSPCE founders' warrants and (iv) the shares that may be issued upon the exercise of the BSA stock warrants shall not exceed 250,000 shares. However, this cap will be increased by the additional number of shares to be issued, in accordance with contractual provisions, to preserve the rights of holders of securities and other rights conferring access to shares.

(2) The purchase or subscription price per share will be set by the board of directors on the day the option is granted, within the limitations set by law and this resolution, but shall not be less than ninety-five percent (95%) of the average share price over the twenty trading days before the date of the board's decision to award the options, rounded to the next lowest euro, nor, in the case of stock options, 80% of the average purchase price of treasury shares held by the Company, rounded to the next lowest euro.

(3) These amounts cannot be combined. The maximum total amount for capital increases in par value terms is set at €210,000. The total par value of issues of debt securities of the Company conferring equity rights in the Company may not exceed €30,000,000.

(4) The share issue price shall be at least equal to the weighted average trading price over the last three trading days before the price is set, discounted, if applicable, by the maximum issue discount allowed by law (currently 5%), and adjusted by the difference in their dividend entitlement dates. However, the issue price of securities conferring equity rights shall be such that the amount, if any, received immediately by the Company or that it may receive subsequently, is, for each share issued as a result of the issue of these securities, at least equal to the minimum issue price defined above.

(5) Up to a maximum of 10% of the Company's capital (as of the transaction date) per 12-month period, the board may disregard the price-setting conditions specified in the above resolutions and set the issue price of common shares and/or marketable securities conferring immediate or future access to equity rights as follows:

- the issue price of common shares shall be at least equal to the weighted average of the price over the last three trading days before the date on which it is set, less a possible maximum issue discount of 20%, which shall in no case be less than the par value of one share of the Company on the issue date of the relevant shares. However, in the event securities conferring equity rights are issued, the issue price of the shares that may result from the exercise, conversion or exchange thereof may, at the board's discretion, be set by reference to a calculation formula it defines and applicable after such securities are issued (e.g., when they are exercised, converted or exchanged), in which case the aforementioned maximum issue discount may be determined, at the board's discretion, on the date the formula is applied (and not the date the issue price is set); and

- the issue price of marketable securities conferring equity rights shall be such that the amount the Company receives immediately plus, if applicable, the amount it may subsequently receive is, for each share issued in consequence of the issue of these securities, at least equal to the issue price defined in the paragraph above.

(6) These amounts are not cumulative. The maximum cumulative ceiling authorized for nominal capital increases is € 210,000. The total nominal amount of issues of debt securities representing the Company giving access to the Company's share capital may not exceed € 50,000,000,

(7) 15% or any other fraction that would have been determined by decree

(8) the issue price of the issued shares will be determined by the Board of Directors and will be at least equal to the average of the volume-weighted average trading prices for the last 3 trading days preceding the price of the issue possibly reduced by a maximum discount of 20%, taking into account, if applicable, their date of entitlement; it being specified that (i) in the event of the issue of securities giving access to the share capital, the issue price of the shares likely to result from their exercise, conversion or exchange may be fixed if necessary, at the discretion of the board of directors, by reference to a calculation formula defined by the latter and applicable subsequent to the issue of such securities (for example upon their exercise, conversion or exchange) in which case the maximum discount referred to above may be considered, if the Board deems it appropriate, on the date of application of the said formula (and not on the issue price setting date), and (ii) the issue price of the securities giving access to the the capital, if any, issued pursuant to this resolution shall be such as the sum, if any, immediately received by the Company, plus any sum that may be the exercise or conversion of the said securities, that is, for each share issued as a result of the issue of such securities, at least the minimum amount referred to above,

(9) The issue price of a BSA will be determined by the Board of Directors on the day of issue of the said BSA based on the characteristics of the BSA and will be at least equal to 5% of the average volume weighted average price. the last five (5) trading days on the regulated market of Euronext Paris prior to the date of allocation of said BSA by the Board. The subscription price of one ordinary share of the Company on the exercise of a BSA, will be determined by the Board of Directors at the time of allocation of the BSA and must be at least equal to the higher of the two following values:

- the selling price of a closing share on the regulated market the day before the decision of the board to award the BSA; and

- the weighted average of the quoted prices for the twenty trading days preceding the day of the board's decision to award the BSA

## 5.2.2 Information about the Company's capital which is under option or subject to a conditional or unconditional agreement to be placed under option

To the Company's knowledge, there are no call or put options or other commitments to the Company shareholders, or granted by the Company's shareholders, concerning the Company's shares.

## 5.2.3 History of the corporate capital

### 5.2.3.1 Historical evolution since January 1<sup>st</sup>, 2017

Issue Date	Type of transaction	Capital	Issue premium	Number of shares issued	Total number of shares comprising the capital	Par value	Corporate capital	Issue price per share
June-17	Acquisition of AGA	200€	(200) €	2,000	6 861 763	0.1€	686 176€	-
December-17	Acquisition of AGA	3, 629€	(3,629) €	36,290	6 898 053	0.1€	689 805€	-
December-17	Acquisition of AGA	270€	(270) €	2,700	6 900 753	0.1€	690 075€	-
December-17	Acquisition of AGA	1, 000€	(1,000) €	10,000	6 910 753	0.1€	691 075€	-
March-18	Acquisition of AGA	600€	(600) €	6,000	6 916, 753	0.1€	691 675€	-
June-18	Exercise of SO	9€	1,720 €	91	6 916, 844	0.1€	691 684€	19€
December -18	Acquisition of 'AGA	1, 440€	(1,440) €	14,400	6 931, 244	0.1€	693 124€	-

### ▪ Share price variation – Risk of price variation

The securities of the Company were listed on the regulated market of Euronext Paris on February 14, 2012 at the introductory price of € 15.88.

In 2018, the share price traded at a high of €20.70 on April 26, 2018 and a low of €10.48 on November 23<sup>rd</sup>, 2018. At the end of December 2018, the share price was €16.54, i.e., giving the Company a market capitalization of €114.6 million.

In the early months of 2019, the share price rose from €16.54 on January 1, 2019 to €14.14 on April 9, 2019, giving the Company a market capitalization of €98 million.

