



**ADOCIA**

# Innovative Medicine

for everyone, everywhere

# 2021

## Universal Registration Document

This is a translation into English of the universal registration document of the Company issued in French and it is available on the website of the Issuer

*This is a free translation into English of the universal registration document of Adocia issued in French and it is available on the website of the Issuer. This free translation is for an informational purpose only.*

# ADOCIA

innovative medicine  
for everyone, everywhere



A French société anonyme (corporation) with €727 095.60 in share capital.

Registered office: 115 avenue Lacassagne

69003 Lyon, France

Lyon Trade and Companies Registry No. 487 647 737



The Universal Registration Document was filed on April 21, 2022 with the AMF, as the competent authority under Regulation (EU) 2017/1129, without prior approval in accordance with Article 9 of that Regulation.

The Universal Registration Document may be used for the purposes of a public offering of financial securities or the admission of financial securities to trading on a regulated market if it is supplemented by a transaction note and if necessary, a summary and all the amendments to the universal registration document. The assembly then formed is approved by the AMF in accordance with Regulation (EU) 2017/1129.

The Universal Registration Document as Annual Financial Report in pdf format is a reproduction of the official version of the Universal Registration Document as Annual Financial Report 2021 that was prepared in ESEF format and that 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)). Copies of this universal registration document are available free of charge from the Company at 115, Avenue Lacassagne, 69003 Lyon.

## NOTICE

In this universal 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 270258 San Diego, CA 92198-2258, U.S.A.

The consolidated financial statements prepared under IFRS for the fiscal year ended December 31, 2021, are presented on pages 128 to 166 of this universal registration document. The statutory auditors’ report on the consolidated financial statements prepared under IFRS for the fiscal year ended December 31, 2021, is presented on pages 167 to 173 of this universal registration document.

The corporate financial statements prepared under French GAAP for the fiscal year ended December 31, 2021, are presented on pages 174 to 194 of this universal registration document. The statutory auditor’s report on the corporate financial statements prepared under French GAAP for the fiscal year ended December 31, 2020 is presented on pages 195 to 201.

Pursuant to Article 19 of Commission Regulation (EC) No. 2017/1129 of June 14, 2017:

- The consolidated financial statements for the year ending on December 31, 2020, and the related statutory auditors’ reports presented respectively in paragraph 4.1 and 4.2 of the 2020 universal registration document filed with the AMF on April 20, 2021, with reference D.20-0330
- The consolidated financial statements for the year ending on December 31, 2019, and the related statutory auditors’ reports presented respectively in paragraph 4.1 and 4.2 of the 2019 universal registration document filed with the AMF on April 22, 2020, with reference D.19-0328

are incorporated by reference in this universal registration document.

The non-included parts of this(ese) document(s) are either irrelevant for the investor or covered elsewhere in the universal 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 universal registration document contains, in particular in section 1.2 “*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 universal 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 universal 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 universal 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 1.4 “*Risk Factors*” of this universal 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 universal registration document may also have a material adverse impact.

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# 01



# Presentation of Adocia and its activities

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# 1 PRESENTATION OF ADOCIA AND ITS ACTIVITIES

## 1.1 About Adocia and its evolution

### 1.1.1. 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.

Its legal entity identifier (LEI) is 969500ZL79KYH9PTY78.

The Company's contact information is shown below:

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

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

### 1.1.2. General presentation of Adocia

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#### 1.1.2.1. Mission

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

Adocia is a clinical-stage biotechnology company that specializes in the development of innovative formulations of already-approved therapeutic proteins and peptides for the treatment of diabetes and other metabolic diseases. In the diabetes field, Adocia's portfolio of injectable treatments is among the largest and most differentiated of the industry, featuring six clinical-stage products and products in preclinical-stage.

Adocia's clinical pipeline contains five innovative insulin formulations for the treatment of diabetes: two ultra-rapid insulin formulations based on rapid insulin lispro (BioChaperone® Lispro U100 and U200), a combination of long-acting insulin glargine and rapid-acting insulin lispro (BioChaperone® Combo) and two combinations of prandial insulin with pramlintide, an analog of amylin (M1 Pram and BioChaperone® LisPram). It also includes an aqueous formulation of human glucagon (BioChaperone® Glucagon) for the treatment of hypoglycemia.

Adocia preclinical pipeline includes bi-hormonal products for the treatment of diabetes: a combination of rapid insulin aspart with pramlintide (BioChaperone® AsPram) and a fixed combination of insulin glargine with an analogue of the GLP-1 receptor (BioChaperone® Glargine Liraglutide). In addition, it includes three multihormonal products for the treatment of obesity: a combination of glucagon and exenatide (BioChaperone® GluExe), a combination of pramlintide



and exenatide (PramExe) and a triple combination of pramlintide, glucagon and exenatide (BioChaperone® PramGluExe).

Adocia bases the development of its pipeline on three technology platforms: 1) the BioChaperone® improves the efficacy and/or the security of therapeutic proteins, while facilitating their use by patients; 2) a platform designed to improve cell therapy techniques thanks to a hydrogel matrix; 3) an oral delivery platform for peptides.

### 1.1.2.2. Significant events in the business development of the Company

As the results of the Company's 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 its founders, 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.

The BioChaperone Lispro program has been licensed twice to the American company Eli Lilly. Between December 2011 and January 2013, a first partnership was signed, which was terminated by joint agreement.

Then, a second agreement, based on the results obtained from two phase 2a studies, was reached on December 19, 2014, on the development of an ultra-rapid insulin with two formulations: BioChaperone Lispro U100 and BioChaperone Lispro U200. Over their partnership, Eli Lilly and Adocia successfully completed 6 clinical studies on BioChaperone Lispro U100 and U200.

On January 26, 2016, Lilly announced its decision to terminate this agreement in order to prioritize an internal project, LY900014 (Lyumjev®). The termination of the contract was followed by two arbitration proceedings, which have been closed since and detailed in section "Disputes" 1.2.8.4 of this present document.

Following the termination of the second partnership, Adocia regained full ownership of the rights that had been licensed and has been continuing to develop its product.

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

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 late 2019, the Company used a financing plan of €15 million in the form of a bond loan with attached warrants (BSA) to finance the development of its products portfolio.

Since, Adocia has continued to develop products under the partnership with Tonghua Dongbao. The Company made progress in the development of its entire portfolio, notably with the M1 Pram project, a co-formulation of synergistic therapeutic hormones pramlintide and M1 insulin.

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In 2020, despite a year disrupted by the Covid-19 pandemic, the Company continued to develop its projects. In August 2020, Adocia was granted a State-guaranteed loan of €7 million, which enabled the Company to have a greater financial visibility and to be in a position of strength to sign a partnership.

2021 was marked by major advances in our insulin portfolio and by the achievement of important proofs of concept on new technological platforms in cell therapy and oral delivery of peptides. To speed up the development of these innovations, Adocia carried out a financing of €7 million made up of, on the one hand, the issuance of bonds convertible into shares subscribed by European investors for an amount of €6 million net and, on the other hand, a share capital increase of €1 million subscribed by Gérard Soula, co-founder of Adocia.

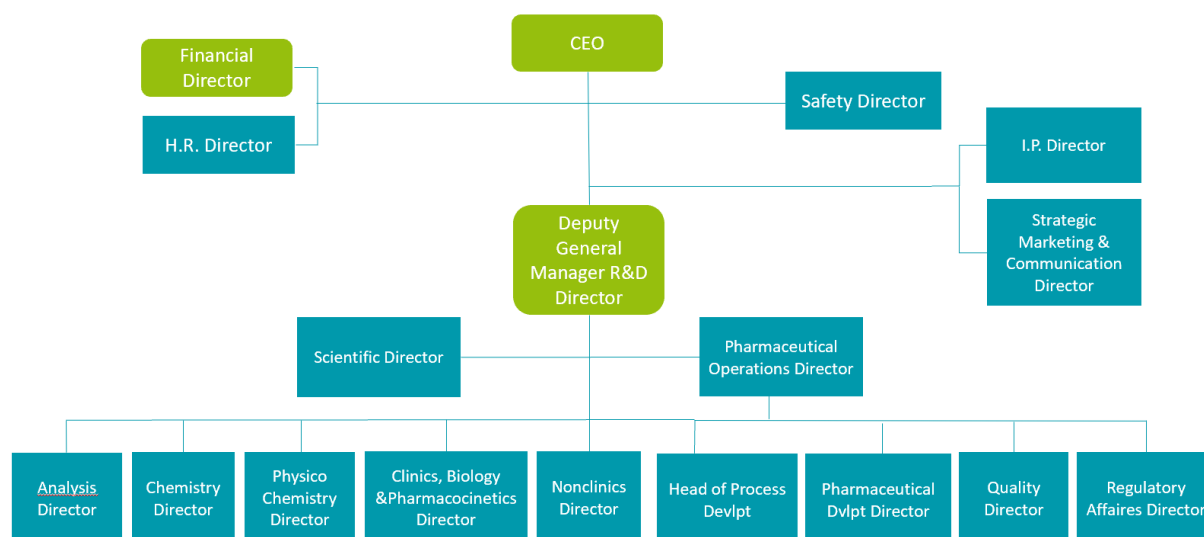
Finally, in a favorable real estate context, the Company completed in March 2022 a sale and leaseback transaction resulting in the sale of the building that it owned, thus enabling it to support its growth while securing the occupation of its historic site.

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### 1.1.3. Organizational chart

#### 1.1.3.1. Organization of the Company

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



#### 1.1.3.2. 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 PO Box 270258 San Diego, CA 92198-2258, U.S.A. Adocia wholly owns its subsidiary Adocia Inc., which at the date of the present registration document had one employee: 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.

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

#### 1.1.3.3. Management

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

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 3.1.2.4 of the current universal registration document.

**Dr. Olivier Soula, PhD, MBA – Deputy General Manager – R&D Director:** cf. paragraph 3.1.2.4 of the current universal registration document.

#### 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.

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### 1.1.4. 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.

The investments made during the last three fiscal years are as follows:

<i>En milliers d'euros</i>	<b>FY 2021 (12 months)</b>	<b>FY 2020 (12 months)</b>	<b>FY 2019 (12 months)</b>
Intangible assets	-	-	13
Property, plant and equipment	-	-	234
Other tangible assets	159	148	1 798
Non-current financial assets	-	12	35
<b>TOTAL</b>	<b>159</b>	<b>160</b>	<b>2 081</b>

#### 1.1.4.1. 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 storage building 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. This work was finalized in 2019.

On March 28, 2022, Adocia completed a sale and leaseback transaction of its building. The sale of the building included all real estate assets for a net amount of close to €19 million corresponding to the sale price (€23.2 million) minus the repayment of the debts (€4.4 million) that were contracted to finance the acquisition of the building in 2016 and that

have been completely repaid in the context of the sale transaction. The lease agreement provides for Adocia staying in the building for a duration of 12 years, with an option for an added 9 years. The annual rent will amount to €1.04 million for the entire surface of the buildings, the car parks, and the storage building.

- **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 universal registration document.

### 1.1.4.2. Major current and future investments

Over the course of 2022, Adocia plans *a minima* investments to purchase the scientific material needed for the research and development activities of its current and future projects.

Further refurbishment of the building will be done if there is new cash-in.

In the lease contract signed on the day of the sale of the building, the lessor has committed to financing up to €5 million of renovation work on the floors yet unoccupied by Adocia by means of an increase in rent.

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## 1.2 Description of activities

### 1.2.1. Missions

Adocia is a French biotechnology company founded in December 2005 by Gérard, Olivier and Remi Soula.

Adocia focuses on the development of innovative medicine, for the treatment of diabetes, obesity and other metabolic diseases.

Since 2005, Adocia's value lies in its ability to formulate already approved therapeutic proteins and peptides to make them more effective, better tolerated or easier for patients to use. To do this, Adocia relies on its patented BioChaperone® technology platform as well as on the know-how carried by a highly qualified team. This historical expertise in formulating therapeutic protein permitted Adocia to currently have six clinical stage products and four preclinical products.

Since 2020, Adocia has brought a new wave of innovations into its pipeline. With its experience in formulation and its knowledge of metabolic diseases, it is naturally that Adocia has brought in three new areas to ensure future innovative growth relays of its pipeline. Currently in preclinic, Adocia's work focuses on:

- A technology platform for cell therapy, primarily focused on its application for diabetes
- A technology platform to enable oral drug delivery of peptides
- Innovative multi-hormonal formulations for obesity treatment, to be delivered by pumps

Adocia's mission is "to deliver more effective treatments, easier to use and more accessible to people with diabetes and other metabolic diseases in order to help them better treat their disease and avoid their long-term consequences".

Adocia aims to demonstrate the clinical proof of concept of its products before licensing them out to a pharmaceutical partner responsible for bringing the product to the market and ensuring its commercialization.

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

- **Adocia, a unique approach to face a triple challenge**

Diabetes and obesity are closely related pathologies. Caused by the dysregulation of certain hormones in common (glucagon, amylin, GLP-1 RA...), they can be both cause and consequence of each other.

In 2021, more than 537 million people have diabetes worldwide, so about one on ten people<sup>1</sup>. Despite significant advancement in the treatment of diabetes over the past 30 years, the medical need remains high, and it is estimated that 79% of people with diabetes live with severe complications<sup>2</sup>. The treatments complexity and the costs associated place an additional strain on people living with diabetes and may be responsible for a decline in treatment adherence, as well as a deterioration in the long-term quality of care.

As for obesity, the disease has been growing rapidly over the last decades. To date, the World Health Organization (WHO) estimates that 1.9 billion people are obese or overweight (BMI > 25 kg/m<sup>2</sup>) in the world.

The question arises of the capacity of the healthcare systems to cope with the colossal expenses generated by these diseases, in a context of an overall increased pressure on health expenditure. In 2021, global spending on diabetes accounted for \$966 billion<sup>1</sup>. The Milken Institute has estimated the direct and indirect health care costs of obesity at \$1.72 trillion per year for the United States alone<sup>3</sup>.

Therefore, Adocia believes that any new treatment must meet a triple 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 patients' compliance without placing further daily constraints on them;
- **Guarantee costs control**: to ensure the greatest number of patients can access the best treatment and to guarantee the sustainability of our healthcare systems.

To meet this triple challenge, Adocia adopts an original strategy based on two axes.

On the one hand, it consists of improving the efficacy and the safety of already-approved therapeutic proteins and peptides, while facilitating their use by patients. In order to do this, Adocia relies on its expertise in hormones formulation and on its proprietary formulation technologies: the BioChaperone<sup>®</sup> platform and the platform for oral drug delivery of peptides.

The formulation approach is simple to implement and provides the opportunity to improve and combine in an original way already-approved proteins. It also takes advantage of the track record of already-used therapeutic proteins in terms of safety, efficacy and production infrastructure. This business-model based on reformulation makes possible to deliver innovative treatments with improved performance while having relatively short and less expensive development cycles, compared to developing new proteins.

By adapting its platforms to each protein to face specific technical challenges, Adocia has developed a differentiated portfolio of innovative formulations of metabolic hormones for the treatment of diabetes and obesity. Each product aims to meet the specific needs of people living with diabetes.

At the same time, Adocia is preparing the innovative treatments of tomorrow and has launched a research program on cell therapy. Today, this technique exists for the treatment of diabetes and consists of transplanting living pancreatic cells into diabetic patients in order to restore glycemic control. However, it is limited to a small population because donors are scarce and it requires immunosuppressive treatments. Adocia's objective is to design an innovative hydrogel matrix capable of maintaining cell activity while protecting them from the degradation by the immune system. In addition to significantly improving the quality of life of patients, this technology can have a real economic impact. Adocia intends to deploy this innovative approach to other cell types and diseases once proof of concept is established, in order to benefit a maximum number of patients.

## 1.2.2. The BioChaperone<sup>®</sup> technology platform

Adocia has designed and developed BioChaperone<sup>®</sup>, a technology platform based on novel polymers, oligomers, and innovative small molecules. BioChaperone<sup>®</sup> molecules can spontaneously form a complex with other molecules, including therapeutic proteins. This technology platform can be leveraged to combine various therapeutic proteins.

<sup>1</sup> International Diabetes Federation, 2021

<sup>2</sup> Hazel-Fernandez & al; American Journal of Managed Care. 2015

<sup>3</sup> America's Obesity Crisis: The Health and Economic Costs of Excess Weight, Milken Institute, Sept. 2020

The non-covalent molecular association helps to increase solubility and efficacy of therapeutic proteins while protecting from enzymatic degradation.

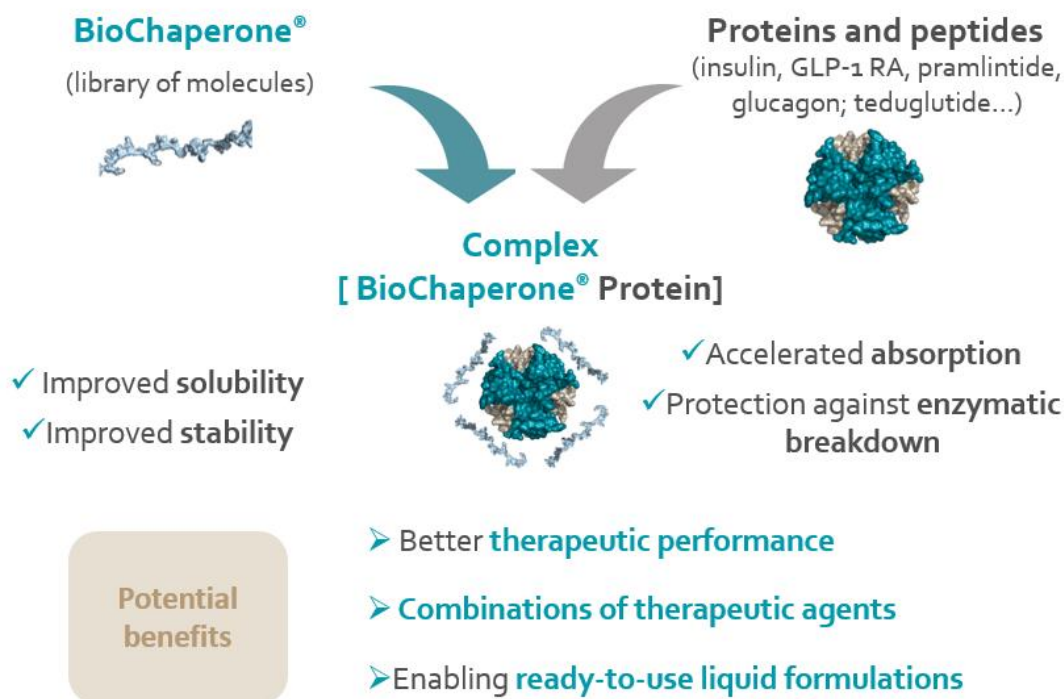
BioChaperone technology is derived from the functional mechanism of heparin. This natural polysaccharide forms molecular complexes with growth factors which increases their solubility and protects them from enzymatic breakdown, thereby extending their time of action. The first generation of BioChaperone molecules developed by Adocia mimicked the properties of heparin with growth factors, while avoiding its anticoagulant effects. The BioChaperone compounds were then developed with the objective to be combined with a wide range of different proteins.

The first innovative BioChaperone polymers were composed of a sugar backbone (e.g., dextran or pullulan) modified by both anionic groups (eg. carboxylates with a negative electric charge) and by hydrophobic amino acids. Subsequently Adocia extended its BioChaperone family to include other shorter compounds (oligomers and small molecules) with the same properties. BioChaperone compounds have no intrinsic biological activity.

BioChaperone compounds form complexes with proteins by non-covalently binding to their surface (adsorption). The complex forms spontaneously and is based on hydrophobic, electrostatic interactions or hydrogen bonds. These BioChaperone polymers interact reversibly and have non-degradative effects on the proteins. When the two constituents are simply mixed in aqueous solution, the complex is formed naturally. 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 produced at industrial scale as it relies solely on the addition of BioChaperone in the formulation process (preservatives, salt, etc.), and does not require additional use of industrial tools. Furthermore, the BioChaperone chemical synthesis processes are simple and low-cost compared to the therapeutic proteins themselves. These two aspects make it possible to envisage the BioChaperone formulations manufacturing costs to be equivalent with those of the original formulations.

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

- 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, to be easier to use for the patient or to offer new applications.

To date, Adocia’s research team has developed more than 500 BioChaperone compounds, an impressive collection that continues to grow over time. The main distinctions among BioChaperone compounds are their size, type and the number of anionic and hydrophobic grafts. This portfolio of molecules was rapidly developed to advance several classes of difficult to formulate therapeutic proteins; notably insulins and other metabolic hormones used in the treatment of diabetes (glucagon, amylin, etc).

BioChaperone technology is protected by several patent families, for BioChaperone molecules alone and for formulations with BioChaperone. In addition, Adocia also has patent families covering compositions which include active ingredients with or without BioChaperone.

### 1.2.3. Pipeline presentation



Over the years, Adocia has developed a broad portfolio of injectable treatments for type 1 and 2 diabetes patients based on its BioChaperone technology and on other innovative formulation strategies. In 2021, Adocia, leveraging the knowledge accumulated over the past 15 years, added a new cell therapy platform technology to its diabetes pipeline.