## 5

## 5.3 Articles of incorporation and statutes

### 5.3.1 Corporate purposes

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The Company's purposes, directly or indirectly, both in France and abroad, are:

- Research and development of polymer materials to create controlled-release systems for peptides and proteins of pharmaceutical interest;
- The registration, study, acquisition and granting of all patents, licenses, processes, trademarks and protection of specialized knowledge in any way arising from or relating to the domains or technologies falling within the scope of the corporate purposes;
- The design, development, manufacture, distribution, import, export and use, by any means, of medicines, proprietary drugs and other healthcare goods;
- Creating, buying, renting and taking all businesses pursuant to lease-management arrangements, and leasing, installing and operating all establishments, businesses, factories and workshops in relation with any of the activities specified above;
- The Company's direct or indirect participation in all financial, real or personal property transactions and in any civil, commercial or industrial companies that may come within the scope of the corporate purposes, or any similar, related or complementary purpose.

### 5.3.2 Management and supervisory bodies

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#### 5.3.2.1 Board of directors

- **Composition of the board of directors (Articles 11.1 and 11.2 of the articles of incorporation)**

The Company shall be administered by a board composed of individuals or legal entities whose number shall be determined by an ordinary general shareholders' meeting within the limits of the law.

At the time they are appointed, legal entities shall designate an individual as their permanent representative to the board of directors. The term of office of the permanent representative shall have the same duration as the term of office of the legal entity he represents. If the legal entity dismisses its permanent representative, it shall immediately appoint a replacement. The same provision shall also apply in the event of the death or resignation of the permanent representative.

Directors are appointed for a three-year term. Directors' terms of office shall expire at the conclusion of the ordinary general shareholders' meeting that votes on the financial statements for the past fiscal year and that is held in the year during which said directors' terms of office expire.

Directors may be reappointed. They may be removed from office at any time by a decision of a general shareholders' meeting.

In the event of one or more vacancies on the board of directors due to death or resignation, the board may make temporary appointments between two general shareholders' meetings.

Appointments made by the board pursuant to the preceding paragraph shall be submitted for ratification by the next ordinary general shareholders' meeting.

The absence of such approval shall not affect the validity of the board's prior resolutions and acts.

If the number of directors falls below the statutory minimum, the remaining directors shall immediately convene an ordinary general shareholders' meeting for the purpose of completing the membership of the Board.

Company employees may be appointed as directors. However, their employment contract must correspond to actual employment. In such case, employees do not lose the benefit of their employment contracts.

The number of directors who have entered into an employment contract with the Company may not exceed one-third of the directors in office.

The number of directors over the age of 70 may not exceed one-third of the directors in office. If this limit is exceeded during the directors' terms of office, the oldest director shall automatically be deemed to have resigned at the conclusion of the next general shareholders' meeting.

- **Board observers (Article 15 of the articles of incorporation)**

Pursuant to a proposal of the board of directors, an ordinary general shareholders' meeting may appoint board observers. The board of directors may also appoint them directly, subject to ratification by the next general shareholders' meeting.

The board observers, who may not number more than five, shall form a panel. They shall be selected, without restriction, based on their expertise.

They shall be appointed for a term of three years, which shall expire at the conclusion of the ordinary general shareholders' meeting that votes on the financial statements for the previous fiscal year.

The panel of board observers shall review matters that the board of directors or its chairman submits to it for its opinion. The board observers shall attend board of directors' meetings and shall take part in deliberations in a nonvoting capacity. However, their absence shall not affect the validity of the board's decisions.

They shall be given notice of board meetings in the same manner as the directors.

The board of directors may compensate the board observers by allocating an amount from the directors' fees granted annually to the directors by a general shareholders' meeting.

- **Meetings of the board of directors (Article 12 of the articles of incorporation)**

The board of directors shall meet as often as the required by the Company's interests.

The chairman shall give the directors notice of board meetings. Notice may be given by any means, whether written or oral.

The chief executive officer may also request that the chairman convene a meeting of the board of directors to consider a specific agenda.

Additionally, directors representing at least one-third of the members of the board may validly convene a board meeting. In such case, they shall state the agenda for the meeting.

## Information on the Company and the corporate capital

If a works council has been created, the representatives of such council, appointed in accordance with the provisions of the French Labor Code, shall be given notice of all board of directors' meetings.

Board meetings shall be held at the registered office or at any other location in France or abroad.

Decisions of the board shall be valid only if the number of members in attendance is at least equal to half the members.

Decisions of the board of directors shall be made by a majority of votes; in the event of a tie, the chairman of the meeting shall cast the deciding vote.

The board of directors may adopt rules of procedure, which may provide *inter alia* that, for purposes of calculating the quorum and majority, directors who participate in board meetings by videoconference or other means of telecommunication in compliance with the laws and regulations in force will be deemed to be present. This provision shall not apply to the adoption of the decisions referred to in Articles L. 232-1 and L. 233-16 of the French Commercial Code.

Each director shall receive the information necessary to perform his duties and hold his corporate office, and may obtain copies of all documents he deems of use.

Any director may authorize, by letter, telegram, telex, fax, email or any other means of remote transmission, another director to represent him at a board meeting, but each director may only hold one proxy during a meeting.

Copies or extracts of the minutes of board of directors' meetings shall be validly certified by the chairman of the board of directors, the chief executive officer, a director temporarily appointed to act as chairman or an agent duly authorized for such purpose.

### ▪ Powers of the board of directors (Article 13 of the articles of incorporation)

The board of directors shall establish the Company's business policies and ensure they are carried out. Subject to the powers expressly reserved by law to shareholders' meetings and within the limits of the corporate purposes, the board of directors may consider any issue relating to the proper operation of the Company and, by its decisions, shall resolve matters that concern the Company.

In its relations with third parties, the Company shall be bound by the acts of the board of directors that exceed the scope of the corporate purposes, unless the Company proves that the third party was aware, or that in light of the circumstances could not have been unaware, that the act was not within said corporate purposes. However, the mere publication of the articles of incorporations shall not constitute such proof.

The board of directors shall carry out all verifications and audits it deems necessary.

Furthermore, the board of directors shall exercise the special powers conferred on it by law.

### 5.3.2.2 Executive management (Article 14 of the articles of incorporation)

The Company's executive management functions shall be performed, under his responsibility, by the chairman of the board of directors or another individual appointed by the board of directors, who shall hold the title of chief executive officer.