**For the treatment of diabetes,** Adocia’s clinical pipeline as of today features multiple innovative insulin formulations:

- An ultra-rapid insulin **BioChaperone Lispro**, in two strengths, U100 and U200
- A combination of long-acting insulin glargine and rapid-acting insulin lispro: **BioChaperone Combo**,
- Combinations of insulin and amylin analogue (pramlintide), a synergistic hormone to mealtime insulin:
  - A metabolite of insulin glargine (M1) and pramlintide: **M1Pram**
  - Insulin lispro and pramlintide: **BioChaperone LisPram**
  - Insulin aspart and pramlintide: **BioChaperone AsPram**
- A ready-to-use aqueous formulation of human glucagon: **BioChaperone Glucagon**

Adocia also has several projects in **preclinical development**:

- A combination of insulin glargine with GLP-1 Receptor Agonist : **BioChaperone Glargine Liraglutide**
- A hydrogel scaffold ensuring pancreatic cells encapsulation, for cell therapy application

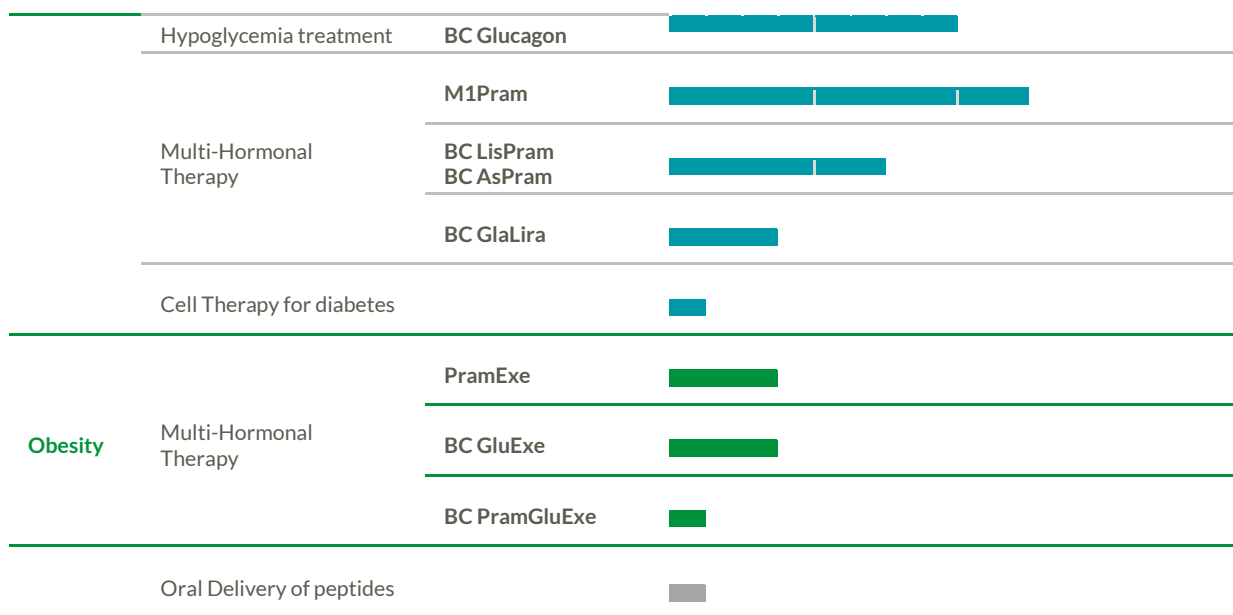
**For the treatment of obesity,** the following products currently in **preclinical development**, are designed for administration via pump:

- A combination of pramlintide with a GLP-1 Receptor Agonist: **PramExe**
- A combination of glucagon with a GLP-1 Receptor Agonist: **BioChaperone GluExe**
- A triple combination of pramlintide, glucagon and a GLP-1 RA: **BioChaperone PramGluExe**

Finally, a platform for **oral drug delivery of peptides** is in **preclinical development** for diabetes, obesity and other metabolic diseases applications

- First application on a GLP-1 receptor agonist for the treatment of diabetes

		Preclinic	Phase 1	Phase 2	Phase 3
Diabetes	Ultra-Rapid Insulin	BC Lispro U100 / U200	[Progress bar showing completion in Preclinic, Phase 1, and Phase 2]		
	Insulins Combination Long acting + Rapid acting	BC Combo U200	[Progress bar showing completion in Preclinic and Phase 1]		



BC: BioChaperone®; Lispro: insulin lispro; BC Combo: BC insulin glargine insulin lispro; M1: A21G human insulin; Lira: Liraglutide, Pram: pramlintide; Glu: Glucagon; Gla: insulin glargine; Exe: exenatide

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## 1.2.4. Adocia's pipeline for the treatment of diabetes

### 1.2.4.1. Diabetes

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

- **Epidemiology**

Diabetes is a chronic disease that regroups type 1 diabetes and type 2 diabetes. It is a global public health issue, and the incidence rate is still increasing. The International Diabetes Federation<sup>4</sup> estimates that between 2021 and 2045, the number of people with diabetes in the world should grow by almost 46% (among the population aged 20 to 79), growing from 537 million to 783 million people affected. While Europe (+ 13%) and North America (+ 24%) should experience growth rates below the world average, albeit high, emerging countries will no doubt have to face a sharp increase in number of people with diabetes. For example, Africa diabetes prevalence is estimated to increase by 134% by 2045. Today, 3 in 4 people (79%) with diabetes live in low-income or middle-income countries.

<sup>4</sup> Diabetes Atlas 10<sup>th</sup> edition (2021), Fédération Internationale du Diabète



Let's also stress that in 2021, an estimated 240 million people are living with undiagnosed diabetes worldwide, meaning almost one-in-two adults with diabetes are unaware they have the condition.

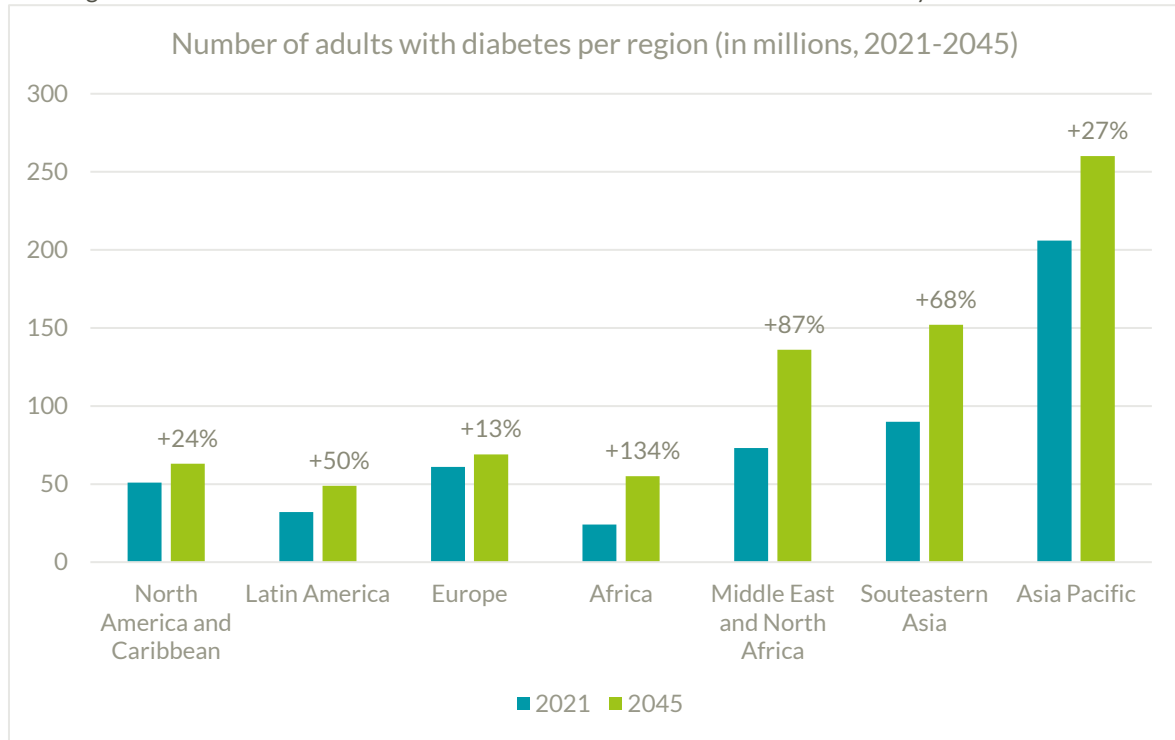


Figure 1 : Estimates of the number of people with diabetes (in millions) among people aged between 20 and 79 years worldwide in 2021 and forecasts for 2045. The percentages show growth rates from 2021 to 2045 per region. Source: International Diabetes Federation, 10<sup>th</sup> edition 2021

▪ 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. Insulin is a hormone produced by the pancreas.

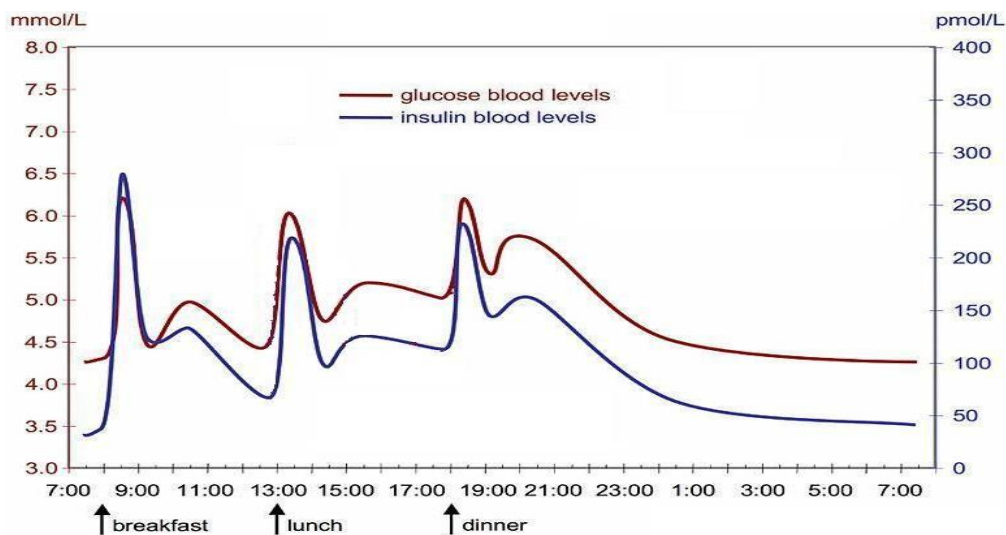


Figure 2 : Schematic representation of daily glycemic (red line) and insulin secretion (blue line) patterns in a person without diabetes

Insulin plays a major role in the control of glycemia by enabling the circulating glucose to enter into the cells. In a subject without diabetes, the surge of glycemia following a meal is immediately counteracted with a rapid increase of endogenous insulin concentration in the blood. This enables the circulated blood glucose to be taken up by the cells

and consequently helps to maintain the glycemia level. The control of glycemia is considered ideal when blood glucose stays between 4.4 mmol/L (0.80 g/L) and 7 mmol/L (1.4 g/L).

However, if the blood glucose concentration goes under 0.80 g/L, the subject enters into a hypoglycemic state, which is hazardous, and could potentially be lethal.

When this concentration goes over 1.4 g/L, the patient enters into a hyperglycemic state which can lead to short-term ketoacidosis. Chronic exposure to hyperglycemic states could result in long-term microvascular and macrovascular complications, which are a major cause of blindness, kidney failure, heart attacks, strokes and lower limb amputation.

In people with diabetes, glucose regulation is impaired, which implies recurrent exposure to both hyperglycemic and hypoglycemia risk.

In 2021, an estimated 6.7 million deaths were attributable to diabetes, which is equivalent to one death every five seconds<sup>5</sup>.

# 1

## Complications of diabetes

Cardiovascular complications are the main cause of mortality in patients with type 2 diabetes. For those patients, cardiovascular morbidity and mortality are multiplied by a factor of 2 to 3 in men and 4 to 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>6,7</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 the accumulation of damages in the retina small vessels. 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.
- Diabetes has also been associated with increased risks of neurological pathologies:
  - 21% of people with type 1 diabetes and 27% of those with type 2 diabetes have depressive symptoms<sup>8</sup>;
  - 70% of people with type 2 diabetes will develop cognitive decline<sup>9</sup> in their lifetime, which can lead to Alzheimer's disease. Alzheimer's disease is sometimes referred to as "type 3 diabetes" in connection with the growing body of data implicating a metabolic brain disorder in this disease. Type 1 diabetes has also been associated with a 73%<sup>10</sup> increased risk of developing dementia.

## Different types of diabetes

**Type 1 diabetes** is a disease caused by an autoimmune reaction. Although most often developed in young people, the pathology can occur at any age. Type 1 diabetes has been estimated to affect 5 to 10% of people with diabetes<sup>11</sup>. A

<sup>5</sup> Diabetes Atlas 10<sup>th</sup> edition (2021), Fédération Internationale du Diabète

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

<sup>7</sup> DTTC study, NEJM, 1993, 329(14); EDIC study NEJM, 2005, 353(25)

<sup>8</sup> De Groot et al, Am Psychol 2016 ; Roy et al J Aff Dis 2012

<sup>9</sup> Ott et al, Neurology 1999

<sup>10</sup> Roriz-Filho et al, Biochim Biophys Acta 2009

<sup>11</sup> Business Insights - The Diabetes Market Outlook to 2016–May 2011

person with type 1 diabetes makes antibodies which attack the beta cells of the islets of Langerhans, located in the pancreas. These cells are responsible for the production of the insulin. 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>12</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>13</sup>. Type 2 diabetes is a progressive disease: insulin resistance begins with excessive insulin production, which degrades the islets of Langerhans. Once this degradation is initiated, the amount of insulin being 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 have already lost half of their beta cells at the time of diagnosis. Genetic predisposition is a predominant factor and being overweight is an aggravating cause of type 2 diabetes.

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.

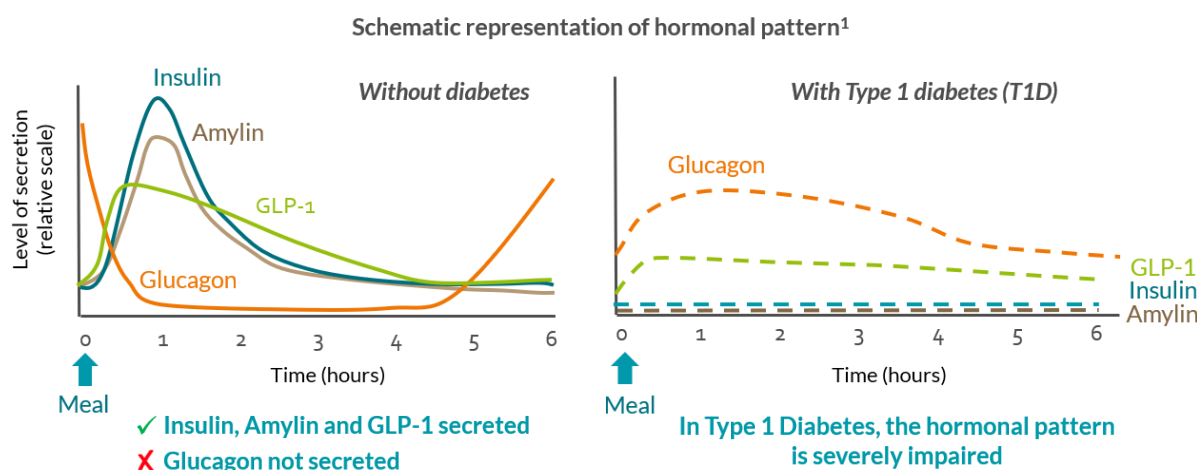


Figure 3: Schematic representation of the secretion pattern of 4 key metabolic hormones around mealtime: insulin, amylin, GLP-1 and glucagon. Source: Adocia, adapted from Toff-Neilsen et al., *J. Clin Endocrinol Metab* 2001;86:3717-3723; Cummings DE et al., *Diabetes* 2001;50:1714-1719; Aronoff SL et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

In particular, four hormones play a key role in controlling glycemia: 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 beta cells in the pancreas, at a 'basal' rate between meals and at a higher level, 'prandial' rate, during food consumption. Insulin promotes uptake of sugar from the blood by signaling on the liver, muscles, and adipose tissues to absorb glucose. Amylin works by suppressing the secretion of glucagon in the pancreas, by promoting a sensation of satiety in the brain and by slowing gastric emptying.

<sup>12</sup> Diabetology Department, Prof. Altman, Georges Pompidou European Hospital (<http://www.hegp.fr/diabeto/causetype1.html>)

<sup>13</sup> Business Insights - The Diabetes Market Outlook to 2016-May 2011

- **GLP-1** (“Glucagon-Like Peptide-1”) also works in synergy with insulin and amylin. GLP-1 is mainly produced in the intestines following a meal. It has several effects which 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; 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 hypoglycemia, which can be immediately debilitating or even fatal if severe, and hyperglycemia, responsible for severe long-term complications<sup>14</sup>.

In each of these four classes, at least one compound has been approved by the FDA.

1

- Insulins:
  - Prandial insulins (short acting hormones, for mealtime usage):
    - Recombinant human insulin (also named « rHI »): Humulin<sup>®</sup>, Eli Lilly; Novolin<sup>®</sup>, Novo Nordisk; Insuman<sup>®</sup>, Sanofi
    - Rapid insulin 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)
    - Ultra-rapid insulin analogs: insulin lispro-aabc (Lyumjev<sup>®</sup>), insulin aspart (Fiasp<sup>®</sup>)
  - Basal (long acting hormones, to control fasting glycemia): insulin glargine (Lantus<sup>®</sup> and Toujeo<sup>®</sup>, Sanofi; Abasaglar<sup>®</sup>, Lilly); insulin detemir (Levemir<sup>®</sup>, Novo Nordisk); insulin degludec (Tresiba<sup>®</sup>, Novo Nordisk)...
  - Premix (insuring both prandial and basal regulation): Humalog Mix<sup>®</sup>, Eli Lilly, NovoMix<sup>®</sup>/Novolog Mix<sup>®</sup>, Novo Nordisk...
- Amylin analog: pramlintide (Symlin<sup>®</sup>, AstraZeneca);
- GLP-1 receptor agonists: exenatide (Byetta<sup>®</sup>, AstraZeneca), lixisenatide (Lyxumia<sup>®</sup>, Sanofi)...<sup>15</sup>
- Human glucagon (Glucagon<sup>®</sup> and Baqsimi<sup>®</sup>, Eli Lilly, and Glucagen<sup>®</sup>, Novo Nordisk)

In people with type 1 diabetes, this physiological hormonal regulation is severely impaired (see figure 3): not only does the destruction of pancreatic beta cells lead to the lack 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.

Therefore, prandial hyperglycemia is potentially caused by three factors: 1) glucagon secretion, which leads to the release of sugars even before the person starts eating; 2) faster gastric emptying resulting in a massive surge of glucose; 3) the absence of insulin, which prevents the uptake of endogenous and exogenous sugars. This in part might explain why prandial insulin injection alone is not enough to completely control post-prandial hyperglycemia in insulin dependent diabetes patients.

### 1.2.4.2. Diabetes treatment and insulin-therapy

Diabetes is a global pandemic affecting 537 million people in 2021. The diabetic population 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 three major players: Eli Lilly, Novo Nordisk and Sanofi, with all three initially focusing on insulin and, more recently,

<sup>14</sup> D. Nathan et al, Diabetes Care 2014 Jan; 37(1): 9-16 (overview of the Diabetes Control and Complications Trial)

<sup>15</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> (abirglutide, GlaxoSmithKline, weekly injection).

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 receptor analogs, glucagon) grew by 18.1% per year between 2008 and 2018, accounting for \$29 billion<sup>16</sup>, i.e., more than 50% of the total market for antidiabetic medications. (cf. figure 4).

The dominance of insulin in this injectable market compared to other drug classes, is explained simply by the fact that insulin is absolutely necessary for the survival of patients with type 1 diabetes. Type 2 diabetes patients will ultimately rely on insulin therapies as well.

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', 'mealtime' or 'prandial' insulins, injected with every meal.

In order to simplify administration schemes, a third type of product, called 'premix', injected twice a day, provide both prandial and basal regulation. The premixes are based on a mealtime insulin, part of which is made slower by co-precipitation with protamine. However, premixes are a sub-optimal solution to using basal insulin (which lasts longer) and mealtime insulin (which works faster) separately.

2021 marked the century of the discovery of insulin by McLeod, Banting and Best. And it was on January 23, 1922, that 14-year-old Leonard Thompson was the first patient to receive insulin<sup>17</sup>. Historically, purified animal insulin was used as the first insulin-therapy, followed in the 1980's by human recombinant. Since the end of 1990's, modified insulin analogs were developed to either accelerate the prandial action (insulin lispro, aspart or glulisine), or to lengthen the basal action (insulin glargine, detemir or degludec). Premixed insulins made from human recombinant insulin and insulin analogs have also been developed.

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

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

Despite the multitude of treatment options for people with type 1 and type 2 diabetes, there is still significant unmet medical needs in the area.

- **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>18</sup>. Generally, there is a strong trend in the endocrinologist community to start evaluating new treatments on more diverse aspects than glycated hemoglobin (HbA<sub>1c</sub>) alone, which only reflects the average glycemia over 3 months.

For instance, it has been proposed<sup>19</sup> to pay closer attention to:

- The "Time-In-Range" (TIR): defined as the time spent in a specific glycemic range 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;

<sup>16</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.

<sup>17</sup> <https://insulin100.utoronto.ca/>

<sup>18</sup> DTTTC, NEJM study, 1993, 329(14); EDIC NEJM study, 2005, 353(25)

<sup>19</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

- The risk of hypoglycemia (the definition of which has recently been revised by several scientific societies): hypoglycemia is a major risk for patients treated for diabetes and can lead to permanent brain damage and death;
- Long-term benefits of certain drugs: for instance, cardiovascular benefits observed with new classes such as GLP-1 receptor agonists and SGLT-2 inhibitors.

In general, there is also a trend toward actively engaging the patient, in order to avoid treatment misuse or discontinuation. The American Diabetes Association's guidelines (ADA) published in January 2022 are also going in that direction, recommending the use of Continuous Glucose Monitoring (CGM) devices in order to gain more insights on the glycemic management<sup>20</sup>.

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

The focus given to specific indicators of glycemic variability has been possible with the rapid evolution of technology: development of increasingly accurate continuous blood glucose monitoring (CGM) devices, ability to use Big Data to address patient behavior, development of decision support algorithms (eg. Sanofi's IBG Star) or control pumps (eg. BetaBionics), etc. Recently, companies such as Eli Lilly or BigFoot entered in collaboration with medtech companies (like Dexcom) to develop complete solutions (also known as "artificial pancreas" or "closed-loop systems") which includes a CGM system, an insulin pump and an algorithm that automatically takes into account blood glucose levels and injects the appropriate dose of insulin. Similar systems using "smart" pens are also under development.

More generally, the various major players in insulin treatment have partnered with big data companies to develop new diabetes monitoring and management solutions (Medtronic-IBM Watson partnerships, 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<sup>®</sup>, Eli Lilly) has been introduced to the European (2015) and American (2016) markets, a few years after similar products were introduced to the Chinese (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, launched in the UK in November 2018, in Japan in 2017, and in the US in August 2020), 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. On July 28, 2021, the FDA (U.S. Food and Drug Administration) authorized the interchangeability at pharmacy level of Lantus and Semglee, which is the first time for an insulin biosimilar in the USA<sup>21</sup>.

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 exempt from the biosimilars competition. For example, Novo Nordisk and Eli Lilly, world leaders in prandial insulins with Novolog<sup>®</sup> and Humalog<sup>®</sup>, developed two ultra-rapid acting insulins, Fiasp<sup>®</sup> (approved in 2018) and Lyumjev<sup>®</sup> (approved in 2020). 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 innovating from already approved products, Adocia responds to these trends in the diabetes market and develops new generations of more efficient treatments, compatible with new technologies and protected by intellectual property (via formulation, BioChaperone, etc.).

<sup>20</sup> Glycemic Targets: Standards of Medical Care in Diabetes—2022 Diabetes Care 2022;45(Suppl. 1):S83–S96

<sup>21</sup> <https://www.fda.gov/news-events/press-announcements/fda-approves-first-interchangeable-biosimilar-insulin-product-treatment-diabetes>

#### 1.2.4.4. BioChaperone Lispro U100 and U200

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

Ultra-rapid insulin is an insulin that has an increased rapid absorption profile compared to 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, in order to limit 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 a shift between insulin on-board and actual glycemia). In the long-term, chronic hyperglycemia is correlated to serious complications.

A mealtime injection, or right-after-mealtime, would enable patients to better determine the appropriate insulin dose because the exact contents of their meal would be known. This would also avoid overdosing or delayed dosing, which can lead to hypo- or hyperglycemia respectively, which both have severe short and long-term consequences. This would 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 Insulin Units/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 be of particular importance for specific populations of people with type 1 or type 2 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 in their children with diabetes at mealtimes or after meals, which, together with prandial insulins currently on the market, can result in hyperglycemia.
- **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 glucose levels. Concentrated ultra-rapid insulin may also facilitate the miniaturization of devices and/or increase autonomy between refills.
- **People with high insulin requirements:** BC Lispro U200, an ultra-rapid concentrated insulin, could improve blood glucose control in these people, while limiting the volume of each injection, and therefore the local pain felt afterwards. It also allows to reduce the disposable use – one pen or catheter lasting twice as long.

- **Previous partnership with Eli Lilly for BC Lispro U100 & U200**

BioChaperone Lispro program was previously licensed on two different occasions to the American company Eli Lilly.

A first partnership was signed between December 2011 and January 2013, when it was agreed upon to terminate it.

Then, based on the results obtained from two phase 2a studies, a second agreement was reached on December 19, 2014 for the development of an ultra-rapid insulin with two formulations: BioChaperone Lispro U100 and BioChaperone Lispro U200. During the term of the partnership, Eli Lilly and Adocia successfully completed 6 clinical studies on BioChaperone Lispro U100 and U200.

On January 26, 2017, Lilly announced its decision to terminate this agreement in order to prioritize an internal project, LY900014 (Lyumjev®). The end of the contract led to two arbitration proceedings which have since been closed<sup>22</sup>.

Following the termination of the second partnership, Adocia regained full ownership of the rights that had been licensed and continued to develop its product.

- **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.

<sup>22</sup> For more information on legal procedures opposing Adocia and Lilly following the termination of this contract, please see section « Litigation » 1.2.7.3 of the present reference document

Adocia received an upfront payment of \$10 million for BioChaperone Lispro. Additionally, Adocia is entitled to receive development milestone payments up to \$35 million 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<sup>®</sup> pharmaceutical excipients.

On October 13, 2021, Adocia announced that THDB has received from the Chinese Regulatory Authority, the CDE, the authorization to initiate the BioChaperone Lispro Phase 3 program in China.

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 Adocia full control over the further development of BioChaperone Lispro. This also opens additional collaboration opportunities with biopharmaceutical companies focused on diabetes with no existing insulin manufacturing facilities and, also, device companies integrating synergies between innovative medicines, devices and care management systems.

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### ▪ Results obtained with BC Lispro U100 & U200

To date, BioChaperone Lispro has been successfully tested in 11 clinical studies, in more than 250 people with type 1 or type 2 diabetes. BioChaperone Lispro has repeatedly shown an ultra-rapid profile compared to reference analog insulins aspart and lispro, whereas it was injected via syringes or insulin pumps. BC Lispro also showed superiority on some pharmacodynamic and pharmacokinetic parameters over Fiasp<sup>®</sup>.

#### 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 Lispro 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.

#### 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 76<sup>th</sup> Scientific Sessions (June 2016, New Orleans, USA) and a further oral presentation by Dr. Heise at the European Association for the Study of Diabetes 52<sup>nd</sup> Annual Conference (September 2016, Munich, Germany).



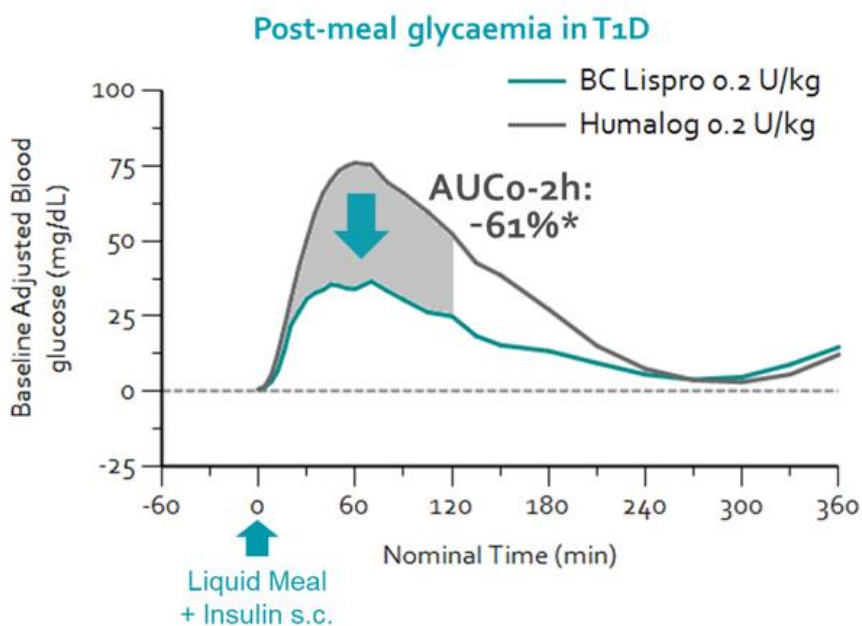


Figure 4: Comparison of the effect on postprandial glycaemia of BioChaperone Lispro U100 vs. Humalog U100 in 38 people with type 1 diabetes. Glycemia is measured for six hours after injecting the treatment at the time of consuming a standardized liquid meal.

**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% C<sub>max</sub> 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.

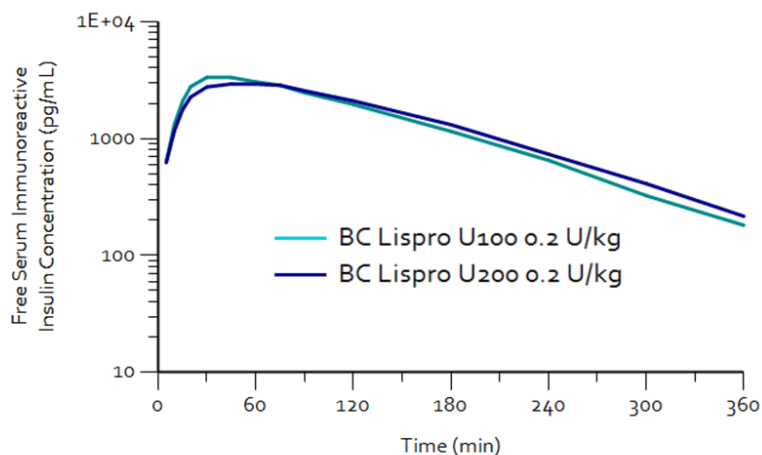


Figure 5: Mean pharmacokinetic profiles (variation in insulin level in the blood) of BioChaperone Lispro U100 (light blue curve) and BioChaperone Lispro U200 (dark blue curve) obtained from 26 healthy volunteers.

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The results of this study were the subject of an abstract published in the Diabetes Care scientific journal at the American Diabetes Association's 76<sup>th</sup> 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 on postprandial glycemic control 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, 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; (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>23</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 77<sup>th</sup> 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 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 were generated to allow the inclusion of Japanese diabetes patients into the Phase 3 program.

<sup>23</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

### 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 glycaemic 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 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  $T_{max}$  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>24</sup>.

### Positive clinical results confirming the ultra-rapid profile of BC Lispro including insulin from its partner Tonghua Dongbao

In January 2021, Adocia announced the positive results of the pharmacological study comparing BC Lispro, formulations using insulin lispro from two different sources: the biosimilar of its partner Tonghua Dongbao (THDB), and Humalog®, marketed by Eli Lilly. From a CMC perspective, all comparability data between THDB's lispro and Lilly's lispro has been generated to date. This bridging study validates the BioChaperone Lispro clinical data, in order to include previously obtained clinical data in the phase 3 dossier.

BC Lispro, formulated with insulin lispro from Tonghua Dongbao, demonstrates significantly faster absorption than the two Humalog® formulations marketed in Europe and the USA; and a stronger early effect. Conversely, the late exposure and late effect of BC Lispro (THDB) is reduced compared to the two Humalog® formulations. All four formulations showed good safety in use and were well tolerated. These results confirm the specific ultra-rapid action profile of BC Lispro, with a safety profile similar to that of Humalog®.

- **Study using the Beta Bionics iLet™ system (n=30)**

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

The iLet is a so called "Hybrid Closed-Loop" system. It consists of an autonomous infusion pump paired with a continuous glucose monitor (CGM). The system uses clinically tested mathematical dosing algorithms driven by

<sup>24</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.

machine learning to calculate and dose insulin as needed. The iLet used in this trial will be set on an insulin-only configuration (another version allows the co-infusion of glucagon).

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. It will compare the pharmacokinetic and pharmacodynamic profiles, intra- and inter-individual, for subjects using the iLet system with insulin lispro, insulin aspart, and BioChaperone Lispro. The co-primary endpoints will be mean continuous glucose monitoring glucose (CGMG) and portion of time spent in severe hypoglycemia (CGMG <54 mg/dL).

Results were delayed until 2021 due to difficulty in supplying equipment by Beta Bionics, independent of Adocia.

### ▪ Next steps

On October 13, 2021, Adocia announced that THDB has received from the Chinese Regulatory Authority, the CDE, the authorization to initiate the BioChaperone Lispro Phase 3 program in China.

Based on BioChaperone Lispro's strong clinical dossier, Adocia is seeking a new partner for entry into phase 3 and commercialization for territories excluded from the licensing agreement with THDB, with a primary focus for partnering on the US, EU, Japan, Latin America, Middle East and North Africa.

### ▪ 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 approval from 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. Fiasp is now available in 33 countries and in 2021 achieved \$265 million dollars in sales (1 748 million DKK)<sup>25</sup>.

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 it has been shown for BioChaperone Lispro U100 in several Phase 1b Studies. This latter effect is desirable as it may reduce the risk of hypoglycemia. In Phase 3 studies, Fiasp confirmed its ultra-rapid absorption profile but did not show superiority in terms of hypoglycemia compared to insulin aspart.

In 2017, when the collaboration with Adocia and Eli Lilly ended, **Eli Lilly** announced that it had developed a competing ultra-rapid insulin project LY900014 (insulin lispro formulated with treprostinil and citrate, among other excipients). In June 2020, Eli Lilly launched Lyumjev®, which presents pharmacokinetic and pharmacodynamic profiles faster than those of Humalog (insulin lispro) in the first minutes after injection. However, Lilly did not demonstrate a faster "fast-out / fast-off" effect than insulin lispro, unlike BioChaperone Lispro. In the Phase 3 trial, Lyumjev met the non-inferiority criterion for reduction in glycated hemoglobin (HbA<sub>1c</sub>) compared to Humalog and demonstrated a better glucose control after a meal. Lyumjev's sales in 2021 are evaluated at 115 million USD<sup>26</sup>.

**Mannkind**, founded in 1991, developed Afrezza®, an inhalable human insulin with an ultra-rapid 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 explicitly on the packaging), regarding the risk of bronchospasm associated with the treatment. In addition, the FDA requested that Mannkind carry out four post-marketing clinical trials. An Afrezza marketing agreement with Sanofi in 2014 was terminated on

<sup>25</sup> Novo Nordisk Annual Report, 2021

<sup>26</sup> GlobalData Forecast, as of 02/02/2022

April 4, 2016. Since then, Mannkind has continued to market Afrezza by its own means (except Brazil where a partnership has been signed with Biomm). In 2020, Afrezza generated \$ 32 million in net income, up by 26% from 2019 (\$25.3 million). The growth is mainly due to an increase in demand, including the sales in Brazil, an increase in prices as well as a more suitable product mix (there are disposable cartridges of 4, 8 or 12 units of insulin).

In June 2020, Arecor announced the results of phase 1 of its ultra-rapid insulin (AT-247). This is a crossover, randomized, double-blind, single-dose, 3-week PK / PD study. Conducted in 19 patients with type 1 diabetes, the trial demonstrated that absorption of AT247 was accelerated compared to NovoRapid® and Fiasp®. Insulin AT247 was detected in the blood 12 minutes (p = 0.0004) earlier than with NovoRapid and 2 minutes (p = 0.0003) earlier than Fiasp. On January 20, 2022, Arecor announced the inclusion of the first patient in a phase 1 study conducted in the US for AT247. The study intends to explore its application in a CSII (Continuous Subcutaneous Insulin Infusion). The study completion is expected in H2 2022.

Thermalin Inc. is also working on ultra-fast, thermo-stable and ultra-concentrated insulins (U500), in particular for patch pump applications. In August 2019, Thermalin announced the selection of T-1123 as a clinical candidate for trials in type 1 and 2 patients<sup>27</sup>.

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 Biodel (which was the subject in 2016 of a "reverse-merger" operation by Albireo, which resulted in the deprioritization of Biodel's historical activities).

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#### 1.2.4.5. 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. Today, 50% of patients on basal insulin do not meet their glycemic control targets<sup>28</sup>.

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-dose 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).

Thank to this simple administration scheme, premixed insulins are therefore particularly recommended for elderly patients. They are also widely used in emerging countries due to an overall lower cost. However, they do not offer ideal medical performance, due 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) and insulin lispro (prandial) 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.

- **Partnership with Tonghua Dongbao Pharmaceuticals Co. Ltd**

In 2018, Adocia and the Chinese insulin leader Tonghua Dongbao Pharmaceuticals Co. Ltd entered a strategic alliance. In April 2018, Adocia granted Tonghua Dongbao Pharmaceuticals Co. Ltd two licenses for the development and

<sup>27</sup> Thermalin Press Release, August 6, 2019

<sup>28</sup> Sanofi communication – Q3 2015 presentation

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. THDB also relies on Adocia's expertise to conduct part of its clinical development in Europe, in preparation for approval in China.

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

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- **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. HumalogMix™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

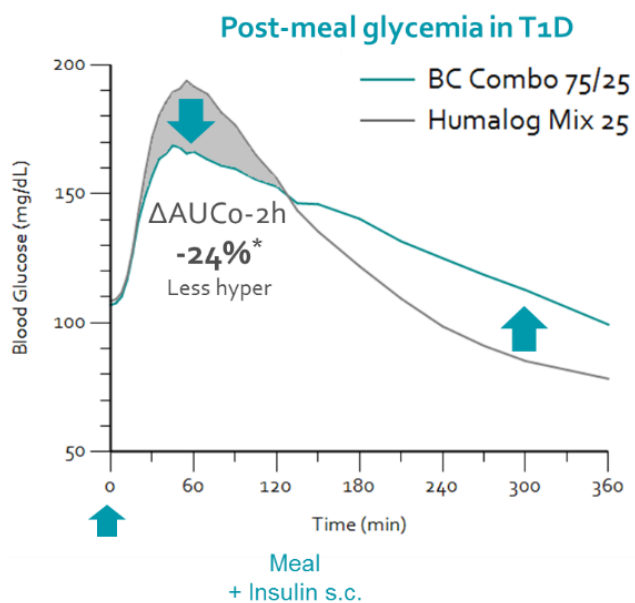


Figure 6: Pharmacodynamic profiles for BioChaperone Combo 75/25 and HumalogMix 25 after a liquid meal obtained from 28 people with type 1 diabetes (NCT#02514954). 1 p=3.10-3.2 p=8.10-3.

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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 76<sup>th</sup> Scientific Sessions (June 2016, New Orleans, USA) and a poster at the European Association for the Study of Diabetes 52<sup>nd</sup> 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 HumalogMix™75/25 (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 ( $AUC_{GIR(0-2h)}$ ) and the delayed basal effect ( $AUC_{GIR(24-30h)}$ ) of these three treatments.

In this study, BioChaperone Combo demonstrated a significantly superior early prandial action and a longer metabolic effect compared to HumalogMix™75/25, which confirms results previously obtained during the first pharmacokinetic and pharmacodynamics study conducted in patients with type 1 diabetes.

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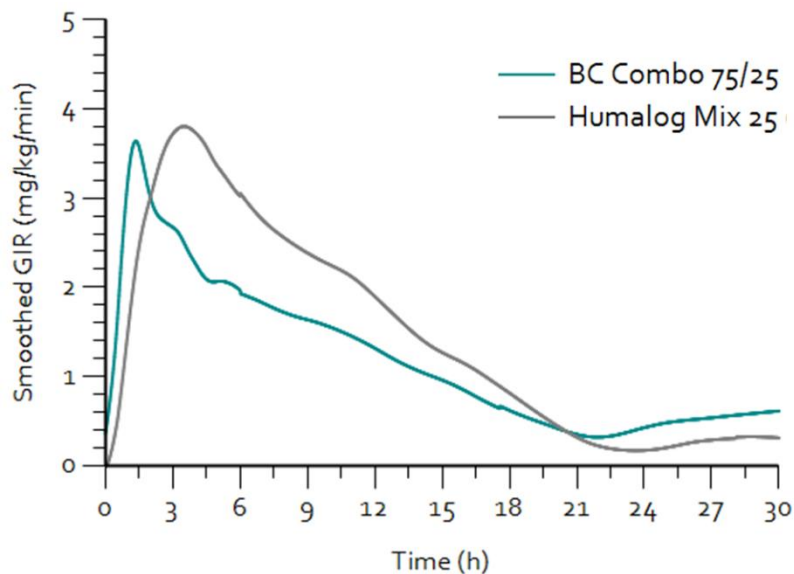


Figure 7: Pharmacodynamic profile (glucose infusion rate) of BioChaperone Combo 75/25 and Humalog Mix 25 for 30 h after injection in 24 subjects with type 2 diabetes under euglycemic clamp conditions (NCT#02514850).

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.

- **Next steps**

In order to register BC Combo in China, Tonghua Dongbao has chosen to rely on Adocia's expertise to conduct part of the clinical development in Europe. In April 2022, the launch of three clinical studies has been validated by Chinese and German regulatory authorities (CDE and BfArM), which will contribute to the dossier for Phase 3 studies in China.



## ▪ Competition

**Premixed insulins** are prandial insulins, with a portion of insulin precipitated with protamine to slow down its effect. These products are 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 premixed insulins made from human insulin, which remain widely used in emerging countries (e.g., Humulin® 70/30 for Eli Lilly and Novolin® 70/30 for Novo Nordisk, as well as many locally developed products). The premix market in the USA represents a turnover of 2.2 billion dollars in 2019. It should be noted that in China, 63% of the volume of insulin sold consists of insulin premix. The turnover of Chinese companies in their market is not precisely known and it is observed that the Chinese market is partially underestimated<sup>29</sup>.

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

- **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®, 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®, 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 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® and Humalog®). 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..

### 1.2.4.6. 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.

It is worth mentioning that an overdose of insulin can cause hypoglycemia. It is therefore the most feared short-term side effect of patients on insulin therapy.

**Severe hypoglycemia** is defined by a blood glucose lower than 50-54 mg/dL. Its symptoms may include dizziness, transient cognitive impairment, convulsion and, in the most severe cases, coma and death. Due to those symptoms,

<sup>29</sup> IQVIA data for 2019

treating severe hypoglycemia very often requires the help of a third party. The prevalence of severe hypoglycemia per year is estimated at 34% in people with type 1 diabetes<sup>30</sup>. Severe hypoglycemia causes more than 300,000 hospitalizations in the United States each year<sup>31</sup>.

In the therapeutic field, human glucagon is the only approved treatment for severe hypoglycemia. Unfortunately, human glucagon is very unstable in an aqueous solution and the only commercially available products during the last decades are multi-step emergency (rescue) kits. Composed of lyophilized human glucagon, the kit requires reconstitution 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>32</sup>.

By using proprietary BioChaperone<sup>®</sup> technology, Adocia is developing 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 the development of completely autonomous devices, using algorithms that react automatically to glycemic variations, without the patient intervening. Recently, several research groups (academic and 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>33</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 glucagon solution. Most of the studies had been conducted using lyophilized glucagon reconstituted every day, which 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.

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### ▪ 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 BioChaperone Glucagon in this first human study. 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<sup>®</sup> HypoKit<sup>®</sup>. The median time to reach a clinically risk-free level of blood glucose of 70 mg/dL was 11 min for BioChaperone Glucagon and almost 7 min for the reconstituted commercial product Glucagen<sup>®</sup>. All patients achieved hypoglycemic resolution within 35 minutes of injection.

### ▪ Next steps

Adocia is actively seeking a partner to continue clinical development with a Phase 1/2 study. This study may be the last before the program enters Phase 3 of its clinical development. At the same time, Adocia has identified a high quality and easy to use injection device for BioChaperone Glucagon.

### ▪ Competition

The product developed by Adocia is an aqueous formulation based on human glucagon, an approved peptide. This is a de-risked approach, compared to formulations proposed by other competitors based on new peptides (glucagon analogs).

For the treatment of severe hypoglycemia, four products are currently on the market:

**“Historical” products to be reconstituted:** Glucagon Emergency Kit (Eli Lilly) and GlucaGen<sup>®</sup> Hypokit<sup>®</sup> (Novo Nordisk). In both cases, these emergency kits require real-time reconstitution of lyophilized glucagon and injection using a syringe. The entire operation takes between 7 and 9 steps. In a real emergency situation, when the patient is

<sup>30</sup> Frier Int. Dia. Monitor 2009

<sup>31</sup> CDC reports, 2014

<sup>32</sup> Yale et al. Faster use and fewer failures with needle-free nasal glucagon versus injectable glucagon in severe hypoglycemia rescue: a simulation study. *Diabetes Technol Ther.* 2017;19:423-432

<sup>33</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

unconscious, these devices have proven to be extremely difficult to use by third parties, especially since they are not always trained in their use. In a study, 130 parents of people with type 1 diabetes are placed in a simulated hypoglycemic emergency situation, 69% of them experienced difficulty handling the emergency kit (GlucaGen Hypokit)<sup>34</sup>. Due to the difficulty of using these products, they remain under-prescribed and under-utilized, leading to frequent interventions by emergency teams. Response time can be fatal.