The chief executive officer shall have the broadest possible powers to act in all circumstances in the name of the Company. The chief executive officer shall exercise his powers within the limits of the corporate purposes and subject to the powers expressly granted by law to shareholders' meetings and to the board of directors.

He shall represent the Company in its dealings with third parties. The Company shall be bound by acts of the chief executive officer that exceed the scope of the corporate purposes, unless the Company is able to prove that the third party was aware, or in light of the circumstances could not have been unaware, that the act was not within said corporate purposes. However, the mere publication of the articles of incorporation shall not be sufficient to constitute such proof.



The chief executive officer may not be more than 75 years old. If the chief executive officer reaches this age limit, he shall automatically be deemed to have resigned. However, the chief executive officer's term of office shall continue until the next board of directors' meeting at which a new chief executive officer is appointed.

If the chief executive officer is a director, the term of his position shall not exceed his term of office as director.

The board of directors may remove the chief executive officer at any time. If the chief executive officer is removed from office without just cause, he may claim damages, unless he also holds the position of chairman of the board of directors.

By a decision adopted by a simple majority of the votes of directors present or represented, the board of directors shall choose between the two methods of executive management referred to in the first paragraph of this section.

Shareholders and third parties shall be informed of this decision in accordance with statutory and regulatory requirements.

The choice made by the board of directors shall remain in effect until a contrary decision of the board or, at the board's discretion, for the duration of the chief executive officer's term of office.

If the Company's executive management functions are performed by the chairman of the board of directors, the provisions concerning the chief executive officer shall apply to him.

In accordance with the provisions of Article 706-43 of the French Code of Criminal Procedure, the chief executive officer may validly delegate to any person of his choice the authority to represent the Company in connection with criminal proceedings that may be initiated against the Company.

Pursuant to a proposal of the chief executive officer, the board of directors may authorize one or more individuals to assist the chief executive officer in the capacity of deputy chief executive officer.

In agreement with the chief executive officer, the board of directors shall determine the scope and duration of the powers granted to the deputy chief executive officers. The board of directors shall set their compensation. If a deputy chief executive officer is a director, the term of his position shall not exceed his term of office as director.

The deputy chief executive officers shall have the same powers with respect to third parties as the chief executive officer; in particular, the deputy chief executive officer may represent the Company before the courts.

No more than five deputy chief executive officers may be appointed.

Pursuant to a proposal of the chief executive officer, the deputy chief executive officer(s) may be removed from office by the board of directors at any time. If a deputy chief executive officer is removed from office without just cause, he may claim damages.

Deputy chief executive officers may not be more than 65 years old. If a deputy chief executive officer in office reaches this age limit, he shall automatically be deemed to have resigned. The deputy chief executive officer's term of office shall continue until the next board of directors' meeting, at which a new deputy chief executive officer may be appointed.

If the chief executive officer leaves office or is unable to perform his duties, unless otherwise decided by the board of directors, the deputy chief executive officer(s) shall remain in office and retain his (their) powers until the appointment of a new chief executive officer.

## 5.3.3 Rights, privileges and restrictions pertaining to the Company's shares

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### 5.3.3.1 Forms of the shares (Article 7 of the articles of incorporation)

Shareholders may choose to hold their fully paid-in shares in registered or bearer form, subject, however, to application of the legal provisions relating to the form of shares held by certain individuals or legal entities. Shares that are not fully paid-in must be held in registered form.

The shares shall be registered in an account under the terms and conditions specified in the applicable laws and regulations.

The ownership of shares issued in registered form shall be effective upon their registration in a registered account.

### 5.3.3.2 Voting rights (excerpted from Article 9 of the articles of incorporation)

Unless the law provides otherwise, and except in the case of double voting rights as set forth below, each shareholder has a number of voting rights and may cast a number of votes at shareholders' meetings equal to the number of fully paid-in shares he owns. Provided they have the same par value, each equity or dividend share is entitled to one vote, except in the case of double voting rights as set forth below.

A voting right equal to twice the voting right attributed to other shares, based on the proportion of the corporate capital they represent, is granted to all fully paid-in shares (regardless of their class) that can be proved to have been registered in the name of the same shareholder for at least two years. The conversion of preferred shares into common shares shall have no impact on the calculation of the holding period. This right is also conferred at the time of issue, in the event of a capital increase carried out by capitalizing reserves, profits or issue premiums, to registered shares granted as bonus shares to a shareholder for existing shares that already entitled him to this right.

### 5.3.3.3 Rights to dividends and profits (excerpted from Articles 9, 21 and 22 of the articles of incorporation)

Each share confers ownership rights to a share of the corporate assets, profits and liquidation surplus in proportion to the number and par value of existing shares.

Whenever it is necessary to hold more than one share, whether or not preferred shares, or securities to exercise any right, the shareholders or holders of securities shall be responsible for pooling the number of shares or securities required.

An amount of at least five percent (5%) shall be deducted from the profits for the fiscal year, reduced by prior losses, if any, in order to constitute the reserve fund known as the "legal reserve fund". Such deduction shall cease to be mandatory when the amount in the statutory reserve fund is equal to one-tenth of the capital.

Distributable earnings shall consist of earnings for the fiscal year, less prior losses and the deduction specified in the previous paragraph, plus earnings carried forward.

If the financial statements for the fiscal year, as approved by a general shareholders' meeting, show a distributable profit, the general shareholders' meeting shall post it to one or more reserve funds that they have the power to appropriate or use, carry it forward or distribute it in the form of dividends.

After having confirmed the existence of reserve funds available to it, a general shareholders' meeting may decide to distribute amounts deducted from such reserve funds. In such case, the decision shall expressly state the reserve items from which the deductions are made. However, dividends shall first be deducted from the distributable profits for the financial year.

The procedures for paying dividends shall be set by a general shareholders' meeting or, failing that, by the board of directors.

However, dividends shall be paid within a maximum period of nine months from the end of the fiscal year.

The general shareholders' meeting convened to vote on the financial statements for the fiscal year may give each shareholder, for all or part of the dividend paid, the choice between receiving the dividend in cash or in shares.

Similarly, an ordinary general shareholders' meeting, acting in accordance with the requirements of Article L. 232-12 of the French Commercial Code, may grant each shareholder an interim dividend and, for all or part of said interim dividend, may give him the choice between receiving the interim dividend in cash or in shares. (...)