**Eli Lilly** received in 2019 the regulatory approval from the American and European regulatory authorities for Baqsimi<sup>®</sup>, a presentation in the form of a single-use nasal spray, which might be apparently easier to use for a naive user. In 2020, Baqsimi's worldwide sales reached \$76.1 million<sup>35</sup>. Baqsimi's sales are forecasted to reach \$277 million in 2026 and to account for 30% of global glucagon sales<sup>36</sup>. In France, Baqsimi was added to the reimbursed drug list on January 19, 2022<sup>37</sup>. In parallel, Eli Lilly ended the development of a soluble glucagon analogue in 2018.

**Xeris** received FDA approval in September 2019 for the use of Gvoke<sup>®</sup>, a liquid formulation of human glucagon (obtained using the organic solvent DMSO), to treat severe hypoglycemia. The company now markets Gvoke as a HypoPen<sup>®</sup> autoinjector pen and as a pre-filled syringe. A kit (vial of liquid glucagon and a syringe) has also recently been launched in the US on March 16, 2022.

In February 2021, the ready-to-use glucagon solution received marketing approval from the EMA, for its commercialization in Europe under the name Ogluo<sup>®</sup>. The first launch happened in the UK in December 2021. Xeris recorded 20.2 million USD in sales in 2020. Consensus estimate that the product will achieve \$288.6 million in 2026<sup>38</sup>.

Xeris also intends to develop this product as mini-pens for moderate hypoglycemia and as cartridges for use in pumps (artificial pancreas or other chronic uses of glucagon). The company is conducting a Phase 2 study in pump for hypoglycemia following bariatric surgery and is conducting a Phase 2 pump trial to reduce exercise-induced hypoglycemia.

**Zealand Pharma** received FDA approval on March 22, 2021 for the use of Zegalogue<sup>®</sup> for the treatment of severe hypoglycemia in patients with diabetes. It is a glucagon analogue, dasiglucagon. Zealand Pharma thus launched its ready-to-use prefilled pen HypoPal<sup>®</sup> in June 2021 in the USA.

Dasiglucagon is developed for three main indications: the treatment of severe hypoglycemia, the use in bi-hormonal pumps ("artificial pancreas") and the chronic treatment of congenital hyperinsulinism (in glucagon pump). The company recently demonstrated the non-inferiority of dasiglucagon, compared to Eli Lilly's glucagon, in a Phase 2b study in Beta-Bionics' artificial pancreas, iLet<sup>™</sup>. The initiation of a pivotal Phase 3 study with this system is scheduled for the year 2021. Finally, the Company has obtained an "orphan drug" indication by the FDA for the use of dasiglucagon to treat congenital hyperinsulinism, project which entered Phase 3 in December 2018.

**Hanmi** is currently developing a long-acting glucagon analogue (HM15136), building on their LAPSCOVERY technology platform. Hanmi is primarily aimed at the treatment of congenital hyperinsulinism and hypoglycemia following bariatric surgery. Hanmi has obtained orphan drug designation for HM15136 from the FDA and EMA.

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.

#### 1.2.4.7. M1 Pram, BC LisPram, BC AsPram: 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

<sup>34</sup> Harris, G et al Practical Diabetes Int. 2001; 18;22-25.

<sup>35</sup> Eli Lilly Financial Workbook

<sup>36</sup> EvaluatePharma<sup>®</sup> Consensus Sales Forecast based on: Morgan Stanley to 2025 (28 Oct 20); Wolfe Research to 2030 (13 Oct 20); Cantor Fitzgerald to 2026 (16 Dec 20)

<sup>37</sup> Arrêté du 19 janvier 2022 modifiant la liste des spécialités pharmaceutiques remboursables aux assurés sociaux - JORF n°0020 du 25 janvier 2022

<sup>38</sup> EvaluatePharma<sup>®</sup> Consensus Sales Forecast based on: RBC Capital Markets to 2024 (07 May 20); Piper Sandler to 2027 (18 Jun 20); SVB Leerink to 2035 (02 Jul 20); Jefferies to 2025 (08 May 20); Mizuho Securities to 2024 (08 May 20)

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 (cf. figure 3). 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®, 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>39</sup>.

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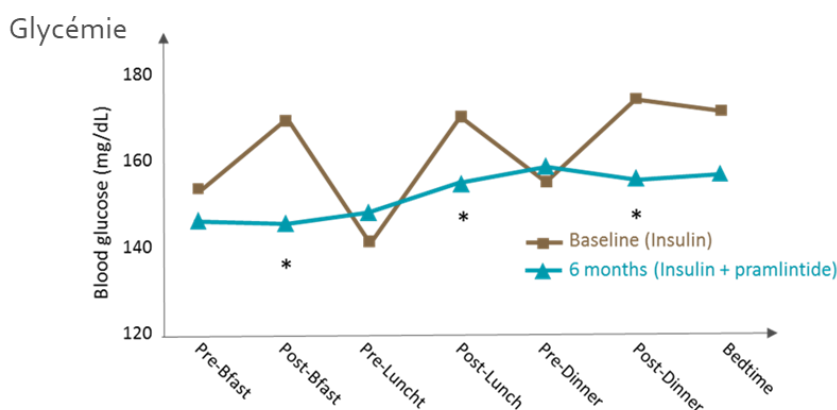


Figure 8: Average daytime glycemia in people with type 1 diabetes, treated by insulinotherapy alone (brown curve) or by insulinotherapy + Symlin®(pramlintide, blue curve), after a 6 months treatment period. Adapted from Guthrie R et al. Diabetes 2005, 54(Suppl 1): A118, \*P <.05. See also Pullman J and 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 combinations is Adocia's objective for the M1 Pram, BC LisPram and BC AsPram programs.

Currently, prandial insulin and pramlintide formulations are not compatible. Adocia has developed various type of combinations:

- Adocia used its formulation expertise to identify a human insulin analogue, M1, that can be co-formulated with pramlintide to provide a stable formulation. M1 is the A21G analog of human insulin. It is also the major metabolite of long-acting insulin glargine, but exhibiting the action profile of a mealtime insulin. As a result, millions of insulin glargine users worldwide have been exposed for years to M1 without M1 being an approved insulin. It is therefore a well-known insulin with an established action and tolerance profile<sup>40</sup>.
- At the same time, Adocia took advantage of its BioChaperonne® technology platform to combine pramlintide with insulin lispro ("BC LisPram"), and with insulin aspart ("BC AsPram"). These insulin analogs are already approved and are both in the public domain.

The formulation strategy is based on the clinical results demonstrating clear medical benefits when the hormones are administered separately. This would allow for a reduced development timeline. Amylin and insulin combinations could support a competitive pricing strategy, taking advantage of already market approved proteins and in the public

<sup>39</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

<sup>40</sup> Bolli et al. Diabetes Care. 2012 Dec; 35(12): 2626-2630. & Lucidi et al. Diabetes Care. 2012 Dec; 35(12): 2647-2649 & Lantus® label, Section 12.3

domain. Developing these three programs in parallel makes it possible to mitigate the risk and enhance partnership opportunities.

- **Clinical results obtained by the Insuline Pramlintide combinations**

Considering the significant clinical benefit of an insulin-pramlintide combination, Adocia has developed three co-formulation approaches. Currently, M1 Pram is the lead formulation. In parallel, Bc LisPram and BC AsPram program are also being developed, particularly for application in pump.

### Clinical results obtained by M1 Pram

#### Phase 1 clinical results – Evaluation of safety, pharmacokinetics and pharmacodynamics of M1 Pram in people with type 1 diabetes (n=24)

In April 2019, Adocia announced positive preliminary pharmacodynamic and safety results for a Phase 1 study of M1 Pram, its ready-to-use co-formulation of pramlintide and M1, mealtime insulin analog A21G of human insulin. In this randomized, double-blind, controlled by an active comparator, three-period crossover trial, 24 participants with type 1 diabetes randomly received a sequence of three treatments, administered at mealtimes (standardized mixed meal). The objective of this study was to investigate the pharmacokinetic, pharmacodynamic, safety and tolerability profiles of a single dose administration of M1 Pram (containing 7.5 units of insulin and 45 µg of pramlintide), compared with those obtained after separate and simultaneous injections of human insulin (7.5 units, Umuline®, Eli Lilly) and pramlintide (45 µg, Symlin®, AstraZeneca) on the one hand, and to those obtained after an injection of the fast-acting insulin analog lispro (7.5 units, Humalog®, Eli Lilly) on the other hand.

Treatment with M1 Pram resulted in a statistically significant reduction of 85% in glycemic excursion during the first two hours, compared to (Mean (± Standard Deviation)  $\Delta\text{AUC}_{\text{Blood Glucose 0-2h}} = 18 (40) \text{ mg}^* \text{ h} / \text{dL}$  vs.  $119 (56) \text{ mg}^* \text{ h} / \text{dL}$ ;  $p < 0.0001$ ) and postprandial glycemic control similar to that of separate injections of Umuline and Symlin (Mean (± Standard Deviation)  $\Delta\text{AUC}_{\text{Blood glucose 0-2h}} = 26 (49) \text{ mg}^* \text{ h} / \text{dL}$ , ns).

All treatments were well tolerated. In particular, the overall number of hypoglycemia was similar between treatments (M1 Pram: n = 2; Symlin + Umuline: n = 2; Humalog: n = 0) and no signs of gastro-intestinal side effects was reported. As a reminder, hypoglycemia and gastrointestinal side effects have previously been associated with the clinical use of Symlin®.

#### Clinical results of Phase 1b, part A - exploratory study of M1Pram in type 1 diabetics (n = 24), receiving a low dose of insulin for a period of 3 weeks, in the clinic and on an outpatient basis

In April 2020, Adocia announces the positive preliminary results of the exploratory Phase 1b - part A study, with M1 Pram in people with type 1 diabetes. This study documents the safety and efficacy of M1 Pram over a 24-day period of repeated administration, including an outpatient period, in order to inform future clinical development. The primary endpoint is the M1 Pram effect on postprandial glycemic control at the end of the 24-day treatment period, compared to mealtime insulin Novolog® (insulin aspart, Novo Nordisk).

This two-period, randomized, double-blind, crossover trial, controlled by an active comparator was to assess the safety and efficacy of M1 Pram. 24 participants with type 1 diabetes received multiple daily doses of either M1Pram or Novolog over two periods of 24 days each (including 4 days in clinic and 20 days under participants' usual life conditions), after a stabilization period to determine the optimal basal insulin dosage.

In a meal-test administered at the clinic on day 24, treatment with M1 Pram allowed a reduction of postprandial glycemic excursion vs. Novolog® by more than 100% during the 2 hours after the meal ( $p = 0.0001$ ) and resulting in an overall decrease of 39% (n.s.) over the first 4 hours. During the 3-week outpatient treatment period, M1 Pram resulted in a 70 min daily increase in the "Tight Time-in-Range" (time spent in a narrow blood glucose target,  $p = 0.001$ ) vs. Novolog®. M1 Pram also allowed an average weight loss of 0.7 kg compared to the initial weight ( $p = 0.012$ ). These results are consistent with the known pharmacological effects of pramlintide. Both treatments were well tolerated, and no serious side effects were seen during the 24 days of treatment.

#### Clinical results of Phase 1b, part B - repeated administration of M1 Pram in people with type 1 diabetes (n = 16) receiving a high dose of insulin, for a period of 3 weeks, with in-clinic and outpatient settings

In September 2020, Adocia announced positive preliminary results from a Phase 1b clinical study with M1 Pram in subjects with type 1 diabetes.

This two-period, randomized, double-blind, crossover trial controlled by an active comparator was to assess the safety and efficacy of M1 Pram. As part of this extension of the initial study, patients requiring more than 40 IU/day of mealtime insulin were recruited, in order to document the safety/efficacy of high ratio of M1Pram. Sixteen subjects with type 1 diabetes received several daily doses of M1Pram and Novolog (insulin aspart, Novo Nordisk) over two periods of 24 days each (including 4 days in-clinic and 20 days in outpatient), after a stabilization period aimed at optimizing the basal insulin regimen. During standardized meals at the clinic on day 24, treatment with individualized doses of M1 Pram resulted in a 69% decrease in glycemic excursion compared to Novolog during the first 4 hours after the meal (primary endpoint: Delta AUC<sub>PG 0-4h</sub>,  $47 \pm 149$  mg.h / dL vs  $145 \pm 162$  mg.h / dL, LSM ratio 0.31 p = 0.0266).

At the end of the treatment period, a significant mean weight loss of 1.6 kg from baseline was observed in people treated with M1 Pram. This weight loss was statistically different from the 0.4 kg weight increase seen in people treated with Novolog (p = 0.0065).

In addition, a treatment satisfaction questionnaire was submitted to all patients after each treatment period. The results reflect the beneficial impact of M1 Pram on individuals, with 87% of them reporting better appetite control thanks to the M1 Pram drug, and 75% of patients recommending it to other people with diabetes.

In terms of safety, both treatments were well tolerated, and no serious treatment-related adverse events were reported. M1Pram showed good local tolerance.

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### BC LisPram and BC AsPram clinical development

#### Phase 1 clinical results - Evaluation of the safety, pharmacokinetics and pharmacodynamics of BioChaperone Insulin-Pramlintide 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 M1 Pram, 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 food intake (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 7.5 insulin units and 45 µg pramlintide), compared on the one hand to separate and simultaneous injections of human insulin (7.5 IU, Humulin®, Eli Lilly) and pramlintide (45 µg, Symlin®, AstraZeneca), and on the other hand to an injection of rapid-acting insulin analog lispro (7.5 IU, Humalog®, Eli Lilly).

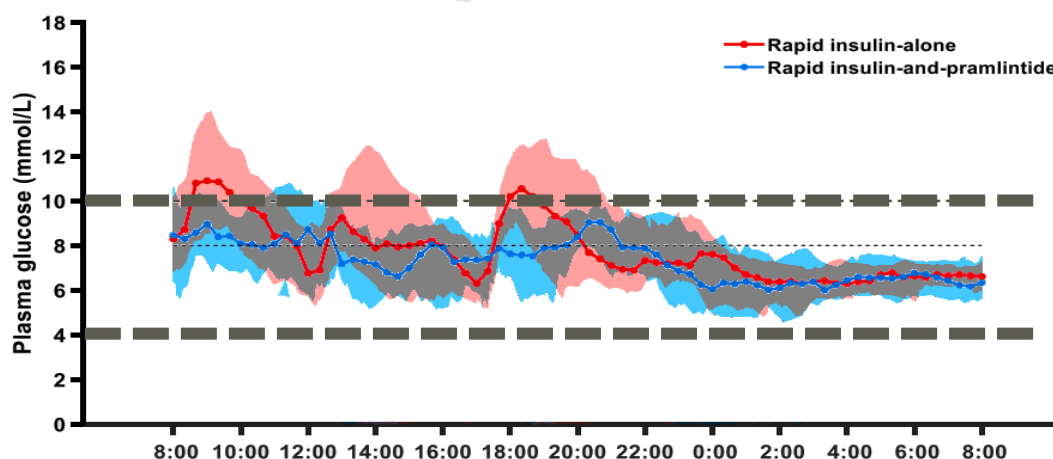
Treatment with BC Pram Ins resulted in a statistically significant 97% reduction of blood glucose excursions over the first two hours compared to Humalog (Mean(±SD) DeltaAUC<sub>GIR 0-2h</sub> = 4 (63) mg\*h/dL vs. 126(74) mg\*h/dL; p<0.0001) and a comparable postprandial glycemic control to that of the separate injections of Humulin and Symlin (LS- Mean DeltaAUC<sub>GIR 0-2h</sub> = 21 (66) mg\*h/dL, n.s.).

All treatments were well tolerated. In particular, 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.

#### Proof of concept obtained at McGill University, Montreal, Canada, n = 29

The clinical proof of concept was established by Dr. Amhad Haidar of McGill University, Canada, comparing the simultaneous administration of insulin lispro and pramlintide via two separate pumps to the administration of lispro alone. Lispro + pramlintide administered simultaneously resulted in a + 10% improvement in time spent in the glycemic target ("time-in-range") compared to Lispro (Humalog®) alone (84% vs. 74%). A satisfaction questionnaire was also sent to the 29 patients included. Of these, 27 would recommend switching from insulin lispro alone to a fixed combination of insulin and pramlintide<sup>41</sup>.

<sup>41</sup> Ahmad Haidar et al. Diabetes Care 2020 Jan; dc191922



Results comparing the time spent in the target area for the 29 patients with type 1 diabetes, treated with insulin lispro alone or with insulin lispro and pramlintide co-administered

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Adocia developed BC LisPram and BC AsPram formulations with the goal of achieving similar results with a formulation that combines the two hormones in one pump.

- **Next steps for Insulines-Pramlintides programs**

#### M1 Pram

Adocia announced on March 10, 2021 that it had started a Phase 2 study with M1 Pram multiple daily injection. This study compares the efficacy of M1 Pram with that of insulin lispro (Humalog®, Eli Lilly) on weight variation and glycemic control, after 16 weeks in 80 patients with type 1 diabetes. Both products are administered in combination with basal insulin. Tolerance criteria are also evaluated. The design is multicentered, open-label, randomized, in parallel-group, versus active-control. Glycemic homeostasis is measured by continuous glucose monitors (CGM) and patient satisfaction is collected via a questionnaire. Results obtained in the first quarter of 2022 will result in a communication.

Adocia plans to explore additional indications for M1Pram as a second step, including treatment of people with Alzheimer's disease<sup>42 43 44</sup>.

#### BC LisPram

On June 29, 2021, Adocia initiated a Phase 1 study in patients with Type 1 diabetes, with BC LisPram administered by pump. This study, in collaboration with Dr. Ahmad Haidar of McGill University in Canada, is designed to evaluate the pharmacokinetics, glycemic control and tolerability of BC LisPram in 16 patients in comparison to rapid insulin lispro. Results are expected in the second quarter of 2022.

- **Competition**

To date and to our knowledge, only **Biozeus**, a Brazilian biotechnology company, **Arecor** and **Xeris Pharmaceutical** are developing a combination of insulin and amylin.

**Biozeus** is working on a long-acting amylin analog (BZ043). In April 2019, they announced that they had demonstrated a normoglycemic effect in animals, in combination with glargine. The program no longer appears active in 2020<sup>45</sup>.

<sup>42</sup> de Groot et al. Am Psychol 2016, Roy et al. J. Aff. Dis. 2012; Ott et al. Neurology 1999

<sup>43</sup> Robin et al. Diabetes Educ 2009, Robin et al. Curr Med Res Opin 2007

<sup>44</sup> Zhu et al. Alzheimer and Dementia 2017

<sup>45</sup> Biozeus Pharmaceuticals, press release 22 avril 2019

In October 2019, **Areacor** announced that it had signed a research, development and commercialization agreement with JDRF for a co-formulation of insulin and amylin for the treatment of diabetes. The JDRF (Juvenile Diabetes Research Foundation) is a global organization funding research for type 1 diabetes. Under this collaboration, Areacor and the JDRF are equally contributing to the development of AT271, a liquid and stable solution of insulin and amylin, taking advantage of Areacor's technological platform: Arestat™. The program has not yet entered the clinical stage<sup>46</sup>.

**Xeris** began a first clinical study in 2019 for their insulin and amylin co-formulation called Xerisol™ (XP-3924). In June 2020, the company announced positive results from a comparative study between Xerisol and Humulin® R in adults with type 1 diabetes. Improved blood sugar control and Xerisol has a good tolerance profile<sup>47</sup>. It is important to note that this study was conducted on only 18 patients, with a single injection, and compared to human insulin. In 2022, XP-3924 does not appear anymore on Xeris' pipeline.

**AstraZeneca**, owning the commercial product Symlin® (pramlintide), has successfully conducted Phase 1 clinical studies of co-administration, using two independent pumps, delivering mealtime insulin and pramlintide. These trials were partially funded by Juvenile Diabetes Research Foundation (JDRF). The positive results are obtained in line with Adocia's approach, which consists of combining the two products in the same formulation for better clinical benefit<sup>48</sup>.

**Novo Nordisk** is also developing a new long-acting amylin analog, called cagrilintide, which is currently tested in several clinical trials (Phase 1 and 2), alone or in combination with semaglutide, Novo Nordisk's last generation GLP-1.

**Zealand Pharma** in collaboration with Boehringer Ingelheim, is also developing ZP-4982, 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.

#### 1.2.4.8. BioChaperone Glargine GLP-1

- **Combinations to intensify treatment for 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>49</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® (Novo Nordisk) combining degludec and liraglutide; and Soliqua®/Suliqua® (Sanofi) made of glargine and lixisenatide.

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®, Novo Nordisk, daily administration) and dulaglutide (Trulicity®, Eli Lilly, weekly administration), in order to develop two potential candidates:

- BioChaperone® 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® Glargine Dulaglutide, with a strong potential for best-in-class performance, based on the excellent pharmacologic profile of dulaglutide and glargine.

<sup>46</sup> Xeris, press release, 18 juin 2020

<sup>47</sup> Xeris, press release, 18 juin 2020

<sup>48</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>49</sup> Sanofi, JP Morgan Healthcare Conference Presentation, San Francisco, January 12, 2015.



These two candidates, 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 and is seeking a partner to continue development.

- **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® (insulin glargine 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. Novo Nordisk fixed set a price for Xultophy equivalent to the cost of acquiring both products individually (ie. Victoza + Tresiba prices) minus a reduction of about 20%. While Sanofi was more aggressive, fixing a pricing structure equivalent to the average price of a GLP-1, a price about 33% lower than that of Xultophy (before negotiations). 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 (or LAPS Insulin Combo HM1422), 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.

#### 1.2.4.9. Cell Therapy

- **Cell therapy: the ultimate goal for people living with diabetes**

25 million of people with type 1 diabetes live without  $\beta$ -cells, destroyed by their own immune system. Cell therapy involves administering living cells to patients in order to restore glycemic control.

Since the 1980s, the transplantation of islets of Langerhans from the pancreas of deceased donors has been possible. However, this technique, although approved by the health authorities, is limited to a small patient population because two major problems persist:

- The scarcity of donors
- The lifelong use of immunosuppressive treatments to prevent rejection of transplanted cells by the immune system, causing a significant increase in the risk of infection and certain cancers.

Today, recent advances in cell biology allowing stem cells to be differentiated into cells like  $\beta$ -cells, will solve the problem of donor shortages and expand treatment to a larger patient population. However, a real challenge remains to overcome: effectively implanting these  $\beta$ -cells for the long term.

To address these issues, Adocia has designed an innovative hydrogel matrix capable of maintaining cell activity while protecting them from rejection by the immune system.

### ▪ *In vitro/In vivo* results and next steps

Adocia has developed a flexible, stable and biocompatible hydrogel matrix. The program was initiated with human islets of Langerhans to demonstrate the proof-of-concept of the tolerance and efficacy of an easily transplantable implant. The process was straightforward and the transplanted islets were functional and rapidly delivering insulin in response to a glucose stimulus. The next step will be to extend the application to stem cells, which will remove the limitations of the number of donors. Other diseases might also benefit from this technology (cancers, diseases of the heart, muscles, immune system...).

A collaboration has been established with Professor Pattou's research team (TRD (Translational Research for Diabetes)/DiabInnov®, Inserm Lille, France), who is internationally recognized in the field of islet of Langerhans transplantation in humans and in preclinical models. Adocia has also surrounded itself with a network of experts in various fields, including the CEED (Centre d'Etudes Européennes pour le Diabète) in Strasbourg, the University Hospital of Montpellier, the Pierre Gilles de Genes Institute, the ESPCI (Ecole Supérieure de Commerce et d'Industrie), and the IRCAD (Institut de Recherche contre les Cancers de l'Appareil Digestif) in Strasbourg.

A family of patents relating to cell therapy was filed in early 2021. The preliminary results obtained *in vitro* and *in vivo* in rats, mice and pigs are promising.

Adocia aims to obtain the proof-of-concept in large animals in 2021, for a potential clinical entry in 2022/2023.

### ▪ Competition

While many research teams are focused on cell biology to obtain  $\beta$  cells from stem cells, Adocia is focused on developing a matrix capable of accommodating these cells. Other public and private research teams are also working on  $\beta$ -cell encapsulation. To date, around ten programs have been initiated based on various technologies. No company has yet entered phase 3. Among the most advanced:

- **ViaCyte** is working on both a polymer device (ePTFE) in collaboration with Gore, and on stem cells, notably via a collaboration with CRISPR Therapeutics. To date, they have two categories of macro-encapsulation devices: on the one hand, PEC-Direct and PEC-QT, which let the micro-vascularization reach the cells, and on the other hand, PEC-Encap, based on Encaptra® technology, which prevents contact between the graft and immune cells and thus prevents the patient's autoimmune response. In 2021, a Phase 1/2 was underway for PEC-Direct and PEC-Encap. The results of PEC-Direct were announced at the end of December 2021. All 26 patients treated still required insulin injections at the end of the study, and had to resort to immunosuppressive treatments<sup>50</sup>. On February 2, 2022, Viacyte announced the inclusion of a first patient in a Phase 1 study of VCTX210, cells edited by CRISPR technology to evade the immune system.
- **Sigilon Therapeutics** is developing a spherical matrix based on alginate (Afibromer™). In 2018, the proof of concept was carried out in primates. On April 4, 2018, a partnership was signed with Eli Lilly for the development of encapsulated cells for cell therapy, for which Sigilon received an initial payment of \$63 million. This technology, developed in parallel for the treatment of hemophilia, was suspended in November 2021 by the FDA, following observations of fibrosis<sup>51</sup>. Sigilon since reduced its workforce by 38% and re-focused on diabetes.
- **Vertex**, which acquired Semma Therapeutic for USD 950 million on September 3, 2019, is developing two approaches to deliver insulin-producing cells: one product requiring immunosuppressive therapy,

<sup>50</sup> Endpoints, Disappointing' ViaCyte data raise questions about future of company's attempted diabetes cure, by Jason Mast on December 22nd, 2021

<sup>51</sup> Sigilon Therapeutics Announces Update on SIG-001 Phase 1/2 Study in Hemophilia A, Nov 29, 2021

the other protecting cells within a PTFE-based medical device. The proof of concept has been obtained in animals. Phase 1/2 preliminary results of VX-880, stem cell-derived pancreatic cells, were communicated in October 2021 and appeared promising, even though immunosuppression is still required.

- **Sernova** is working on different approaches to overcome the immune response: via a conformal coating, in partnership with the University of Miami, and via the development of cell lines designed to evade the immune response, with AgeX. A PTFE device, the CellPouch<sup>®</sup>, is designed to facilitate cell survival and recovery. Results were reported in January 2022: some patients, in addition to an intraportal injection of pancreatic cells, have achieved insulin independence, in addition to an immunosuppressive treatment<sup>52</sup>.
- **Procyon Technologies** signed on December 8, 2020 an exclusive research agreement with Novo Nordisk for the development of an implantable device used to encapsulate  $\beta$ -cells. While Novo Nordisk brings its expertise in stem cells, Procyon's strength lies in the development of a system allowing optimal oxygenation of cells within the implantable device.

Most of these companies focus their research on technologies based on alginate or PTFE (poly-tetra-fluoro-ethylene). Adocia now proposes an innovative approach with a matrix based on an innovative hydrogel.

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## 1.2.5. Adocia's pipeline for the treatment of obesity

### 1.2.5.1. Obesity and its treatment

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>53</sup>. The obesity rate varies from one country to the next one. Amongst the most impacted, we can highlight the USA with 42.2% of adults suffering from obesity (and 65% overweight)<sup>54</sup> and China, where more than half of the population (50.7%) is overweight or obese<sup>55</sup>. Obesity can lead to at least sixty other pathologies, including diabetes, cardiovascular disease, NASH... The Milken Institute has estimated the direct and indirect health care costs of obesity at \$1.72 trillion per year for the United States alone.

Today, 70% of Americans suffering from obesity are trying to lose weight<sup>56</sup>. However, only 2% of those patients use prescription medicines. This percentage can be explained by the small number of drugs available, their sometimes limited efficacy and the lack of persistence of their effects over time. These treatments, oral or injected subcutaneously, allow a rapid loss of 3 to 10% of body mass, but this loss is rarely stabilized in the long term. Moreover, some of these treatments are associated with side effects (nausea, cardiac risk, diarrhea...). Finally, obesity has only recently been considered a serious chronic disease. It is now recognized that obesity is not only a matter of the patient's will, but has a multifactorial origin, including genetics, biology, cultural and socio-economic environment... To accompany the launch of Wegovy<sup>®</sup> (semaglutide 2.4mg) in June 2021, Novo Nordisk has undertaken a strong advocacy work to change the mentalities and the policies of obesity management<sup>57</sup>.

Mechanisms of action include a decrease of the energy intake (via modulation of the food bolus, limitation of nutrients absorption, etc), or an increase in energy expenditure.

Interestingly, many of the hormones involved in weight control are also involved in blood glucose regulation. Amylin, glucagon, GLP-1 receptor agonists, etc., thus play a role both at the peripheral and central nervous system levels.

<sup>52</sup> Press Release - January 10, 2022; The Principal Investigator in Sernova's Type 1 Diabetes (T1D) Trial Confirms Patients with a History of Hypoglycemia Unawareness Are Now Insulin Independent

<sup>53</sup> Key facts about being obese and overweight, WHO, October 2017

<sup>54</sup> NCHS Data Brief, Prevalence of obesity among adults and youth: United States, 2015-2016

<sup>55</sup> The Lancet, Obesity in China, May 24, 2021. [https://doi.org/10.1016/S2213-8587\(21\)00150-9](https://doi.org/10.1016/S2213-8587(21)00150-9)

<sup>56</sup> Mechanisms of Weight Regain following Weight Loss, E. S. Blomain et al., <https://doi.org/10.1155/2013/>

<sup>57</sup> <https://www.itsbiggerthan.com/>

These two pathologies, diabetes and obesity, are thus intimately linked and can be both cause and consequence of each other. In the USA, 65% of adults with type 1 diabetes<sup>58</sup> and 85% of type 2<sup>59</sup> are overweight or obese. Recent studies have shown that a multi-hormonal approach, targeting several metabolic hormone receptors, could increase energy expenditure, promote significant weight loss and improve blood glucose control in obese people<sup>60</sup>. Based on these results, several companies have initiated the development of multi-agonists (e.g. tirzepatide, Eli Lilly's GIP/GLP-1 receptor co-agonist; IBI362, Zealand's Glucagon/GLP-1 receptor co-agonist, etc) or multi-hormonal combinations (e.g. semaglutide-cagrilintide, Novo Nordisk's amylin analog and GLP-1 RA combination).

Adocia, because of its knowledge of metabolic hormones, has naturally extended its formulation expertise to the treatment of obesity.

### 1.2.5.2. Multi-hormonal combination for the treatment of obesity

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Among companies targeting multiple receptors via multi-agonists or multi-hormone combinations, many are seeking to develop weekly formulations, in order to limit the injection burden. However, some of these treatments, including GLP-1 RA in particular, are known to be associated with strong gastrointestinal side effects: nausea, vomiting, diarrhea, pain... Studies have shown that these effects affect treatment adherence, and that 70.1% of diabetic patients taking GLP-1 discontinue their treatment before 2 years<sup>61</sup>. It should be noted that treatment discontinuation often leads patients to return to their original weight, or even gain more weight, due to a metabolic adaptation mechanism. Weekly injections make it impossible for the patient to modulate these effects, which may be felt for several days.

Adocia is therefore proposing a new paradigm in the treatment of obesity by working on combinations of short-acting hormones. Via pump administration, the patient can optimize the dose received at any time and truly personalize his treatment. Initial doses can be finely modulated, and the treatment does not reach concentration peaks as it does with weekly forms. Finally, if patients experience any side effects, they have the option to discontinue them quickly. In contrast to multi-agonist approaches, Adocia's approach using formulations makes it possible to rely on the efficacy and safety profiles of several approved molecules, while promoting the choice of the best ratio between these molecules to optimize the product profile.

Looking for complementary or even synergistic effects, Adocia developed several combinations of key hormones of weight regulation:

- **PramExe:** a combination of the amylin analogue pramlintide and the GLP-1 receptor agonist exenatide
- **BC GluExe:** based on a BioChaperone®, allowing the co-formulation of glucagon and exenatide
- **BC PramGluExe:** based on a BioChaperone®, enabling the triple combination of pramlintide, glucagon and exenatide

Among other effects, it has been previously shown that pramlintide increases satiety and enhances leptin response, exenatide limits food intake while orienting relative preferences towards lower fat and calorie foods, and glucagon signals satiety while increasing energy consumption via activation of brown adipose tissue.

Adocia's objective is to offer an easy-to-use and effective multi-hormonal treatment, with weight loss rates that can exceed 15% or 20%. Through an approach combining "drug and medical device" Adocia can offer the best benefit/risk ratio, thus enabling long-term patient adherence and therefore the best results.

#### ▪ In vitro results and next steps

Promising *in vitro* stability results of PramExe and BioChaperone GluExe have been demonstrated.

<sup>58</sup> Conway et al, Diabetes Med 2010 April; 27(4):398-404. BMI>25, Data for 2004-2007 period

<sup>59</sup> Epidemiology of Obesity and Diabetes and Their Cardiovascular Complications

<sup>60</sup> 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

<sup>61</sup> Real-World Adherence and Discontinuation of Glucagon-Like Peptide-1 Receptor Agonists Therapy in Type 2 Diabetes Mellitus Patients in the United States, Weiss et al. Nov 2020

The pre-clinical proof of concept has been established with BC GluExe on obese mice. After 14 days of treatment, a weight loss of 25% ( $p < 0.001$ ) was observed vs. placebo (vehicle). Adocia's objectives is to test a multi-hormonal combination in human in 2022/2023.

- **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, due to the rapid increase of the obese population and the growing awareness of the benefits of drug-based approaches. The global market was still relatively limited in recent years, with approximately ten approved products, but the appearance of more effective products such as Saxenda<sup>®</sup> and Wegovy<sup>®</sup> is changing the dynamic considerably. In 2020, the market reached \$8.36 billion and is expected to reach \$27.1 billion by 2028, representing a CAGR of 16.7%<sup>62</sup>.

**Saxenda<sup>®</sup>** (liraglutide 3mg, already approved in diabetes as Victoza<sup>®</sup>), a GLP-1 receptor agonist launched by Novo Nordisk in 2015, is administered once daily subcutaneously. Despite its injectable form and its price (~\$15,000 per year in the US), it occupied 79% market share by value of the prescription anti-obesity treatment market in North America in 2020. Saxenda provides a weight loss of 5-10%.

In June 2021, Novo Nordisk is looking to expand its obesity franchise with the launch of **Wegovy<sup>®</sup>** (semaglutide 2.4mg, already approved in diabetes as Ozempic<sup>®</sup>). Intended for a weekly injection, at price parity with Saxenda, Wegovy would allow a weight loss of 17.4% after 68 weeks of treatment<sup>63</sup>. The strong demand encountered at launch time is limited by supply issues experienced by Novo Nordisk. The European launch could be postponed until these problems are resolved. However, the NICE (UK's National Institute for Health and Care Excellence) approved the product on February 8, 2022.

2021 also saw the launch of another product, **Imcivree<sup>®</sup>** (setmelanotide) from Rythm Pharmaceuticals, to treat rare forms of obesity. Following genetic screening, patients with deficiencies in the Pro-Opiomelanocortin (POMC), Proprotein Convertase Subtilisin/Kexin Type 1 (PCSK1), or Leptin Receptor (LEPR) genes can benefit from this injectable treatment, which promises an average weight loss of 10% at one year. With a true "rare disease" approach, setmelanotide has received orphan drug designation and a priority review voucher. Targeting a population of a multiple of 100 worldwide, Rythm Pharmaceuticals has not set up a sales force and offers its treatment at \$290,000-\$300,000 per year in the US.

There are currently 83 products in clinical development to treat obesity, with various approaches in terms of mechanism of action and expected efficacy. This includes the multi-agonistes targeting receptors of GLP-1, glucagon or GIP (Glucose-dependent Insulinotropic Polypeptide).

Among the most anticipated products in development is tirzepatide (Eli Lilly co-agonist GLP-1 and GIP), currently in Phase 3 for obesity. Experts expect a real blockbuster, with applications for NASH (Phase 2), cardiovascular benefits and HFpEF (Heart Failure with preserved Ejection Fraction - Phase 3) and type 2 diabetes (in pre-registration). Six Phase 3 studies are being conducted in parallel for obesity (SURMONT) and weight losses in the order of 11% (15mg - 40 weeks) are expected, based on the SURPASS-1 study conducted in type 2 diabetic patients.

Also expected is cagrilintide (AM833), a long-acting amylin analog developed by Novo Nordisk, either alone or in combination with semaglutide. Currently in Phase 2, cagrilintide could reach the obesity market in 2025 and offer a weight loss of 10.8% (4.5 mg - 20 weeks). Novo Nordisk is also developing its oral form of semaglutide (Phase 3), to be administered to obese patients at a dose of 50mg.

Another company is also betting on pump administration to deliver short-acting hormones, in order to better control side effects and personalize treatment to each patient. San Plena, which was created in December 2021 as a joint venture between Zhipp (a spin-off from Imperial College London) and EoFlow (a Korean company marketing patch pumps), is working on a PYY agonist<sup>64</sup>. A weight loss of 10 to 15% in 2-3 months is expected.

<sup>62</sup> BioSpace, Obesity Treatment Market Size to Reach USD 27.10 Billion in 2028, Jul 01, 2021

<sup>63</sup> « Step-4 » clinical trial, Novo Nordisk

<sup>64</sup> Zhipp and EoFlow Announce Joint Venture for Development of Innovative Solutions for Treatment of Obesity & NASH, Dec 28, 2021

## 1.2.6. The platform for oral delivery of peptides

### 1.2.6.1. Market trends

Peptides and proteins are widely used as drugs, particularly in the treatment of chronic diseases such as diabetes. However, almost all of these drugs exist only in injectable form, which is very restrictive for patients and hinders the adoption of these products, especially in the case of chronic diseases that require numerous and regular injections. One of the main barriers to diabetes treatment intensification is the "injectable" nature of the options currently available. It faces the reluctance of some patients, who also need to be properly trained in the proper injection technique, which can impact the time and resources of healthcare professionals<sup>65</sup>.

Oral forms could thus help overcome delays in treatment intensification, improve patient adherence and compliance, and help them achieve their therapeutic goals.

Analysts agree that the simplification of administration with oral forms (GLP-1, insulin, etc.) will be the main growth driver in the diabetes and obesity market. Thus, major research efforts have been made in recent years to obtain oral formulations of proteins and peptides.

However, the technological challenge is significant because these molecules are naturally degraded in the digestive tract before reaching the bloodstream. Due to this low bioavailability, only five peptides are currently available on the market in oral form. Four are cyclic and of relatively low molecular weight (cyclosporine, 1.2 kDa; voclosporine, 1.2 kDa; octreotide, 1.0 kDa; desmopressin, 1.1 kDa). To date, only one linear peptide has been formulated for the oral route: semaglutide (4.1 kDa).

Novo Nordisk, in reformulating its flagship product Ozempic® (semaglutide weekly injection, 0.25 mg, 0.5 mg, 1 mg) has proposed a real game changer: Rybelsus® (semaglutide, daily oral administration, 3 mg, 7 mg, 14 mg). Using SNAC Eligen technology (developed by Emisphere Technologies), Novo Nordisk has established the ability to produce oral formulations of peptides, protecting them from degradation in the stomach and increasing their absorption. It should be noted that the bioavailability of semaglutide is around 1%, the rest being degraded in the gastrointestinal tract.

In response to this strong market need, Adocia has developed a technology platform based on its formulation expertise to increase the absorption efficiency of peptides in the gastrointestinal tract, which would allow for the transition from injectable to oral forms. Adocia's objective is to obtain a better performance than the established reference.

- **Adocia's preclinical program**

Currently in preclinical development, Adocia's delivery technology optimizes the bioavailability of orally administered peptides. *In vitro*, efficacy has been demonstrated at low concentrations. Applied to semaglutide, *in vivo*, Adocia's formulation has achieved performance similar to that of Rybelsus. Adocia's objective is to test its oral delivery technology in human in 2022.

- **Competition**

Many companies have realized the importance of oral formulations for improving patient compliance and quality of life. These formulations can be a real growth driver for peptides or proteins already offered as injectable forms.

**Novo Nordisk** has reformulated its flagship product Ozempic® (semaglutide weekly injection, 0.25 mg, 0.5 mg, 1 mg) has proposed a real game changer: Rybelsus® (semaglutide, daily oral administration, 3 mg, 7 mg, 14 mg). Approved by the FDA in September 2019 for the treatment of type 2 diabetes, analysts predict it will be the biggest growth in the GLP-1 class. Launched in 29 countries, 2021 sales approached \$765 million. Sales grew 168% (CER) between 2020 and 2021, with demand coming from all regions of the world<sup>66</sup>. Novo Nordisk is also planning to expand its oral semaglutide line, with the initiation in 2021 of Phase 3 programs of Rybelsus® in high doses: at 25 and 50 mg for people with type 2 diabetes, and at 50 mg for people with obesity.

<sup>65</sup> Will oral semaglutide be a game-changer in the management of type 2 diabetes in primary care? Primary Care Diabetes, S. Seidu et al. Feb 2021

<sup>66</sup> Annual Report 2021 Novo Nordisk - CER : Constant Exchange Rate

To gain access to this oral delivery technology, Novo Nordisk paid \$1.35 billion in November 2020 to acquire Emisphere Technologies<sup>67</sup>. This transaction gives Novo Nordisk full ownership of the SNAC Eligen (sodium N-[8-(2-hydroxybenzoyl)amino] caprylate) technology.

Novo Nordisk is also working with MIT (Massachusetts Institute of Technology) and BWH (Brigham and Women's Hospital) on a completely different approach to enable oral delivery of large molecules. The collaboration resulted in the SOMA (Self-Orienting Millimeter-Scale Applicator) robotic pill, licensed exclusively to Novo Nordisk for clinical development. On March 9, 2022, a new agreement was signed extending the collaboration to 2026, expanding the scope to include the creation and integration of bioelectronic devices, biosensors, and stimulus-sensitive delivery devices.

**Oramed** has tackled the challenge of formulating human insulin and exenatide (GLP-1 RA) in oral forms. Based on the POD™ (Protein Oral Delivery) technology, the active proteins are encapsulated in a capsule protecting them from the acidity of the intestine, combined with protease inhibitors to limit enzymatic degradation. The bioavailability of the drug is further enhanced by a permeation enhancer that facilitates the passage of the protein through the intestinal barrier. Their insulin (ORMD-0801) is currently in Phase 3 for type 2 diabetes, and in Phase 2 for type 1 diabetes and NASH. Exenatide (ORMD-0901) is in Phase 1.

**Eli Lilly** is also working on an orally administered GLP-1 RA, with LY3502970 (OWL 833 - licensed from Chugai). It is important to stress that LY3502970 is non-peptidic (GLP-1R NPA – Non Peptidic Agonist). It is currently in Phase 2 for type 2 diabetes patients.

**Entera Bio** addresses osteoporosis (EB613) and hypoparathyroidism (EB612) with oral formulations of PTH 1-34 (parathyroid hormone). The company is also seeking to improve the bioavailability of peptides via an absorption enhancer (SNAC) and protease inhibitors. Both products have completed Phase 2 studies. On January 4, 2022, Entera Bio reported a successful EoP2 (End of Phase 2) meeting with the FDA, opening the possibility of a Phase 3 entry in 2022 for EB613<sup>68</sup>.

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## 1.2.7. Intellectual Property

### 1.2.7.1. 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 2021, the Company refocused its business on the treatment of diabetes and obesity, which is reflected in its patent portfolio. Two new technology platforms were also added, for cell therapy and oral delivery of peptides.

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 35 years' experience in this field. Mr. Olivier Soula, Deputy General Manager and R&D Director has more than 20 years of experience in R&D management, first with Flamel Technologies and then with Adocia.

<sup>67</sup> Novo Nordisk to Acquire Emisphere Technologies for \$1.35 Billion, November 06, 2020

<sup>68</sup> Entera Bio Announces Successful EB613 End-of-Phase 2 Meeting with FDA: FDA Agrees to Phase 3 Twelve Month Study with Lumbar Spine BMD (bone mineral density) as the Primary Endpoint, January 4, 2022

### 1.2.7.2. Procedures for the protection of Intellectual Property

- **IP department and external Industrial Property consultancy**

The Intellectual Property department is under the responsibility of Walter Roger, IP Director and comprises two people at the date of this universal 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.

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 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 in 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).

### 1.2.7.3. 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 submitted in France or via an European patent application (in English). 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.

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## ▪ 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; In this strategy 3, direct filings can be made simultaneously with the filing of the PCT application, in order to obtain protection, in particular in non-PCT member states.

## ▪ 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 patents:

- 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;
- In addition, depending on the evolution of legislation, patent applications relating to specific therapeutic applications, dosages and / or methods of treatment are also filed to supplement the protections.