### 5.3.3.4 Preemptive rights

Shares in the Company carry a preemptive right to subscribe to capital increases in accordance with the requirements of the French Commercial Code.

### 5.3.3.5 Restrictions on voting rights

No provision of the articles of incorporation restricts the voting rights attached to shares.

### 5.3.3.6 Identifiable bearer shares

The Company may, in accordance with applicable statutory and regulatory requirements, at any time and at its own expense, request from any authorized body the name or, in the case of a legal entity, the corporate name, nationality and address of holders of shares that confer an immediate or future voting right at its own shareholders' meetings, as well as the number of shares held by each of them and, if applicable, any restrictions on these shares.

### 5.3.3.7 Buyback by the Company of its own shares

See section 5.1.4 "Acquisition by the Company of its own shares."

## 5.3.4 Requirements for amending shareholders' rights

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The rights of shareholders as described in the Company's articles of incorporation may only be amended by an extraordinary general meeting of the Company's shareholders.

## 5.3.5 General shareholder's meetings

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### 5.3.5.1 Holding of shareholder's meetings (Article 19 of the articles of incorporation)

General shareholders' meetings shall be convened and shall meet in the manner prescribed by law.

If the Company wishes to give notice of meetings electronically, instead of by mail, it must first obtain the agreement of the shareholders concerned, who shall provide their email address.

Meetings shall be held at the registered office or at any other location specified in the notice of meeting.

The right to attend meetings is governed by the applicable statutes and regulations and requires, in particular, registration of the shares in the name of the shareholder or of the intermediary registered on his behalf, by midnight,

## Information on the Company and the corporate capital

Paris time, on the second business day before the meeting, either in the registered securities accounts held by the Company or in the bearer share accounts held by the authorized intermediary.

Shareholders who do not attend a general shareholders' meeting personally may choose one of three following options:

- appointing a proxy under the conditions permitted by the statutes and regulations;
- voting by mail; or
- sending a proxy form to the Company without naming a proxy;
- in accordance with the requirements prescribed by the laws and regulations.

In accordance with the requirements prescribed by the statutes and regulations in force, the board of directors may arrange for shareholders to participate and vote by videoconference or means of telecommunication that allow them to be identified. If the board of directors decides to exercise this right for a particular shareholders' meeting, such board decision shall be mentioned in the announcement and/or notice of the meeting. Shareholders who participate in shareholders' meetings by videoconference or any of the other means of telecommunication referred to above, as selected by the board of directors, shall be deemed present for the purposes of calculating the quorum and majority.

Shareholders' meetings shall be chaired by the chairman of the board of directors or, in the absence thereof, by the chief executive officer, by a deputy chief executive officer if he is a director, or by a director specifically appointed for such purpose by the board. Failing that, the shareholders' meeting shall elect its own chairman.

The duties of vote counter shall be performed by the two participants at the shareholders' meeting who are present and hold the highest number of votes, and who agree to perform such duties. The officers shall appoint a secretary, who may but is not required to be a shareholder.

An attendance sheet shall be kept, in accordance with the requirements prescribed by law.

An ordinary general shareholders' meeting can be validly conducted pursuant to a first notice of meeting only if the shareholders present or represented hold at least one-fifth of the shares having the right to vote. An ordinary general shareholders' meeting convened pursuant to a second notice of meeting may deliberate validly regardless of the number of shareholders present or represented.

Decisions of ordinary general meetings shall be adopted by a simple majority of the votes cast by the shareholders present or represented.

An extraordinary general shareholders' meeting can be validly conducted pursuant to a first notice of meeting only if the shareholders present or represented hold at least one-fourth of the shares having the right to vote. An extraordinary general shareholders' meeting can be validly conducted pursuant to a second notice of meeting only if the shareholders present or represented hold at least one-fifth of the shares having the right to vote.

Decisions of extraordinary general meetings shall be adopted by a two-thirds majority of the votes cast by the shareholders present or represented.

Copies or extracts of shareholder meeting minutes may be validly certified by the chairman of the board of directors, a director who holds the position of chief executive officer or the secretary of the meeting.

### 5.3.5.2 Powers of shareholders' meetings

Ordinary and extraordinary general shareholders' meetings shall exercise their respective powers in accordance with the requirements prescribed by law.

### 5.3.6 Provisions that may have the effect of delaying, deferring or preventing a change of control

The Company's articles of incorporation contain no provisions that may have the effect of delaying, deferring or preventing a change of control.

### 5.3.7 Specific provisions governing changes in the capital

The Company's articles of incorporation contain no specific provisions governing changes in its capital.

## 5.4 Major shareholders

### 5.4.1 Change in the Company's capital structure over the past two years on an undiluted basis

	Situation as of December 31, 2018			Situation as of December 31, 2017		
	Number of shares	% of capital	% of voting rights	Number of shares	% of capital	% of voting rights
<b>Soula Family</b>	<b>1 527 983</b>	<b>22,0%</b>	<b>31,6%</b>	<b>1 519 483</b>	<b>22,0%</b>	<b>31,6%</b>
G�rard Soula	898 463	13,0%	18,7%	898 463	13,0%	18,7%
Olivier Soula	305 490	4,4%	6,3%	299 490	4,3%	6,2%
R�mi Soula	306 540	4,4%	6,3%	304 040	4,4%	6,3%
Laure Soula	17 490	0,3%	0,4%	17 490	0,3%	0,4%
<b>Financial Investors</b>	<b>1 178 856</b>	<b>17,0%</b>	<b>23,9%</b>	<b>1 133 138</b>	<b>16,4%</b>	<b>23,5%</b>
Innobio (a)	671 641	9,7%	13,5%	625 923	9,1%	13,1%
Fonds BioAM (b)	112 716	1,6%	2,3%	112 716	1,6%	2,4%
<i>Subtotal (a)+(b)</i>	784 357	11,3%	15,8%	738 639	10,7%	15,4%
Fonds Amundi	1 570	0,0%	0,0%	1 570	0,0%	0,0%
Fonds Viveris	32 368	0,5%	0,6%	32 368	0,5%	0,6%
Or�o Finance	40 561	0,6%	0,8%	40 561	0,6%	0,8%
SHAM (1)	320 000	4,6%	6,7%	320 000	4,6%	6,7%
<b>Employees</b>	<b>104 305</b>	<b>1,5%</b>	<b>1,6%</b>	<b>89 310</b>	<b>1,3%</b>	<b>1,3%</b>
Scientific committees (BSA)	700	0,0%	0,0%	700	0,0%	0,0%
Directors (BSA)	0	0,0%	0,0%	0	0,0%	0,0%
Treasury shares	10 555	0,2%	0,0%	7 516	0,1%	0,0%
<b>Other shareholders (2)</b>	<b>4 108 845</b>	<b>59,3%</b>	<b>42,8%</b>	<b>4 160 606</b>	<b>60,2%</b>	<b>43,5%</b>
<b>TOTAL</b>	<b>6 931 244</b>	<b>100,0%</b>	<b>100,0%</b>	<b>6 910 753</b>	<b>100,0%</b>	<b>100,0%</b>

(1) SHAM: Soci t  Hospitali re d'Assurance Mutuelles

(2) Including any shares held in bearer form by the Company's historical financial investors, as well as shares held by investors who took part in the private placement carried out in March 2015 (KKR filed a threshold crossing declaration).

As of the date of this reference document, the Company is not aware of any significant changes in its shareholding structure since December 31, 2018.

## Information on the Company and the corporate capital

### Threshold crossing of KKR & Co. L.P.:

By mail received on May 22, 2018, KKR & Co. LP (9 West 57th Street, Suite 4200, New York 10019, United States) stated that it had crossed indirectly, on May 17, 2018, the 5% threshold ADOCIA and indirectly hold 343,995 ADOCIA shares representing as many voting rights, ie 4.97% of the capital and 3.58% of the voting rights of this company, distributed as follows:

	Shares	% capital	Voting rights	% voting rights
KKR GMO II Holding L.P.	324 540	4.69%	324,540	3.38%
KKR Partners II (International) L.P.	19 455	0.28%	19 455	0.20%
<b>TOTAL KKR &amp; CO. L.P.</b>	<b>343 995</b>	<b>4.97%</b>	<b>343 995</b>	<b>3.58%</b>

This threshold crossing results from a sale of ADOCIA shares on the market. On this occasion, KKR GMO II Holdings LP crossed individually the same threshold

5

## 5.4.2 Distribution of capital and voting rights as of December 31, 2018 on a fully diluted basis

	Situation as of December 31, 2018 (non diluted basis)			Situation as of December 31, 2018 (diluted basis) (1)		
	Number of shares	% of capital	% of voting rights	Number of shares	% of capital	% of voting rights
<b>Soula Family</b>	<b>1 527 983</b>	<b>22,0%</b>	<b>31,6%</b>	<b>1 846 133</b>	<b>24,7%</b>	<b>33,1%</b>
G�rard Soula	898 463	13,0%	18,7%	1 057 463	14,1%	19,3%
Olivier Soula	305 490	4,4%	6,3%	429 640	5,7%	7,2%
R�mi Soula	306 540	4,4%	6,3%	341 540	4,6%	6,3%
Laure Soula	17 490	0,3%	0,4%	17 490	0,2%	0,3%
<b>Financial Investors</b>	<b>1 178 856</b>	<b>17,0%</b>	<b>23,9%</b>	<b>1 178 856</b>	<b>15,8%</b>	<b>22,7%</b>
Innobio (a)	671 641	9,7%	13,5%	671 641	9,0%	12,8%
Fonds BioAM (b)	112 716	1,6%	2,3%	112 716	1,5%	2,2%
<i>Subtotal (a)+(b)</i>	784 357	11,3%	<b>15,8%</b>	784 357	10,5%	15,0%
Fonds Amundi	1 570	0,0%	0,0%	1 570	0,0%	0,0%
Fonds Viveris	32 368	0,5%	0,6%	32 368	0,4%	0,5%
Or�o Finance	40 561	0,6%	0,8%	40 561	0,5%	0,8%
SHAM (1)	320 000	4,6%	<b>6,7%</b>	320 000	4,3%	6,3%
<b>Employees</b>	<b>104 305</b>	<b>1,5%</b>	<b>1,6%</b>	<b>267 850</b>	<b>3,6%</b>	<b>3,1%</b>
Scientific committees (BSA)	700	0,0%	0,0%	42 100	0,6%	0,4%
Directors (BSA)	0	0,0%	0,0%	20 000	0,3%	0,2%
Treasury shares	10 555	0,2%	0,0%	10 555	0,1%	0,0%
<b>Other shareholders (2)</b>	<b>4 108 845</b>	<b>59,3%</b>	<b>42,8%</b>	<b>4 108 845</b>	<b>55,0%</b>	<b>40,5%</b>
<b>TOTAL</b>	<b>6 931 244</b>	<b>100,0%</b>	<b>100,0%</b>	<b>7 474 339</b>	<b>100,0%</b>	<b>100,0%</b>

(1) As of December 31, 2017, the dilutive instruments issued by the Company consist of (i) 75,695 shares (after accounting for the 10-for-1 stock split decided by the general shareholders' meeting of October 24, 2011), which were issued as bonus shares by the Company to key employees and are in the vesting period, as more fully described in section 5.1.5 of this reference document; (ii) 41,400 BSA stock warrants conferring the right to subscribe for 41,400 shares (after accounting for the 10-for-1 stock split decided by the general shareholders' meeting of October 24, 2011); (iii)

20,000 BSA stock warrants conferring the right to subscribe for 20,000 shares granted to independent directors; (iv) 370,000 BSPCE founders' warrants conferring the right to subscribe for 370,000 shares; and (v) 36,000 stock options conferring the right to subscribe for 36,000 shares.

(2) SHAM : Hospital Mutual Insurance Compan

(3) Including any shares held in bearer form by the Company's historical financial investors.

### 5.4.3 Major shareholders not represented on the board of directors

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The Innobio and Bioam Funds are major shareholders of the Company, holding 11.3% of the capital and 15.8% of the voting rights as of December 31, 2018. They are represented on the board of directors by their management company Bpifrance Investments.

Société Hospitalière d'Assurance Mutuelles (SHAM) holds 4.6% of the Company's capital and 6.7% of its voting rights. It is not represented on the board of directors.