## ▪ Portfolio

A review of the portfolio is carried out regularly and notably led to the discontinuation of certain patents granted or patent applications which were no longer relevant to ongoing projects.

To date, inventions are protected by patent application filings comprising 39 distinct families. Adocia's portfolio contains more than 250 patents and patent applications belonging to the Company, of which 200 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, 2021:

Territories	Patents	Ongoing patent applications
France	15	5
USA	18	14
Europe (European patent)	6	27
Algeria	0	4
South Africa	0	9
Saudi Arabia	2	7
ARIPO <sup>69</sup>	0	1
Australia	2	3
Bahrein	0	2

<sup>69</sup> ARIPO: African Regional Intellectual Property Organization

## Presentation of Adocia and its activities

Brazil	0	6
Brunei Darussalam	0	2
Cambodia	0	1
Canada	0	7
China	5	14
South Korea	1	6
Egypt	0	2
United Arab Emirates	0	5
Eurasia (Eurasian patent)	1	8
Hong Kong	2	11
India	0	10
Indonesia	0	5
Israel	2	5
Japan	1	6
Kuwait	0	2
Macao	2	2
Malaysia	0	3
Mexico	2	5
New Zealand	0	3
Nigeria	0	1
OAPI <sup>70</sup>	0	1
Uzbekistan	0	2
Pakistan	0	2
Philippines	0	6
Qatar	0	2
Singapore	1	8
Thailand	0	4
Taiwan	0	2
Vietnam	0	2
PCT	NA	7
<b>TOTAL</b>	<b>61</b>	<b>207</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 tens of 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, EP2918804 in Europe, CN104902922 in China and JP6322642 in Japan.

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

<sup>70</sup> OAPI: African Intellectual Property Organization

The project for the combination of basal insulin, notably glargine insulin, and prandial insulin, comprises around 15 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 insulin 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.

We may also mention the applications WO12019110773, WO2019110774.

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. The applications WO2019110837 et WO2019110836 concern also the glucagon.

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 applications WO2018122278, WO2019110788 et WO2019110797.

Adocia has also developed a formulation including a combination of prandial insulin and glucagon suppressor with prandial effect. This works was the subject of application WO2019020820, which led to patent applications in many countries and regions, including Europe, the United States, China, Japan and India. It should be noted that a US patent has already been issued (US10610572B2).

In addition, Adocia is developing products to treat metabolic diseases and in particular obesity. Various families have been filed, including WO2021152184 relating to the combination of an amylin receptor agonist and a GLP-1 receptor agonist.

In early 2021, the Company filed an application related to cell therapy, a new area of research.

In 2020 and 2021, Adocia has also filed applications for combinations of different APIs that could yield very interesting results in terms of patients' treatment. However, these applications are not yet published.

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

## 1.2.8. Major Contracts

Significant contracts for the Company, other than those entered into in the ordinary course of business, are as follows:

### 1.2.8.1. 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.

### 1.2.8.2. 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.

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.

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### 1.2.8.3. 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's press release of January 27, 2017 available on the Company website).

- **Licenses granted by Adocia to Tonghua Dongbao Pharmaceuticals Co. Ltd**

On April 26, 2018, Adocia and Tonghua Dongbao Pharmaceuticals Co. Ltd Pharmaceuticals announced 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 insulin lispro 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, 350/50 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.

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#### 1.2.8.4. 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 concerned some \$11 million and other specific compensation for changes made to the development plan during the collaboration. The arbitration court found in favor of Adocia in the first phase of arbitration against Eli Lilly in August 2018 and Adocia announced via a press release the same month that the company would 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 was seeking monetary damages in excess of \$1.3 billion (before taking into account the interests pre- and post-judgment) as well as others specific relief. In the second phase of this arbitration, Lilly filed counterclaims against Adocia seeking approximately 188 million including prejudgment interest. These counterclaims were based on an allegation that Adocia concealed its discoveries and confidential information which were at issue in Adocia's claims. Adocia denied Lilly's claims.

In August 2019, the American Arbitration Association Panel rejected the additional claims submitted by Adocia as well as the counterclaims of Eli Lilly.

On September 30, 2019, Adocia announced receipt of the payment of USD 14.3 million corresponds to the USD 11.6 million in damages plus interest awarded to Adocia in August 2018 by an American Arbitration Association Panel presiding over Adocia's arbitration claims against Eli Lilly as compensation of a contractual milestone payment disputed by Lilly.

The arbitration procedure is now finalized.

- **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 9, 2018. Lilly's complaint sought 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 on February 27, 2018. US Patent No. 9,993,555 is entitled "Rapid-acting insulin

compositions” and was issued on June 12, 2018. Lilly contended in its complaint that it filed the action because Adocia had asserted that Lilly’s patents reflected Adocia’s inventive contributions.

In September 2019, Adocia and Eli Lilly agreed together to file a consent judgment to conclude the civil litigation initiated by Eli Lilly at the Court of the Southern District of Indiana in October 2018. The consent judgement was registered by the Court of the Southern District of Indiana in October 2019 and concluded this litigation. Each party will cover its own legal fees and associated costs, without any further financial consequence.

Consequently, the litigation in the Court of the Southern District of Indiana is now fully concluded.

### 1.2.8.5. Insulin supply agreements

Adocia and Tonghua Dongbao Pharmaceuticals Co. Ltd announced on June 1<sup>st</sup>, 2018 an expansion of their strategic alliance 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 already commercializes human insulin products in China and in other markets, Tonghua Dongbao Pharmaceuticals Co. Ltd develops in parallel several insulin analogs. Notably, its insulin glargine was approved in China at the end of 2019, 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.

### 1.2.8.6. Bond loan concluded with IPF Fund II

On October 11, 2019, the Company signed a bond financial line with IPF Fund II to finance its growth.

This financing line consists in a bond issue, structured in two tranches of equal amounts, of a total number of 15 million euros of bonds (“Bonds”) to each of which is attached a warrant (the “BSA”), hereinafter collectively referred to as the “OBSA”, for a maximum amount of principal loan of 15 million euros.

The Bonds were issued in two tranches, each for a principal amount of 7,500,000 euros (the « Tranche A » and “the Tranche B” and together the “Issue” entirely reserved for IPF Fund II SCA, SICAV FIAR (hereinafter referred to as “IPF Fund II”).

The first tranche (Tranche A), amounting to 7.5 million euros, was subscribed on October 11, 2019, at the signing of the contract. The second tranche (Tranche B) was subscribed on December 10, 2019.

In return for this loan, the Company issued BSA giving right to Adocia’s shares (1 Bond = 1 BSA) with characteristics detailed below.

In addition, the Company granted IPF Fund II a pledge on part of its assets (bank accounts, securities accounts, trade receivables, stock) as well as a pledge of certain key Adocia patents (« *Core IP* »).

▪ **The terms and conditions of the Bonds are as follows:**

- Nominal Amount of the bond issue: EUR 15,000,000 in two tranches: Tranche A: EUR 7,500,000; Tranche B: EUR 7,500,000.
- Initial par value: 1 euro per Bond.
- Issue date: Tranche A: October 11, 2019 and Tranche B: December 10, 2019.
- Maturity: the twentieth quarter falling after the issue date of each tranche.
- Interest: EURIBOR + 8% (Cash margin) +3% (PIK margin).
- First redemption of the capital deferred for a 12-month period, then the reimbursement will be of 10%, then 20%, finally 30% and at last 40% the last year.

- Early redemption possible at any time, subject to early redemption fee, for an amount of 8% if the exit occurs during the first year, 7% in the course of the second year and finally 6% the third year.
- Security: customary security interests granted to the benefit of the bondholders' body (pledge of the bank accounts and securities accounts, pledge of the trade receivables, pledge of the stock, and pledge of Adocia's key patents registered in France, in Europe, in the United States and in China).
- Assignment: the bonds can be freely assigned to any fund or financial institution, to the exclusion of any competitor of the Company or any fund managing or having invested in a competitor of the Company.

- **The main terms and conditions of the warrants are as follows:**

- Number of warrants: 15,000,000, i.e. 7,500,000 under Tranche A and 7,500,000 under Tranche B, creating the right for each tranche to subscribe to a number of ordinary shares of the Company equals to 15% of the amount drawn, i.e. an amount of 1,125,000 euros each tranche, divided by the share strike price.
- Exercise price: 8.57 euros, it being specified that, in the event the Company issues new shares (excluding employee and manager incentive scheme) at a lower price during the warrants' exercise period, the IPF warrants exercise price shall be reduced to 95% of the lower of the said issue prices, it being specified that the issue price cannot be lower than 80% of the average of weighted average market price over the three stock market sessions preceding a new share issue.
- Number of shares that may be issued upon exercise of the warrants: in respect of each tranche, 131,271 ordinary shares representing 1.89% of the Company's share capital as of the date of the contract signature, i.e. on October, 2019, in respect of each tranche<sup>71</sup>.
- Exercise period: in whole or in part, for a minimum aggregate exercise price of 100,000 euros, once or several times, at any time from their issue date until October 10, 2026.
- Listing of the warrants: the warrants shall not be listed but can be detached from the OBSAs at any time and, from that date, freely assigned under the same conditions as the Bonds.

- **Granted security**

The Company consented a pledge on certain of its assets in order to secure the repayment of the bonds issued by the Company, in particular:

- a pledge on French law of the bank accounts and share accounts of the Company;
- a pledge of the key IP rights (Core IP) of the Company registered in France, in Europe, in the USA and in China insured by the conclusion of a patents deed of pledge on French law, a deed of pledge on New York State law and a pledge deed on Chinese Law on the following families of patents :
  - Insulin FAST (BC lispro and HinsBet): WO2014076423
  - Combination of basal insulin, notably glargine insulin, and prandial insulin: WO2019110773
  - Combination of prandial insulin and suppressor of glucagon with prandial effect: WO2019020820
- a pledge of the trade receivables of the Company evidenced in the form of a deed of pledge of receivables on French law;

Being specified that the implementation of additional security could in the future be required by IPF Fund II, in particular on stock/inventory with a value greater than 250,000 euros and intellectual property rights developed or acquired in the future.

This security may be implemented by IPF Fund II in the event of default of payment by the Company or at the request of IPF Fund II in the event of any event of default stipulated in the issued contract. The implementation of this security would result in the judicial allocation, the forced sale or, as the case may be, the transfer of ownership of the pledged asset to the benefit of IPF Fund II.

<sup>71</sup> Excluded adjustment of the price of the BSA as detailed above

### ▪ Commitment made

Under the terms of the loan obtained, the Company notably made a commitment to comply with the following obligations :

- no contract of new debt (beyond a threshold by type of debt and an overall ceiling of 6.5 million euros in debt),
- no grant of new security or guarantee,
- have an amount of cash to cover 6 months of operating cash flow including debt service (cash covenant),
- no change in activity substantially,
- no sell of assets other than in the ordinary course of business, to acquire or create joint ventures without the prior consent of IPF Fund II,
- respect all legal and regulatory obligations that are applicable to the Company.

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Failure to comply with these commitments, to which it would not be remedied within 10 working days of the occurrence or of their notification by IPF Fund II (or immediately with regard to non-compliance with the cash covenant) could lead IPF Fund II to declare the early payment of the lease and to proceed with the implementation of the security described above.

### ▪ July 2020 debt restructuring

In July 2020, in a context marked by the Covid-19 pandemic, the Company obtained a restructuring of the debt with a new payment deferral of additional 12 months, the final maturity dates of the two tranches remaining unchanged.

In return for this arrangement, the Board of Directors of the Company allocated a total number of 35,005 share subscription warrants (BSA) free of charge to the IPF Fund II SCA SICAV FIAR, under terms and conditions similar to the warrants allocated to IPF Fund II SCA SICAV FIAR under the main contract, with an exercise price of the warrants of 7.70 euros. The number of BSA issued corresponds to 15% of the deferred capital, that being 300,000 euros. Excluding any adjustment of the exercise price, the number of shares that may be issued on the date of signature of the amendment in July 2020 was 38,961, that being approximately 0.5% of the Company's capital.

Furthermore, the Company agreed to modify the cash covenant from 6 to 7 months of Operating Cash Flow with a commitment to maintain a minimum cash position of \$16 (sixteen) million.

As of December 31, 2020, the Company was in compliance with the commitments described above.

### ▪ Restructuring of covenants in September 2021 and following the sale and leaseback agreement in March 2022

At the end of August 2021, the Company obtained a temporary adjustment of its cash covenants pending (i) the completion of additional financing planned for October 31, 2021 at the latest and (ii) the sale of the building scheduled for March 31, 2022 at the latest.

In this context, the minimum amount of cash required to be available has been temporarily reduced to 10 million euros, with a 1% increase in interest rates (cash margin and PIK margin) over the relevant period.

IPF authorizes the Company to sell its real estate assets but asks in return for the possibility of allocating part of the sale price to the early repayment of its loan, up to a maximum of 2 million euros as of August 31, 2022.

## 1.2.8.7. State-Guaranteed Loan (PGE) Contracts

In August 2020, Adocia was granted a loan of €7 million from BNP, HSBC, LCL and Bpifrance Banks, in the form of a State-Guaranteed Loan (PGE).

These loans are guaranteed by the French State up to 90% of the amounts due and are not subject to any payment during the first year. At the end of the first year, the repayment of the principal may again be deferred and amortized over a maximum period of 5 years, at the option of the Company. These loans will carry annual fixed interest rates of between 0.25% and 1.75% for the first year.



### 1.2.8.8. Issuance of convertible bonds at a variable price

On October 26, 2021, the Company issued 6,568,422 convertible bonds into shares with a par value of one euro each for a total amount of 6 million euros net subscribed by Vester Finance and two other European investors.

These convertible bonds were issued at a price equal to 95% of their nominal value. The convertible bonds will not bear interest and may be converted into ordinary shares at the request of the holder, at any time and at a subscription price per share (the "Conversion Price") equal to the lower of (i) 11.87 euros and (ii) 93% of the lower of the daily VWAPs (volume-weighted average share price) over a period of 15 days preceding each conversion request, without this price being lower than the limit set by the General Meeting of Shareholders of the Company on May 20, 2021, i.e. 80% of the volume-weighted average price of the last three trading sessions preceding the conversion request.

The convertible bonds may also be converted or redeemed (in cash or in convertible bonds) at the request of the holder in the event of an event of default.

The convertible bonds have an initial maturity of 24 months, extendable under certain conditions. In the event that the convertible bonds have not been fully converted and/or redeemed at maturity, they will be fully repaid by the Company at 100% of their nominal value.

As of December 31, 2021, a portion of these bonds had been converted (970,000 bonds, i.e. 14.77% of the total amount issued), giving rise to the issue of 123,960 shares.

Please refer to section 4.3.3.7 of this Registration Document for more information on these bonds.

The impact on debt and equity is presented in more detail in note 10 of chapter 4 of the consolidated financial statements.

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### 1.2.8.9. 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 totalling 800,000 euros 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 euros 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 euros 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 fulfil its obligations, OSEO would have a right to demand the repayment of the advance granted.

In 2015, the Company noted the end of the program and proceeded with the reimbursements provided in the event of commercial failure of the program in 2017 and in 2018. An expertise commissioned by BpiFrance is planned for the year 2020 and should make it possible to close this file in the coming months.

## 1.3 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, 2021 and December 31, 2020, 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.

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### 1.3.1. Main activities during the year

2021 was marked by major advances in our insulin portfolio and by the achievement of important proofs of concept on new technological platforms in cell therapy and oral delivery of peptides. In addition, the financial operation carried out in the last quarter strengthened the resources available to support the company's growth.

#### Significant progress made on mature projects in our pipeline:

- BioChaperone® Lispro: approved to enter Phase 3 in China

In October 2021, Tonghua Dongbao received approval from the CDE (Center for Drug Evaluation) to start the Phase 3 program of BC Lispro ultra-fast insulin for the treatment of type 1 and type 2 diabetes in China. The operational start of Phase 3 in China should trigger a milestone payment to Adocia, expected in the second quarter of 2022. In parallel, the preparatory work for the Phase 3 studies in the United States and Europe has successfully been completed. Our commercial activities are aimed at finding a partner capable of financing the pivotal program until marketing authorization is obtained in these regions.

- M1Pram and BioChaperone® LisPram: intensified clinical development efforts

Adocia has intensified the clinical development of its two product candidates, M1Pram and BC LisPram, positioned respectively for the auto-injector pen and pump markets. These fixed combinations of insulin and amylin analogs are expected to provide an improvement in medical service, as compared to rapid insulins administered alone, through weight loss in obese or overweight diabetic patients. These rapid insulins are essential to the survival of many patients and generate more than \$9 billion in revenue each year. These combinations are intended to improve glycemic control whilst generating weight loss in overweight or obese diabetic patients. In the United States, 65% of type 1 diabetic patients and 85% of type 2 diabetic patients are overweight or obese<sup>72,73</sup>.

A Phase 2 study (CT041) was initiated in March 2021 with M1Pram as an auto-injector pen. This comes after the establishment of proof of concept in humans in a study from 2020 that demonstrated improved glycemic control and very significant weight loss, as compared to the reference rapid insulin aspart, in just 3 weeks of treatment. The CT041 study, which aims to confirm these results over a 4-month period in type 1 diabetic patients, has been designed to define all of the parameters of a future Phase 3 program. The results will be communicated in the second quarter of 2022.

Concurrently, a proof-of-concept study in humans has been initiated with BC LisPram. This combination has been specifically designed for automated pump administration using an algorithm. This study is being conducted in collaboration with Dr. Ahmad Haidar of McGill University (Canada) and results are expected in Q3 2022.

<sup>72</sup> Conway et al, *Diabetes Med* 2010 April; 27(4):398-404. BMI>25, Data for 2004-2007 period

<sup>73</sup> *Epidemiology of Obesity and Diabetes and Their Cardiovascular Complications*

## New proprietary technology platforms in new growth markets

- Revolutionizing islet transplantation (AdoShell® technology)

In January 2021, Adocia announced the filing of patents on a hydrogel matrix designed to improve islet transplantation cell therapy techniques. The function of this matrix is to maintain transplanted cells' secretory activity, while protecting them from the immune system. Adocia's objective is to create an organoid capable of secreting insulin in response to glycemic variations, thus avoiding the use of immunosuppressive drugs. An academic collaboration has been established with several teams, including Inserm with Professor François Pattou, a world specialist in islet transplantation. Animal trials are underway, prior to human implantation trials.

- Combining hormones to treat obesity

In 2021, Adocia also initiated new projects in the field of obesity. Patient management is undergoing major changes, due, on the one hand, to gradual recognition of obesity as a pandemic requiring drug treatment, and, on the other hand, to the discovery of the efficacy of certain hormones - which are also involved in diabetes - in controlling weight. These treatments make it possible to avoid recourse to bariatric surgery. These products are intended to be administered in pump so that the patient can set up, with the support of a doctor, a personalized treatment adapted to lifestyle. Patents have been filed by Adocia on these pump-administered hormone combinations. The objective is to prepare a proof-of-concept study in humans by 2022/2023. These hormonal combinations could also be developed in other medical indications such as NASH (Non-Alcoholic Steatohepatitis) and type 2 diabetes.

- Delivering peptides in oral form that were previously administered by injection (AdOral® technology)

Adocia has developed a technology that can enable oral delivery of peptides by limiting their natural degradation in the digestive tract before reaching the bloodstream. Initial results obtained in preclinical studies have shown an increase in the absorption efficiency of peptides by the gastrointestinal tract, which would allow for a switch from injectable to oral forms.

This new technological platform opens up numerous applications for oral forms of molecules intended, in particular, for the treatment of diabetes and obesity.

### The company's cash position was strengthened in October 2021 by a financing transaction and in March 2022 by a real estate transaction:

- The financing transaction carried out in October was for 7 million euros

In October 2021, the Company carried out a financing transaction through (i) the issue of 6,568,422 bonds convertible into shares with a par value of one euro each for a total amount of 6 million Euros net subscribed by Vester Finance and two other European investors and (ii) a capital increase of 1 million Euros, the subscription of which was reserved for the benefit of Gérard Soula, the Company's Chairman and CEO and a shareholder, by way of the issue of new ordinary shares.

- Governance reinforcement

In June 2021, Adocia strengthened its Board of Directors with the appointment of three new independent members: Dr. Claudia Mitchell, Senior Vice President in charge of Portfolio Strategy at Astellas Pharma; Dr. Katherine Bowdish, President and CEO of PIC Therapeutics; and Stéphane Boissel, CEO of SparingVision

## 1.3.2. Presentation of the financial statements

### 1.3.2.1. General information

The Company's principal activity is research and development of innovative formulations of pre-approved therapeutic proteins. It has in particular 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.

### 1.3.2.2. 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 have not been met and the Company therefore does not capitalize its development costs.

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### 1.3.3. Financial position and appropriation of profit

#### 1.3.3.1. Components of income

The following table summarizes the Company's income statement under IFRS for the fiscal year ended December 31<sup>st</sup>, 2021, and provides a comparison with fiscal year 2020.

<i>In (€) thousands</i>	<b>FY 2021 (12 months)</b>	<b>FY 2020 (12 months)</b>
<b>Revenue (a)</b>	<b>1 444</b>	<b>841</b>
Research and collaborative agreements	983	0
Licensing revenues	461	841
<b>Other revenue (b)</b>	<b>4 611</b>	<b>5 992</b>
Research tax credit	4 611	5 992
Grants, public financing, others	0	0
<b>Operating revenue (a) + (b)</b>	<b>6 055</b>	<b>6 833</b>
Research and development expenses	(20 016)	(22 547)
General and administrative expenses	(5 404)	(5 434)
<b>Operating expenses</b>	<b>(25 421)</b>	<b>(27 981)</b>
<b>OPERATING INCOME (LOSS)</b>	<b>(19 366)</b>	<b>(21 148)</b>
<b>FINANCIAL INCOME (LOSS)</b>	<b>(3 388)</b>	<b>(2 147)</b>
<b>EXCEPTIONAL INCOME (PROFIT)</b>	<b>0</b>	<b>0</b>
Tax	0	(29)
<b>NET INCOME (LOSS)</b>	<b>(22 754)</b>	<b>(23 324)</b>
Base earning per share (€)	(3,2)	(3,3)
Diluted earning per share (€)	(3,2)	(3,3)
<b>GROUP NET PROFIT (LOSS)</b>	<b>(22 754)</b>	<b>(23 324)</b>

- **Operating income**

The Company's operating income resulted from collaboration and licensing agreements and public funding of research costs. In 2021, operating income amounted €6 million compared to €6.8 million in 2020, based on the following breakdown:

<i>In (€) thousands</i>	<b>FY 2021 (12 months)</b>	<b>FY 2020 (12 months)</b>
<b>Revenue (a)</b>	<b>1 444</b>	<b>841</b>
Research and collaborative agreements	983	0
Licencing revenues	461	841
<b>Grants, public financing, others (b)</b>	<b>4 611</b>	<b>5 992</b>
<b>OPERATING REVENUE (a) + (b)</b>	<b>6 055</b>	<b>6 833</b>

In 2020, revenue resulted in €0.7 million from the initial upfront payment of \$50 million (€41.1 million) in April 2018 at the signature of the two partnership and licensing agreement with Tonghua Dongbao. These revenues related to R&D services provided by Adocia to Tonghua Dongbao, are recognized based on progress, in accordance with IFRS 15, by comparison between the costs incurred by Adocia and the total budget estimated to date over the term of the contract. The Company had also rebilled Tonghua Dongbao a PK/PD study for the 2020 financial year that amounted to €0.1 million.