### 5.4.4 Voting rights of major shareholders

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A voting right equal to twice the voting right attributed to other shares, based on the proportion of the corporate capital they represent, is granted to all fully paid-in shares (regardless of their class) that can be proved to have been registered in the name of the same shareholder for at least two years.

This right is also conferred at the time of issue, in the event of a capital increase carried out by capitalizing reserves, profits or issue premiums, to registered shares granted as bonus shares to a shareholder for existing shares that already entitled him to this right.

### 5.4.5 Control of the Company

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As of the date of this reference document, no single shareholder owned a percentage of the capital sufficient to create a presumption that it controls the Company, within the meaning of Article L. 233-3 of the French Commercial Code.

The Company has therefore not been required to take measures to ensure that such control is not improperly exercised.

No shareholders' agreement is in force as of the date of this reference document, other than the collective undertaking to retain their securities in the Company (known as a "Dutrel" agreement) concluded by Gérard Soula, Olivier Soula, Rémi Soula and Laure Soula pursuant to Article 787 B of the French General Tax Code.

The Company's main shareholder is the Soula family group, which currently includes Gérard Soula (the chairman and CEO), Olivier Soula (the deputy CEO), Remi Soula, Laure Soula and Sylvie Soula. Gérard Soula and Olivier Soula are members of the Company's board of directors, respectively as chairman and director, along with four other directors (Olivier Martinez, Laurent Arthaud representing Bpifrance Investment, Dominique Takizawa and Ekaterina Smirnyagina). The Soula family group files consolidated declarations and has requested and obtained a waiver from the obligation to launch a public offer triggered by the fact that the Soula family group has crossed the 30% threshold.

### 5.4.6 Agreements that may lead to a change in control

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No specific provision of the issuer's articles of incorporation, or of any charter or rules of procedure could have the effect of delaying, deferring or preventing a change in its control.

## 5.4.7 Pledges of the Company's shares

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None.

## 5.5 Regulated agreements

The regulated agreements that exist to date are described in the statutory auditors' special reports presented below.

No agreement was entered into during the past fiscal year between (i) the chief executive officer, the deputy chief executive officer, any director or any shareholder of the Company holding more than 10% of the voting rights, and (ii) the Company's subsidiary.

### 5

### 5.5.1 Intra-group agreement

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An annual contract for services ("Services Agreement") was entered into between Adocia and Adocia Inc. in March 2015. That contract provides for the re-invoicing of costs incurred by the Company in connection with its business, plus a 10% fee to cover the operating costs of the U.S. subsidiary.

The impact of the creation of this new company on the financial statements as of December 31, 2018 is limited. Expenses totaling €1.1 million are for the payroll costs of two employees and their travel and entertainment expenses.

### 5.5.2 Related-party transactions

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None.



## 5.5.3 Statutory auditors' report on regulated agreements made in the fiscal year ended December 31, 2018

**ODICEO**  
115, boulevard de Stalingrad  
CS 52038  
69616 Villeurbanne Cedex  
S.A. au capital de € 275.000  
430 130 393 RCS Lyon

Commissaire aux Comptes  
Membre de la compagnie  
régionale de Lyon

**ERNST & YOUNG et Autres**  
Tour Oxygène  
10-12, boulevard Marius Vivier Merle  
69393 Lyon Cedex 03  
S.A.S. à capital variable  
438 476 913 R.C.S. Nanterre

Commissaire aux Comptes  
Membre de la compagnie  
régionale de Versailles

### Adocia

Annual General Meeting held to approve the financial statements for the year ended December 31, 2017

#### Statutory auditors' report on related party agreements and commitments

To the Annual General Meeting of Adocia,

In our capacity as statutory auditors of your Company, we hereby present to you our report on related party agreements and commitments.

We are required to inform you, on the basis of the information 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, as well as the reasons justifying why they benefit the Company. We are not required to give our opinion as to whether they are beneficial or appropriate or to ascertain the existence of other agreements and commitments. It is your responsibility, in accordance with Article R. 225-31 of the French Commercial Code (*Code de commerce*), to assess the relevance of these agreements and commitments prior to their approval.

We are also required, where applicable, to inform you in accordance with Article R. 225-31 of the French Commercial Code (*Code de commerce*) of the continuation of the implementation, during the year ended December 31, 2017, of the agreements and commitments previously approved by the Annual General Meeting.

We performed those procedures which we deemed necessary in compliance with professional guidance issued by the French Institute of Statutory Auditors (*Compagnie nationale des commissaires aux comptes*) relating to this type of engagement.

#### Agreements and commitments submitted for approval to the Annual General Meeting

We hereby inform you that we have not been notified of any agreements or commitments authorized and concluded during the year ended December 31, 2017 to be submitted to the Annual General Meeting for approval in accordance with Article L. 225-38 of the French Commercial Code (*Code de commerce*).

**Agreements and commitments previously approved by the Annual General Meeting**

We hereby inform you that we have not been notified of any agreements or commitments previously approved by the Annual General Meeting, whose implementation continued during the year ended December 31, 2017.

Villeurbanne and Lyon, April 17, 2018

The Statutory Auditors  
*French original signed by*

ODICEO

ERNST & YOUNG et Autres

Agnès Lamoine

Mohamed Mabrouk







**6**  
**COMPLEMENTARY  
INFORMATIONS**



## Chapter 6

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## 6 COMPLEMENTARY INFORMATIONS

### 6.1 Persons responsible

#### 6.1.1 Persons responsible for the registration document

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G rard Soula, Chairman and Chief Executive Officer

#### 6.1.2 Responsibility statement

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“Having taken all reasonable measures to this effect, I hereby certify that the information contained in this registration document is, to my knowledge, accurate and contains no omissions likely to affect its import.

I hereby certify that, to my knowledge, the financial statements were prepared in accordance with applicable accounting standards and provide a true and fair view of the assets, financial position and results of the Company and its subsidiary and that the management report information indexed in paragraph 6.5.2 accurately reflects changes in the business, results and financial position of the Company and its subsidiary and describes the principal risks and uncertainties they face.

I have obtained a letter from the statutory auditors certifying completion of their work, in which they state that they have verified the information provided in this registration document regarding the financial position and financial statements, and that they have read the registration document as a whole.