As of December 31, 2021, the turnover of €1.4 million comes mainly from:

- the licensing agreements signed in April 2018 with the company Tonghua Dongbao Pharmaceuticals for an amount of €0.4 million
- the rebilling of Tonghua Dongbao for additional services provided at the request of the partner for the 2021 financial year, particularly for the BC Combo project. These services amounted to close to €1 million.

The portion of the initial payment yet to be recognized as revenue, as of December 31, 2021, amounts to € 0.7 million and is recognized as deferred income.

Other operating income mainly consists of the Research Tax Credit which amounted to €4.6 million as of December 31, 2021 compared to €6 million as of December 31, 2020.

#### ▪ Operating expenses

The table below shows a breakdown of operating expenses by function for the fiscal years ended December 31<sup>st</sup>, 2021 and December 31<sup>st</sup>, 2020:

<i>In (€) thousands</i>	<b>FY 2021 (12 months)</b>	<b>FY 2020 (12 months)</b>
Research and development expenses	(20 016)	(22 547)
General and administrative expenses	(5 404)	(5 434)
<b>OPERATING EXPENSES</b>	<b>(25 421)</b>	<b>(27 981)</b>

Research and development expenses mainly consisted of the 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), and pharmaceutical products and other raw materials. In 2021, these expenses amounted to €20 million versus €22.5 million in 2020.

The activities in the 2021 financial year focused on the development of the Company's portfolio, especially the new projects in the diabetes and obesity field (Cell Therapy, Oral Delivery and Obesity) and the clinical development of the M1 PRAM (ADO09) project, combination of insulin prandial and pramlintide (insulin analog).

General and administrative expenses mainly included 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.

General expenses amounted to €5.4 million in 2021 and are stable compared to 2020.

Research and Development expenses represented almost 79% of the operating expenses in 2021 compared to 80% in 2020.

The table below shows a breakdown of operating expenses by type of expense for the fiscal years ended December 31<sup>st</sup>, 2021, and December 31<sup>st</sup>, 2020:

<i>In (€) thousands</i>	<b>FY 2021 (12 months)</b>	<b>FY 2020 (12 months)</b>
Purchases used in operations	(1 264)	(1 457)
Payroll expense	(11 434)	(11 857)
Share-based payments	(197)	(267)
External expenses	(11 102)	(13 010)
Taxes and contributions	(265)	(257)
Depreciation, amortization & provisions	(1 158)	(1 133)
<b>OPERATING EXPENSES</b>	<b>(25 421)</b>	<b>(27 981)</b>

The cost of consumed materials, products and supplies decreased by €0.2 million between 2020 and 2021, totaling €1.3 million.

**Payroll expenses** totaled €11.4 million in 2021 compared to €11.9 million in 2020, i.e., a decrease of €0.5 million. The decrease is mostly due to the decrease in staff from 133 Full Time Equivalents (FTE) in 2020 to 122 FTE as of December 31, 2021.

**The share-based payments** line of €0.2 million in 2021 reflects the impact of the plans implemented in previous years. 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 nor cash position.

**External charges** include the costs of preclinical studies, clinical trials, subcontracting expenses, intellectual property costs, professional fees, and general expenses. These expenses amounted to €11 million as of December 31, 2021, a decrease of €1.9 million compared to 2020. The €1.9 million variation is mostly due to the decrease in R&D external expenses related to reduced activity in preclinical and clinical studies.

**Taxes totaled** €0.3 million in 2021 at a stable level compared to 2020.

**Depreciation and amortization totaled** €1.2 million as of December 31, 2021, compared to €1.1 million in 2020.

- **Net financial income/expense**

<i>In (€) thousands</i>	<b>FY 2021 (12 months)</b>	<b>FY 2020 (12 months)</b>
<b>Cost of net financial debt</b>	<b>(3 553)</b>	<b>(1 852)</b>
Cash and cash equivalents income	1	(14)
Interest on conditional advances	(2 249)	(2 052)
Fair value revaluation of OCA 1023	(1 078)	0
Fair value revaluation of IPF's share subscription warrants	(227)	214
<b>Foreign exchange gains and losses</b>	<b>176</b>	<b>(304)</b>
<b>Other financial income and expenses</b>	<b>(11)</b>	<b>10</b>
<b>FINANCIAL INCOME (LOSS)</b>	<b>(3 388)</b>	<b>(2 147)</b>

The negative net financial income amounted €3.4 million as of December 31, 2021, due to the following:

- Interest generated on the bond issue with IPF Fund II in October 2019 (€2.1 million),
- Impact, with no consequence on the Company's cash position, of the fair value measurement of the OCA 123 (see paragraph 4.1.5.2 about the implementation of IFRS 9 and IAS 32 on accounting for the bond issue OCA 123),
- Impact, also with no consequence on the Company's cash position of the revaluation of €0.2 million of the fair value of the warrants granted to IPF Fund II (see paragraph 4.1.5.2 about the implementation of IAS 32 on accounting for the IPF bond issue),,
- Exchange rate gain (€0.2 million).

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

#### ▪ Corporation tax

The carryforward tax losses, after allocation of the fiscal deficit subject to the standard tax rate for the 2021 financial year, was €190.7 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

	FY 2021 (12 months)	FY 2020 (12 months)
<b>CONSOLIDATED NET PROFIT / LOSS (in euros thousands)</b>	(22 754)	(23 324)
Average number of shares	7 057 600	6 973 639
<b>NET EARNINGS (LOSS) PER SHARE (in euros)</b>	(3,2)	(3,3)
<b>NET EARNINGS (LOSS) PER SHARE FULLY DILUTED (in euros)</b>	(3,2)	(3,3)

The net loss for 2021 amounts to € 22.8 million, compared to a net loss of €23.3 million in 2020. The net loss per share thus amounts to €3.2 compared to a net loss of €3.3 per share in 2020.

### 1.3.3.2. Balance sheet analysis

#### ▪ Non-current assets

Non-current assets (not including the impact of IFRS 5) amounted to €8 million at the end of 2021, compared with €8.7 million in 2020. Indeed, fixed assets (in net value) decreased by €0.7 million between 2020 and 2021. This decrease reflects the amortization of fixed assets for the period that is partly compensated by some investments made during the year 2021.

In compliance with IFRS 5, €6.9 million of net assets have been reclassified in a separate sub-heading after other current elements (see paragraph 4.1.5.3 – note 2 about the implementation of IFRS 5 for the accounting of Assets and Liabilities classified as held for the purpose of the sale).

#### ▪ Current assets

Current assets amounted to €22.1 million on December 31st, 2021 compared to €52.2 million on December 31st, 2020, consisting of the following items:

- "Cash and cash equivalents" decreased from €28.1 million as of December 31st, 2020 to €15.2 million as of December 31st, 2021. The net cash consumption for the 2021 financial year amounts to €19.9 million and is below the one of the previous year (€22.5 million) on a comparable basis (not including financing operation).

- Other current assets amounted to €6.2 million as of December 31st, 2021, and consisted in particular in the receivable related to the research tax credit (CIR) of €4.6 million. As of December 31st, 2020, this item amounted to €7.8 million, of which €6 million related to CIR.

- **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 amount to €3.8 million compared to €4.9 million at the end of December 2020. The change in this item (-€1.1 million) reflects the decrease in R&D activities (external expenses) over the period.
- "Financial debt" totaling €34.5 million as of the end of December 2021, increasing by €6.3 million compared to the previous year. Net financial debts (excluding the impact of derivative instruments) amounted to €33.3 million at the end of December 2021 compared to 27.3 at the end of December 2020. The €6 million increase mainly comes from the convertible bond financing operation done in October 2021 that resulted in a net receipt of €6 million. A part of these bonds was converted at the end of December, the balance being recorded as liabilities according to IFRS 9 and IAS 32 standards.
- "Long-term provisions" mainly comprise provisions of retirement benefits, which totaled €1.4 million for fiscal year 2021 versus €2.2 million for fiscal year 2020.
- "Other liabilities" for 2021 included tax and social security liabilities which amounted to €3.3 million. The increase of this item compared to 2020 (+€1 million) is mostly related to the provisioned bonuses for the 2021 financial year. As of December 31, 2021, other liabilities also included €0.7 million, versus €1.1 million in 2020, in deferred revenue related to the agreements signed with Tonghua Dongbao Pharmaceuticals Co. Ltd, in April 2018.

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### 1.3.4. 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, 2020, and December 31, 2021, which are presented in section 4.1.6 and Chapter 5 of this universal registration document.

#### 1.3.4.1. Debt financing

Thanks to its research activities, the Company has benefited from reimbursable grants from BpiFrance and COFACE, without bearing any interest, for a total amount of €4.1 million.

As of December 31st, 2021, the outstanding amount of the loans receives from BpiFrance were €0.5 million and relates solely to the repayable advance of €0.8 million received in 2012 for the development of a formulation of fast-acting "human" insulin and the Phase 2a clinical study. In 2015, the Company noted the end of the program and proceeded with the reimbursements provided in the event of commercial failure of the program in 2017 and 2018. An expertise commissioned by BpiFrance was realized in 2020 and should make it possible to close this dossier in the coming months. Details of this repayable advance can be found in chapter 1.3.7 of the present universal registration document.

In addition, the Company uses other financial liabilities to finance the acquisition of lab equipment and materials. Future obligations under these leasing contracts amounted to €0.1 million as of December 31st, 2021.

Bank loans were contracted in 2016 for €5.5 million to finance the purchase of the building where the research center and headquarters of the Company are located. Additional funding of €0.3 million was released in 2017. Between March and May 2019, the Company contracted a loan of €1.2 million to finance the renovation of two 450 m<sup>2</sup> areas for the Analytical department, one for offices, the other for laboratories. These loans have been entirely paid off as part of the building sale in March 2022 (see chapter 4 of the present document). As of December 31, 2021, the loans have been reclassified as short-term financial liabilities on the balance sheet for a total amount of €4.4 million.

In 2019, the Company subscribed to a bond issue, with warrants, for a total of €15 million from IPF Fund II, through two tranches of €7.5 million each, on October 11th, 2019, and December 10th, 2019. This contract is detailed in paragraph 1.3.7.5 of the present universal registration document.



In July 2020, in a Covid-19 pandemic context, the Company obtained a restructuring of the debt with a new payment deferral of another 12 months, the final maturity dates of the two tranches remaining unchanged.

In return for this arrangement, the Board of Directors of the Company allocated to the IPF Fund II SCA SICAV FIAR a total number of 35,005 share subscription warrants (BSA), under terms and conditions similar to those warrants allocated to IPF Fund II SCA SICAV FIAR under the main contract, with an exercise price of the warrants of €7.70.

In August 2020, Adocia was granted a loan of €7 million from BNP, HSBC, LCL and BpiFrance Banks, in the form of a State -Guaranteed Loan (PGE). These loans are not subject to any payment during the first year. In June 2021, the Company chose to defer repayments for another year, the first capital repayments being due in August 2022 with an unchanged maturity in August 2026.

A bond issue was contracted in **October 2021**. On October 26, 2021, the Company proceeded with the issuance of 6,568,422 bonds convertible into shares of a nominal value of one euro each (the "OC") for a total net amount of €6 million subscribed by Vester Finance and two other European investors. The OC were issued at a price equal to 95% of their nominal value. The OC will not bear interest and may be converted into common shares at the request of the holders at any time and at a variable subscription price per share ("the **Conversion Price**") defined by contract.

As at 31 December 2021, part of these bonds had been converted (970,000 bonds or 14.77% of the total amount issued) and resulted in the issue of 123,960 shares. The valuation of these OCA, at the date of subscription and closing of the accounts, was entrusted to an independent actuary. Based on this approach, the fair value of the OCAs is € 7.5 million as at 26 October 2021 and € 6.3 million as at 31 December 2021.

As of December 31st, 2021, financial debt amounted to €34.5 million, with a less than a year component of €16.2 million.

### 1.3.4.2. Cash flows

<i>In (€) thousands, Consolidated financial statements, IAS/IFRS</i>	<b>FY 2021 (12 months)</b>	<b>FY 2020 (12 months)</b>
Net cash flow generated by operating activities	(19 234)	(21 854)
Net cash flow in connection with investment transactions	(361)	(204)
Net cash flow in connection with financing transactions	6 644	6 512
<b>Changes in net cash</b>	<b>(12 951)</b>	<b>(15 547)</b>
Cash and cash equivalents at the start of the year	28 114	43 661
Cash and cash equivalents at year-end	15 163	28 114

- **Net cash flow from operations**

For fiscal year 2021, net cash outflows related to operations amounted to €19.2 million compared to a net cash outflow of €21.9 million in the previous year. This change mainly reflects a slightly lower level of expenses than the previous year, mostly related to the decrease in R&D activities (external expenses) over the period.

- **Net cash flow from investments**

Cash used in investing activities amounted to €0.4 million, compared to 0.2 million euros last year. This change reflects the few investments made over the year 2021.

- **Net cash flow from financing transactions**

In 2021, cash consumption related to financing transactions is mainly due to the subscription of the bond issue (OCA 1023) for an amount of €6 million. Adocia has indeed done a €7 million financing in October 2021 including, on the one hand, a convertible bond issue subscribed to by European investors for a total net amount of €6 million and, on the other hand, an increase in capital of €1 million subscribed by Gérard Soula, co-founder of Adocia.

In 2020, cash consumption related to financing transactions was mainly due to the subscription of PGE loans for an amount of €7 million.

### 1.3.4.3. Funding sources needed in the future

In order to meet the financial commitments made to its lenders (see 4.1.5.4 §.10 financial liabilities) and given (i) the cash position of €15.2 million at 31 December 2021, (ii) the receipt of €19 million in March 2022 related to the sale of the headquarters (iii) the expected receipt in the second quarter of 2022 of the milestone payment from Tonghua Dongbao following the start of phase 3 of the BC Lispro and (iv) the forecasts made, the company will have to conclude a partnership agreement or a capital raising operation during the fourth quarter of 2022.

Management is confident that it will be able to obtain new sources of financing or, failing that, obtain a new temporary arrangement of its financial ratios to be respected in the context of the loans granted to the company.

### 1.3.5. Foreseeable developments, future prospects and significant events after the end of the fiscal year

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#### 1.3.5.1. Trend information

See section 1.2 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.

#### 1.3.5.2. Profit forecasts and estimates

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

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

After a year marked by a global health crisis, the Company's research and development activities have gradually returned to a normal level, with a work organization that integrates more telecommuting. Nevertheless, containment measures and travel constraints continued to disrupt the search for partnerships. The main risk factors of this epidemic have been identified and detailed in section 1.4.1.3 of this Universal Registration Document. The materialization of these risks could have a downward impact on the level of the Company's forecasted expenses, as well as on the expected revenues from collaborations, which is difficult to quantify with precision at the date of this document.

## 1.4 Risk factors

The Group operates in a changing environment involving risks, some of which are beyond its control. Investors are invited to take into consideration all of the information contained in this universal registration document, including the risk factors described in this chapter before deciding to acquire or subscribe for shares in the Company.

The Company has carried out a review of the risks which could have a significant unfavorable effect on the Company, its activity, its financial situation, its results, its prospects or on its capacity to achieve its objectives and which, in this context are important before making any investment decision. As of the date of this universal registration document, the Company is not aware of any significant risks other than those presented in this section.

These risks are grouped according to 4 categories, without hierarchy between them: business-related risks, financial risks, risks of dependence on third parties and regulatory and legal risks, it being specified that within each of among them, the most important risk factors are presented, according to the Company's assessment on the date of the Universal Registration Document, first. The occurrence of new events, either internal to the Company or external, is therefore likely to modify this order of importance in the future.

The section below presents the summary of the main risk factors identified by the Company and indicates for each of them, the probability of occurrence as well as their negative impact on the Company on the date of this reference document. The probability of occurrence is assessed on four levels ("Very likely", "Most likely", "Fairly likely" and "Unlikely") and the consequences in terms of negative impact are assessed on three levels ("High", "Medium" and "Low"). In each section below, the risk factors are presented in decreasing order of importance, according to the

Company's assessment as of the date of this reference document. The occurrence of new events, either internal to the Company or external, is likely to modify this order of importance in the future.

Reference	Risk factor	Occurrence probability	Impact
<b>1.4.1</b>	<b>Risks linked to the company's activity</b>		
1.4.1.1	The Company is dependent on its capacity to innovate and conclude partnership agreements	most likely	high
1.4.1.2	Research and development programs are long, time consuming and expensive and may have an uncertain outcome	most likely	high
1.4.1.3	The spread of a Covid-19 pandemic can disrupt the activity of the Company, in particular the development of its research programs	most likely	high
1.4.1.4	The products resulting from the Company's research are positioned in competitive and rapidly changing markets	most likely	high
<b>1.4.2</b>	<b>Risks related to the financial position of the company</b>		
1.4.2.1	The company has a history of significant operating losses that could continue	most likely	high
1.4.2.2	The Company may need to strengthen its equity or to resort to additional financing in order to ensure its development	most likely	high
1.4.2.3	The Company is exposed to the risk of an increase in interest rates	unlikely	average
1.4.2.4	The market price of the Company's shares is likely to be affected by significant volatility	very likely	average
1.4.2.5	The Company risks being more exposed to currency risks	most likely	low
<b>1.4.3</b>	<b>Risks related to dependence on third parties</b>		
1.4.3.1	The marketing of the Company's product candidates depends on the actions taken by its partners, which are beyond the Company's control	most likely	high
1.4.3.2	The Company sources from third parties to obtain specific proteins in sufficient quantity and quality	most likely	high
1.4.3.3	The Company is dependent on its subcontractors to carry out its preclinical, clinical activities and manufacture of clinical batches	most likely	average
<b>1.4.4</b>	<b>Regulatory and legal risks</b>		
1.4.4.1	The Company operates in an increasingly restrictive regulatory environment	most likely	high
1.4.4.2	The protection of the Company's patents and other intellectual property rights is uncertain and may be insufficient to protect it from its competitors.	most likely	high
1.4.4.3	Third parties could assert property rights over the inventions that the Company develops	most likely	average
1.4.4.4	The responsibility of the Company could be brought into play for product liability	unlikely	low
1.4.4.5	Following the pledge made for the benefit of IPF, the Company may not have its intellectual property	most likely	average
1.4.4.6	The use of chemicals and hazardous substances could lead to accidents	unlikely	low

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## 1.4.1. Risks associated with the Company's activity

### 1.4.1.1. The Company is dependent on its capacity to innovate and conclude partnerships agreements.

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

As of the date of this universal registration document, the Company has licensed two of its products (BC lispro and BC Combo) to a Chinese partner, the company Tonghua Dongbao, which continues their development, in particular clinical and regulatory, and which must then ensure the production and the marketing in China and in other territories as defined in the contract.

The Company is looking for a partner who could continue the clinical development and commercialize the BC lispro product in territories that have not been granted to the Chinese partner, i.e. Europe, Japan and the United States. While the Company is making its best efforts to be creative and explore different possibilities, it is not certain that it will be able to find a commercial or financial partner to fund the continuation of its mature products.

The Company has developed a portfolio of products based on its BioChaperone® technology and focused on the treatment of diabetes, mainly based on insulin. Based on the experience and expertise of its teams, it seeks to enrich its portfolio of innovative products, in particular by working on combinations of hormones or by seeking to extend the application of its innovations outside of diabetes. Thus, in 2021, the Company announced that it had launched new research programs on cell therapy and oral delivery of protein. But these research programs aiming 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:

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- 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.

Therefore, it is not certain that the Company will be able to identify new product candidates through its internal research. The Company could also focus its efforts and its human and financial resources on candidates who could prove unsuccessful.

Finally, the products developed by the Company may not be sufficiently reliable, effective, and innovative to attract major players in the pharmaceutical, biotechnology and medical device industry and convince them to conclude license and collaboration agreements relating to products and technologies of the Company.

If despite of all these efforts, the Company is unable to conclude license and collaboration partnerships for these innovative products, it may lack the necessary funding to continue the internal development of its leading products. Failure to enter into such agreements could further delay or even impeded the development, manufacture and / or marketing of attractive leading products or any other product and have a significant adverse effect on the financial position and operational results of the Company, insofar as income from license agreements on candidate products could be delayed or even never materialize. In such a case, the Company could choose not to market, nor to continue the development of the leading products.

#### 1.4.1.2. Research and development programs are lengthy, time-consuming and costly processes, the outcome of which remains uncertain

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 development stage, the Company must then develop and design clinical trials to test its specific properties. In order to conduct clinical trials, the Company must first obtain the necessary authorizations to carry out these trials in the countries where it intends to market its product. The Company cannot predict how long it will take the regulatory authorities to review the trial protocol and approve the files submitted to them. For example, for the launch of Phase 3 clinical trials in China, Tonghua Dongbao, the Company's Chinese partner, filed an application with the CDE (Center for Drug Evaluation) in March 2021. However, the processing of the application was delayed by the internal reorganization of the Chinese regulatory agency, and the Company was not granted final approval until October. Once this authorization is received, the actual start of the clinical trial may still take some time depending on the number of patients included in these trials and the number of sites involved. As of the date of this document, the first injection on the first patient had not yet been performed.

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 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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#### 1.4.1.3. The spread of a Covid-19-type pandemic could disrupt the Company's business, in particular the development of its research programs

The Covid-19 pandemic that occurred in early 2020 has severely disrupted the global economy. Containment measures adopted by the different countries have limited the spread of the pandemic, pending the launch of vaccination campaigns in 2021. At the time of writing, a more contagious but less critical variant is circulating in a largely vaccinated population.