April 11<sup>th</sup>, 2019.

G rard Soula

Chairman and Chief Executive Officer

#### 6.1.3 Person responsible for financial information

---

Ms. Val rie Danaguezian

Chief Financial Officer

Address: 115, Avenue Lacassagne, 69003 Lyon

Telephone: +33 (0) 4 72 61 06 10

Fax: 33 (0) 4 72 36 39 67

Email: [contactinvestisseurs@adocia.com](mailto:contactinvestisseurs@adocia.com)

## 6.2 Statutory Auditors

### 6.2.1 Principal Statutory Auditors

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#### **ODICEO**

represented by Mrs. Agnes Lamoine, partner

115, Boulevard Stalingrad, 69100 Villeurbanne,

member of the Lyon regional statutory auditors' association,

Appointed through a decision of the sole shareholder on July 31, 2006 until the shareholders' meeting convened to vote on the financial statements for the fiscal year ended December 31, 2011. This term of office was renewed for the first time by the shareholders' meeting held on June 15, 2012 and a second time by the shareholders' meeting held on May 17<sup>th</sup>, 2018, for a period of six fiscal years, expiring at the end of the ordinary shareholders' meeting convened to vote on the financial statements for the fiscal year ended December 31, 2023.

#### **Ernst & Young et Autres**

represented by Mr. Mohamed Mabrouk, partner

1-2 place des saisons, 92400 Courbevoie La Défense,

member of the Versailles regional statutory auditors' association,

Appointed at the combined shareholders' meeting held on October 24, 2011 for a period of six fiscal years, which will expire at the end of the ordinary shareholders' meeting convened to vote on the financial statements for the fiscal year ended December 31, 2016. This term of office was renewed by the shareholders' meeting held on June 27, 2017 for a period of six fiscal years, which will expire at the end of the ordinary shareholders' meeting convened to vote on the financial statements for the fiscal year ended December 31, 2022.

#### 6.2.1.2 Alternate Statutory auditors

##### **Mr. Pierre Grafmeyer**

115, Boulevard Stalingrad, 69100 Villeurbanne,

member of the Lyon regional statutory auditors' association,

Appointed through a decision of the sole shareholder on July 31, 2006 until the shareholders' meeting convened to vote on the financial statements for the fiscal year ended December 31, 2011. This term of office was renewed by the shareholders' meeting held on June 15, 2012 for a period of six fiscal years, which will expire at the end of the ordinary shareholders' meeting convened to vote on the financial statements for the fiscal year ended December 31, 2017.

Mr. Pierre Grafmeyer's term of office as alternate statutory auditor was not renewed at the shareholders' meeting of May 17, 2018, since this appointment is not required as the statutory auditor is not a member of the Board, nor a natural person, nor a single-member legal person.

During the period covered by the historical financial information, there was no resignation or removal of one of the statutory auditors.

## 6.3 Information from third parties, experts' statements and declaration of interests

None

## 6.4 Documents available to the public

Copies of this registration document are available free of charge at the Company's registered office at 115 Avenue Lacassagne, 69003 Lyon. In addition, an electronic version is available on the Company's website ([www.adocia.com](http://www.adocia.com)) and the AMF website ([www.amf-france.org](http://www.amf-france.org)).

The articles of incorporation, minutes of shareholders' meetings and other corporate documents of the Company, as well as historical financial information and any assessment or statement made by an expert at the Company's request which must be made available to shareholders pursuant to the applicable legislation may be consulted free of charge at the Company's registered office.

Regulatory information within the meaning of the General Regulation of the AMF is also available on the Company's website ([www.adocia.com](http://www.adocia.com)).

## 6.5 Cross Reference tables

### 6.5.1 Annual financial report cross reference table

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2 Corporate annual financial statements -French GAAP	4.3
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4 Management report	see index below
5 Chairman's report on internal control	See index below
6 Annual information document	1.4
7 Information on statutory auditors' fee	4.3.3.7
8 Statutory auditors' report on the annual financial statements prepared under French GAAP and IFRS	4.2 et 4.4

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4 Progress made or difficulties encountered	1.3
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<b>Annual management report</b>	<b>Chapter(s)/Section(s)</b>
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## 6.6 Glossary

<b>AFSSAPS</b>	Agence Française de Sécurité Sanitaire et Produits de Santé/ <i>French Agency for the Safety of Health Products</i> . This authority evaluates the safety of use of health products, monitors them, controls their quality in the laboratory and inspects their sites of manufacturing, distribution and testing, and also circulates information for the correct use of health products.
<b>Amphiphile</b>	Chemical compound simultaneously possessing a hydrophilic group (soluble in water or a solvent) and a hydrophobic group (insoluble in water or a solvent). The hydrophilic or hydrophobic characters of the groups are related in particular to their capacity or lack thereof to form electrostatic interactions with water or a solvent.
<b>Anionic group</b>	Negatively charged group of ions (anions)
<b>Ankylosis</b>	Immobility of a joint caused by injury or disease.
<b>Arteriopathy</b>	Any diseases of arteries.
<b>Bedsore (eschar)</b>	Skin lesion resulting from decreased blood flow following an ischemic process
<b>Biosimilar</b>	Generic form a drug whose patent has expired.
<b>Chronic lesion</b>	Significant loss of superficial skin tissues (dermis and epidermis), generally characterized by the absence of healing after 6 weeks of its occurrence and regardless of the conditions of patient management.
<b>Coacervation</b>	The separation of certain macromolecular solutions into two phases.
<b>Complex</b>	Structure formed from several independent chemical entities.
<b>Compliance</b>	The extent to which a patient follows the treatment prescribed.
<b>Crohn's disease</b>	Chronic inflammatory disease of the digestive tract.
<b>Deamidation of asparagine</b>	Non-enzymatic and spontaneous process that converts asparagine, an amino acid of proteins, into aspartic acid.
<b>Dermatitis</b>	A skin reaction caused by exposure to substances that are allergens or irritants.
<b>EMA</b>	European Medicines Agency. This authority evaluates and supervises the development of new drugs for human and veterinary use in the European Union.
<b>Endothelial barrier</b>	Selective permeability barrier enabling and regulating exchanges of molecules of varying sizes (water, salts, proteins, etc.) between the blood and tissues

<b>Enzymatic breakdown</b>	This process involves the destruction of intramolecular bonds of a protein and generally results in the production of smaller molecules. Enzymes, that are also proteins, accelerate the natural phenomenon of protein degradation in the body.
<b>Epidermoid carcinoma</b>	A form of skin cancer.
<b>Erysipelas</b>	Non-necrosing infection of the dermis or epidermis.
<b>European Pharmacopoeia</b>	Collection of quality control requirements of medicinal preparations drafted by the European Directorate for the Quality of Medicines and Healthcare, an organization of the European Council.
<b>Excipient</b>	Any substance in a drug product other than the drug substance(s).
<b>FDA</b>	Food and Drug Administration. American agency responsible for approving drugs and medical devices for marketing.
<b>Glucose clamp technique</b>	Reference method used in clinical research to measure sensitivity to insulin.
<b>Glycoregulation</b>	Regulation of the level of blood glucose, or glycemia, by the endocrine system.
<b>Good Manufacturing Practices</b>	Notion of quality assurance, established by the European Commission and applied to the manufacturing of drugs for human or veterinary use.
<b>Graft</b>	A chemical group bound to the molecule in question.
<b>Granulation tissue</b>	Temporary tissue covering a lesion during the healing process.
<b>Growth factor</b>	Protein required for the growth or regeneration of a tissue or organ.
<b>Heparin</b>	Anticoagulant substance present in the body.
<b>ICH</b>	International Conference of Harmonization. International body composed of American, European and Asian health authorities, as well as pharmaceutical companies.
<b>Immunogenicity</b>	Capacity of an antibody to cause an immune reaction.
<b>Incidence</b>	Number of new cases of a pathology found during a given period and for a given population.
<b>Ischemia</b>	Reduced blood flow to an extremity or an organ.
<b>Islets of Langerhans</b>	Located in the pancreas, they contain three types of cells, each secreting a different hormone: i) insulin that lowers blood glucose levels, ii) glucagon that raises blood glucose and iii) gastrin that controls the process of digestion.

<b>IU</b>	International Unit. In pharmacology it is the unit of measurement of the quantity of a substance, based on its biological activity. One IU of insulin is the biological equivalent of about 45.5 µg of pure crystallized insulin.
<b>kDa (kiloDalton)</b>	Unit used to measure the molecular weight of molecules and atoms. The value of one Dalton is the atomic weight of the hydrogen atom.
<b>Leukemia</b>	Bone marrow cancer with anarchic proliferation of white blood cells.
<b>Ligand</b>	In chemistry, this is an atom, ion or molecule having the capacity to bind to one or several central atoms or ions.
<b>Lymphoma</b>	Malignant tumor of the lymphatic system.
<b>Marketing Authorization (MA)</b>	Approval of a medicine by health authorities prior to its commercialization.
<b>Multiple sclerosis</b>	Disease of the central nervous system, in particular the brain, optic nerves and spinal cord.
<b>Muscular dystrophy</b>	A progressive degenerative disease of the body's muscles.
<b>Muscular hypoxia</b>	Insufficient oxygenation of muscle tissues.
<b>National Consultative Ethics Committee</b>	Independent French advisory body whose principal mission is to provide opinions and reports dealing with ethics as pertaining to scientific progress.
<b>Necrotizing fasciitis</b>	Infection caused by group A <i>Streptococcus</i> .
<b>Nerve fiber (axon)</b>	Single extension emerging from the cell body of neurons whose function is to transport nerve impulses.
<b>Neuropathy</b>	Any disease of the nervous system.
<b>Osteoarticular lesion</b>	A lesion involving both bones and joints.
<b>Pancreas</b>	Gland in proximity to the stomach.
<b>Pharmacodynamics</b>	Study of the effects of a drug on the body, in particular the interaction between its cell receptor and the therapeutic substance.
<b>Pharmacokinetics</b>	Study of the fate of a drug in the body and the body's effect on the drug as a function of time. The pharmacokinetics of a drug can be broken down into four phases: absorption, diffusion in the body, metabolism of the drug and its elimination by the body.
<b>Polymer</b>	Chemical compound formed by molecules whose feature is the repetition of one or several atoms or groups of atoms.

<b>Polysaccharide</b>	Complex sugar composed of several simple sugars of the same family of polymers.
<b>Prevalence</b>	A measure of the health status of a population at a given time, expressed as the ratio of the number of patients to the total population.
<b>Primary dressing</b>	Different types of dressings that are in direct contact with the lesion: sheets cut to size, paste, powder, that keep the lesion warm and moist and enable exudates to be absorbed.
<b>Proof of concept</b>	Demonstration of the feasibility and efficacy of a therapeutic product.
<b>Protein</b>	Macromolecule composed of amino acids linked by peptide bonds and that ensure myriad functions in the body.
<b>Regenerative medicine</b>	The use of human cells to repair or improve the functions of a damaged organ.
<b>Rheumatoid arthritis</b>	Chronic, inflammatory, degenerative disease characterized by the inflammation of several joints.
<b>Sanies</b>	Fetid purulent matter mixed with blood.
<b>Somatic cells</b>	All cells except germ, or sex cells.
<b>SOP</b>	Standard Operating Procedure. A written detailed procedure to ensure the comparability and uniformity of studies of the performance of a given pharmaceutical product.
<b>Sorbitol</b>	A sugar-alcohol.
<b>Stasis</b>	Reduction or cessation of the circulation of a fluid.
<b>Streptococcus</b>	A genus of bacteria, certain species of which are pathogens, i.e. sources of infections.
<b>Transgenesis</b>	The set of techniques used to introduce a foreign gene in the genome of an organism to obtain a genetically modified organism.
<b>Tryptophan</b>	An amino acid forming proteins. It is called essential because it cannot be synthesized by the body and must be provided by the diet.
<b>UDRP procedure</b>	Uniform Dispute Resolution Policy. Principles of the Internet Corporation for Assigned Names and Numbers (ICANN) to resolve disputes involving domain names.
<b>United States Pharmacopeia – National Formulary</b>	Collection of quality control requirements of medicinal preparations, excipients and medical devices drafted by the United States Pharmacopeial Convention. The FDA is responsible for ensuring compliance with these requirements in the United States. These standards have been developed

and used in more than 130 counties in the world.





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