Should the coronavirus continue to spread in different forms of severe variants, the development of Society's research programs could be severely disrupted:

- On the one hand, by limiting the personnel who can travel to the Company's research site, and by disrupting the continuity of supplies of raw materials, consumables and protections necessary for the personnel to ensure the development of the Company's research programs; and
- On the other hand, by affecting the activity of the subcontractors on which the Company is dependent (see in this sense the risk described in section 1.4.3 of this document), and by generating in particular:
  - delays in the transmission and analysis of the results obtained on the completed preclinical and clinical studies;
  - difficulties in the continuation of clinical and preclinical studies launched by the Company or the delay or cancellation of new studies already planned, due in particular to a delay in the recruitment of patients;
  - a limitation of the human resources available for the conduct of these studies or, concerning preclinical studies, difficulties in supplying animals,
  - difficulties in convincing future partners of the effectiveness of its drug candidates in the absence of new clinical or preclinical results.
  - delays on the part of the administrative authorities in obtaining the authorizations necessary to launch the Company's clinical trials,
  - slowdowns in the necessary interactions with local authorities, ethics committees or other regulatory authorities due, in particular, to limitations in human resources or forced holidays of employees of said authorities, or the refusal of these administrative authorities, such as the FDA, ANSM or EMA, to accept data from clinical trials conducted in affected geographic areas;

- changes in local regulations due to the measures taken with regard to the COVID-19 coronavirus epidemic or its variants, which could force the Company to modify the protocols and modalities of its clinical trials, which could thus result in unforeseen costs, or even in the interruption of these trials.

Furthermore, the collaboration between the Company and its partner in China could be impacted by difficulties or delays in the activities carried out by its partner to bring the licensed products of BC lispro and BC Combo to the market, within the deadlines initially provided.

In addition, the difficulties or even the inability for the employees, collaborators, or partners of the Company, taking into account travel restrictions, to travel in order to ensure the latest method transfers, technical assistance and validation of regulatory advancements and clinics could also slow the development of the Company's research programs.

Similarly, given the containment measures, the Company could be penalized by a lack of visibility with the scientific and financial community due to the cancellation of international congresses and conferences.

Finally, this situation could make it more difficult for the Company to obtain, in due time, the additional funds necessary for its development (see section 1.4.2.2 of this universal registration document).

In conclusion, in a context of crisis that could persist, the Company cannot be assured that its research program, in particular the preclinical and clinical studies, can be implemented under the conditions and within the deadlines provided if the one or more of the risks mentioned above should materialize. The materialization of these risks could thus have a significant unfavorable effect on the activity of the Company, in particular by lowering the level of forecast expenditure, as well as expected income from collaborations, difficult to quantify with precision at the date of this universal registration document.

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#### 1.4.1.4. The products resulting from the Company's research are positioned in competitive and rapidly changing markets

Research on products incorporating the Company's technologies is positioned in markets in which there are already therapeutic products, the use of which is sometimes very widespread. In addition, competing therapeutic products or technologies, whether existing, under development or even unknown to date, could, in the more or less near future, take significant market shares and limit the Company and its partners' capacity to market products incorporating the Company's technologies successfully.

The markets in which the Company and its current and future partners are present and intend to develop are experiencing, and should continue to experience, rapid and significant technological upheavals. In fact, the diabetes market in which the Company is positioning itself is undergoing strong change with the development of increasingly precise blood glucose monitoring (CGM) devices, with the use of Big data to measure patient behavior and the development of algorithms to assist in decision-making or pump monitoring. The Company must therefore integrate market research and technologies into its search for candidate products in order to license innovations that meet market needs.

Competitors of the Company and its current and future partners could develop new therapeutic products and innovative technologies that are more effective, more reliable and / or less expensive than those developed by the Company or its partners, which could make the products candidates and / or the Company's current or future technologies not competitive enough, obsolete, or unprofitable.

The Company's competitors could benefit from:

- considerably greater financial, technical and human resources than those available to the Company at each stage of the discovery, development, manufacturing and marketing processes;
- greater experience in the field of preclinical trials, in the conduct of clinical studies, in obtaining regulatory authorizations, in the marketing of drugs, in patent disputes and in the manufacture and marketing of pharmaceutical products;
- products already approved or in an advanced stage of development;
- recommendations or decisions regarding reimbursements which would be more favorable for products of comparable efficiency;
- stronger protection thanks to their patents;

- more innovative drug delivery technologies or devices; and or
- collaboration agreements with key players and major research organizations in the Company's target markets.

Furthermore, even if the leading products of the Company and its partners obtain the required regulatory authorizations, their acceptance by the targeted medical community is in no way guaranteed. The Company cannot guarantee that the marketing of products incorporating its technologies will take place, a fortiori, within the estimated deadlines, or that the medical community will give them a favorable reception or that its partners will deploy the resources necessary for the success of their marketing.

If the Company and its partners fail to market the product for lack of sufficient acceptance by the market or of the means implemented for the marketing or the resolution of other problems post-marketing, the Company and its partners will have devoted financial means, development resources and precious time to research programs that will not ultimately have produced commercially viable products. The activity of the Company, its operating results and its prospects could under these conditions be significantly affected.

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## 1.4.2. Financial risks

### 1.4.2.1. The Company has a risk of significant operating losses that could persist

The Company has posted operating losses every year since its creation in 2005. As of December 31, 2021, its cumulative net losses presented under IFRS rules (including losses carried forward) were €94.9 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 limit its operating losses or become profitable in the long term, the Company must manage to collect revenues which, at this stage, could be from two sources:

- **Income related to the conclusion of license and collaboration agreements**

- The business model of the Company is based on the signing of partnerships which must generate income in the form of initial payments, milestone payments and then royalties on sales made by the partner.
- The conclusion of a major license and collaboration contract with a partner can have an immediate effect on the profitability of a given fiscal year.
- Thus, the signing in 2018 of the partnership with the Chinese company Tonghua Dongbao was accompanied by the payment of an initial amount of \$ 50 million and enabled the Company to generate a net profit and a positive change in cash flow on the exercise.
- This type of income depends on our ability to enter into such agreements.
- On the other hand, the next income expected under this contract are payments which depend on the achievement of scientific objectives (payment in stages) which do not depend solely on the actions of the Company, insofar as certain activities are carried out directly by the partner. If the project does not

meet the planned objectives, the Company could therefore not receive all of the revenues provided for in the contract.

- To ensure its financial profitability, and pending the potential income provided for in this contract, the Company must enter into other partnerships, which may not be achieved or may not be done under reasonable conditions.
- In addition, in France, the allocation of carryforward loss is capped at 1 million euros, increased by 50% of the fraction of profits exceeding this ceiling. The unused balance of the deficit remains transferable to the following years and is chargeable under the same conditions without limitation in time. It cannot be excluded that future tax developments in the area of corporate taxation will call into question, in whole or in part, the allocation of these previous deficits to future profits or limit them over time. Such a change would have a significant impact on the level of net losses displayed by the Company.

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#### ▪ Research tax credit

- To finance its activities, the Company benefits from certain tax advantages such as the Research Tax Credit ("CIR"), which consists in the French State offering a tax credit to companies investing significantly in research and development. Research expenses eligible for the CIR include in particular salaries and wages, depreciation of research equipment, provision of subcontracted services to approved research organizations (public or private) and intellectual property costs.
- The Company has benefited from the research tax credit each year since its creation, which has been systematically reimbursed after the filing of the corresponding application given its status as a European SME. The loss of this status would no longer open the right to immediate reimbursement but to reimbursement at the end of the three-year period.
- Thus, in 2021, the Company received the sum of 6 million euros in reimbursement of the CIR declared as expenses generated in 2020.
- For 2021, the Company recorded an amount of CIR of 4.6 million euros which appears in its receivables and for which it will request reimbursement in 2022.
- Concerning 2021 and the years to come, a questioning by the tax administration of the methods of calculation of research and development expenses retained by the Company, or the loss of the profit of the CIR following a change of regulations or to a dispute from the tax administration cannot be totally excluded, even if the Company considers that it is in order with the requirements of documentation and eligibility of expenses. If such situations occur, it could have a material adverse effect on the results, financial condition, and prospects of the Company.

Failing to become profitable and to remain profitable, the Company risks seeing the stock market price of its shares decline, and its ability to raise funds, develop its activity, diversify its product offering or continue its altered operations.

#### 1.4.2.2. The Company may need to strengthen its equity or resort to additional financing in order to ensure in particular its development.

Historically, the Company has financed its growth mainly by strengthening its equity base through capital increases. For the acquisition of the building in February 2016, the Company used traditional bank loans, which were then supplemented to finance the renovation of the building.

At the end of 2019, the Company has used a financing of 15 million through a bond issue with warrants attached. This bond issue includes financial covenants and customary security interests, in particular the pledge of certain intellectual property rights.

In 2020, the Company obtained a state-guaranteed loan (PGE) of 7 million euros in the context of the health crisis linked to Covid-19.

In 2021, the Company carried out a financing operation by issuing new shares to Gérard Soula, for an amount of 1 million euros, and an issue of bonds convertible into shares at a variable price for a total amount of 6 million euros net.

The Company will continue to have significant financing needs in the future for the development of its technologies and the pursuit of its strategy, but it may not be able to finance its own growth. In addition, the Company could find itself obliged to repay all or part of its loans, convertible or non-convertible bonds and other debts, in particular in the



event of an event of default under one or more of its financing agreements. Such events could require it to seek alternative sources of financing, by increasing its equity through a capital increase and/or taking out bank loans.

The Company may not be able to raise additional capital when it needs it, or it may not be available on financially acceptable terms to the Company. If the necessary funds are not available, the Company may have to:

- postpone, reduce or cancel research programs;
- obtain funds through partnership agreements which could force it to renounce rights to certain of its technologies or certain of its products;
- grant licenses on all or part of its portfolio to partners or third parties; or
- conclude new collaboration agreements which could be less favorable to it than those which it could have obtained in a different context.

In addition, to the extent that the Company raises capital by issuing new shares, the participation of its shareholders could be diluted, particularly in a context where the value of the Company's share has reached a historically low level, which could result in a potentially significant dilution of the current shareholders.

The Company is actively seeking partners for the mature projects in its portfolio and continues their development while nonetheless focusing its expenses on priority projects and activities.

The Company's cash and cash equivalents amounted to almost € 15.2 million as of December 31, 2021 compared to € 28 million as of December 31, 2020.

To respect the financial commitments made to its lenders (see 4.1.5.4 note 10 financial debt) and taking into account (i) the cash position of 15.2 million euros at December 31, 2021 (ii) the receipt, in March 2022, of 19 million from the sale of the headquarters in March 2022, (iii) the milestone payment from Tonghua Dongbao in the second quarter of 2022 following the start of phase 3 of BC Lispro, and (iv) the forecasts made, the company will have to conclude a licensing agreement or a capital raising operation in the fourth quarter of 2022.

Management is confident that it will be able to obtain new sources of financing or, failing that, obtain a new temporary arrangement of its financial ratios to be respected in the context of the loans granted to the company.

### 1.4.2.3. The company is exposed to an increase in interest rates

In 2015, the Company contracted a loan from two banks to finance the acquisition of the building in which its research center and head office are located. These loan contracts were negotiated at a fixed rate over a period of 12 years. With the sale and leaseback operation completed in March 2022, these debts have been completely repaid at the time of the present document.

In 2019, the Company contracted a loan from IPF Fund II (IPF) for an amount of 15 million euros with an interest rate calculated on the Euribor + margin and a maturity of 5 years. Since the signing of the contract, taking into account a negative Euribor, a floor at 0% has been applied. However, over the term of the loan, the Company could be impacted if the Euribor were to rise and rise above the floor.

In addition, the Company is exposed to variations in interest rates in the context of the management of its cash and cash equivalents. The Company's cash and cash equivalents amounted to € 15.2 million as of December 31, 2021 and nearly € 28 million as of December 31, 2020. This item is made up of term deposits, accounts paid at fixed rate and investments in monetary SICAVs. The Company's investment policy is based exclusively on liquid products without capital risk.

The Company strives to reduce the credit risk associated with its cash and cash equivalents by ensuring the quality of the financial institutions to which it entrusts its investments.

The Company is not guaranteed to benefit from the same rates when renewing its term accounts when they mature.

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

The price of the Company's shares is subject to significant volatility. Thus, on December 31, 2021 the Company's share price traded at €8.1, compared to €8.30 on December 31, 2020. The average daily trading volume which was 23 813

shares traded per day in 2020 has slightly decreased in 2021 to 15 724 shares traded per day. The public float remained steady in 2021 and was around 60% at the end of December 2021.

As of April 12<sup>th</sup>,2022, shares traded at €4.9 with an average volume of 20 199 shares traded since the beginning of the year, a slight increase compared to the previous 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.

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#### 1.4.2.5. The Company risks being more exposed to currency risks

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.

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.

### 1.4.3. Risks associated with dependence on third parties

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#### 1.4.3.1. The commercialization of the Company's products depends on the actions taken by its partners which are beyond the Company's control

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

The current and future partners of the Company could also encounter difficulties in obtaining technical and clinical validations for products incorporating its technology. Delays or failures resulting therefrom could delay or even jeopardize the marketing of the products concerned.

The success of the Corporation's partnership agreements rests on the efforts and activities of its current and future partners, who benefit from a great latitude in determining the methods for pursuing planned activities, as well as the quality and nature of the efforts and means that will apply to partnership agreements. These partners may also be unable to successfully develop and market the Company's product candidates.

The Company cannot guarantee its ability to form and renew partnerships. Nor can it guarantee the scientific and/or commercial success of a partnership, nor have the assurance of receiving income on the basis of one of these agreements. For example, in December 2011, the Company entered into a first license and collaboration agreement with Eli Lilly for the development of a fast-acting analog insulin (BC lispro). In 2013, the Company and Eli Lilly decided to terminate the said license agreement. In 2014, in light of the clinical results obtained, Eli Lilly signed a new license agreement with Adocia, again for the formulation of a fast-acting analog insulin (BC Lispro). In January 2017, Eli Lilly announced its decision to end this collaboration.

The following factors are particularly likely to cause the collaborations established by the Company to fail:

- the partners may not use all the means necessary to obtain the expected results within the framework of the agreements concluded with the Company. Budget restrictions within these partners or priority given to other development programs, in particular, could delay or even prevent the validation of the potential of products incorporating the Company's technology, an essential step for the success of its commercial policy;
- conflicts could arise between the Company and some of its industrial partners. There is a risk that the Company's partners will conceive or seek to establish a commercial activity using technology that competes with that of the Company or all or part of the Company's technology, or decide to favor the internal development of products intended for markets in competition with the candidate products of the Company, which would be de facto competitors of the activity of the Company (refer to the paragraph on the risks linked to competition below);
- current or future partners could limit or even terminate their collaboration with the Company, which could lead to additional costs, delays and development difficulties, obtaining authorizations by regulatory authorities and successful marketing of product candidates of the Company, and have a significant unfavorable effect on its activity, its financial situation, its revenues, its development and its prospects. Such restrictions or stops could impede the Company in its efforts to attract new partners or seriously damage its image in the industry and the financial community. They could also cause a loss of expertise for the Company and even lead to the disclosure of important confidential information in the research and development system of the Company, even though the partners concerned would be contractually bound to an obligation of confidentiality towards it .

In addition, the Company derived a large part of its 2018 revenues from the license and collaboration agreement concluded with the Chinese company Tonghua Dongbao Pharmaceuticals Co. Ltd. Following the signature in April 2018 of two contracts relating to the development of an ultra-rapid formulation of insulin called BioChaperone Lispro and a formulation of slow and fast insulin called BioChaperone Combo, Adocia received a total initial amount of \$ 50 million. Under the terms of this agreement, the Company was likely to receive (i) subsequent payments of up to \$ 85 million (if the product successfully passed certain major clinical and regulatory phases) and (ii) royalties on sales. (for more information on this partnership, see section 1.2.8.3 "Licenses granted by Adocia to Tonghua Dongbao Co. Ltd" above).

The Company cannot guarantee that collaboration with a partner will make it possible to reach the clinical and regulatory stages determining the payment of expected income. When Eli Lilly decided to terminate the contract in January 2017, the Company was faced with a difficult situation that forced it to review its development plan. Any decision by a future partner to terminate their agreement with the Company could jeopardize their business, operating results and prospects.

If the partnerships do not generate the benefits expected by the Company, its business, operating results, and prospects could be significantly affected.

### 1.4.3.2. The Company sources from third parties the supply of specific proteins in sufficient quality and quantity.

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.

Finally, within the framework of its partnership with the company Tonghua Dongbao, Adocia benefits from a supply contract for insulin lispro (API) and glargine (API) according to which it is expected that the Chinese company will produce and supply Adocia with insulin according to defined specifications and agreed quality standards. However, the Company does not control the ability of its partner to comply with European and American regulatory standards and to supply, within the required deadlines, quantities of products of sufficient quality.

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.

### 1.4.3.3. The Company is dependent on its subcontractors to carry out its preclinical and clinical activities, and the manufacture of clinical batches.

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 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.

## 1.4.4. Regulatory and legal risks

### 1.4.4.1. The protection of the Company's patents and other intellectual property rights is uncertain and may be insufficient to protect it against its competitors

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.

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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.

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 protect and maintain the intellectual property of its products or its candidate products, and to protect its know-how, it could lose its competitive advantage and be exposed to more intense competition likely to have a significant unfavorable effect on its business, operating results and prospects.

Furthermore, the Company cannot guarantee the adequate protection of its technologies and its innovative formulations of therapeutic proteins developed from its technologies, which are closely linked to its know-how and its trade secrets, against competitors or against risk of usurpation or circumvention. In fact, in the collaboration and research contracts that it concludes, the Company may be required to provide its contracting parties, in different forms, certain elements of its know-how, protected or not by patents, and in particular information, data or information regarding its research, technologies or products.

The Company seeks to limit the communication of key elements of its know-how to third parties to only the information strictly necessary for the collaboration it maintains with them and it ensures contractually that these third parties undertake not to divert, use or communicate this information, in particular by means of confidentiality clauses. The Company cannot however guarantee that these third parties comply with these agreements, that it will be informed of a violation of these clauses, or that the compensation that it could possibly obtain will be sufficient with regard to the damage suffered.

In addition, these collaboration and research contracts expose the Company to the risk of seeing its contracting parties claim the benefit of intellectual property rights over its inventions, its knowledge, or its results. Finally, these agreements could give rise to intellectual property rights held in co-ownership or in exclusive operating concessions under conditions unfavorable to the Company.

Thus, the Company cannot guarantee with certainty that:

- its know-how and trade secrets will not be usurped or circumvented;
- its competitors have not already developed a technology or products similar to its own;

- the extent of the protection conferred by patents and trademarks is sufficient to protect it against competition and the patents and trademarks of third parties covering similar products or devices; and
- no contracting partner will claim the benefit of intellectual property rights over his inventions, his knowledge or his results.

The protection by the Company of its intellectual property rights represents a significant cost linked, in particular, to the costs of filing and maintaining patents and to the management of its other intellectual property rights. This cost could increase, especially if the Company is forced to take legal action to assert its rights. In addition to these costs, any legal action proving necessary for the purposes of enforcing the Company's intellectual property rights, protecting its or its know-how, or determining the validity and scope of its intellectual property rights, could have a significant unfavorable effect on the Company's income and financial position and not provide the protection sought.

Thus, the Company was engaged in legal proceedings against its former partner, the company 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 for the violation by Lilly of several collaboration and confidentiality agreements. The Tribunal issued its decision in August 2019 and dismissed Adocia's request.

Similarly, monitoring unauthorized use of products and technologies is difficult, and the Company cannot be certain that it will be able to prevent unauthorized diversion or use of its products and technologies, especially in foreign countries where its rights would be less well protected.

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#### 1.4.4.2. The Company is operating in an increasingly restrictive regulatory environment

One of the most significant challenges faced by 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 ANSM\*, 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. Failure by a Company partner to obtain marketing authorization for one or more products incorporating its technologies or obtaining authorization once the deadlines have passed could significantly affect the Company's ability to generate income.

These delays in obtaining a regulatory authorization could:

- significantly impact the commercial exploitation of a product developed by the Company or its partners,
- impose costly procedures on the Company or its partners,
- reduce the advantages that the Company and its partners could have over their competition, and
- significantly impact the collection of revenues and royalties by the Company.

Under these conditions, several years could elapse before the product is made available to the end user, if necessary, mainly due to the time required for carrying out clinical trials, developing products and obtaining a marketing authorization.

Once the marketing authorization has been obtained, the Company still runs the risk of having the product approved for a less broad indication than that requested, or that the authorization includes restrictions on the use of the product, such as a "black-box" type mention or when the authorization is subsequently suspended, in the event, for example, of non-compliance with the manufacturing rules or discovery of an undesirable side effect in particular. All of these risks can have a substantial effect on the ability of the Company and its partners to generate revenue.

### 1.4.4.3. Third parties could assert property rights over the inventions that the Company develops

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 realization of one or more of these risks could have a significant unfavorable effect on the activity of the Company, its financial situation, its results, its development, and its prospects.

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### 1.4.4.4. Following the pledge granted to IPF, the Company may not have all of its intellectual property

In order to guarantee the repayment of the obligations subscribed by IPF on October 14, 2019, the Company has granted a pledge on some of its assets and in particular its intellectual property rights in France, Europe, United States of America and China (see paragraph 1.2.8.6 of this universal registration document).

In the event of non-compliance by the Company with the commitments made for the benefit of IPF, the latter could obtain the allocation of the pledged intellectual property rights.

The Company has the option of requesting the lifting of this pledge in the context of certain transactions and subject to certain conditions related to the cash position.

In the event that the Company does not meet the required conditions, and in the case of such a transfer of ownership, the ability of the Company to grant a license to the products covered by these intellectual property rights could be found affected or delayed, which could therefore have a material adverse effect on the activity of the Company, its financial situation, its results, its development, and its prospects.

### 1.4.4.5. 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 1.4.5 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.

#### 1.4.4.6. The use of chemicals and hazardous substances could lead to accidents

The Company is subject to a set of environmental, health and safety laws and regulations. Biological research and development activities require the use of certain biological materials or hazardous chemicals, which produce waste which must be eliminated. The Company has contracted with a specialized company for the management and disposal of this waste.

Although the Company has adopted a policy adapted to this type of risk traditionally identified in biological research laboratories, it cannot exclude the risk of injury, accidental contamination or occupational diseases linked to the handling of chemical materials in its laboratories. In the event of an accident, the Company could be held liable and be forced to pay significant damages to the personnel concerned.

Likewise, the regulations currently in force could be subject to major changes leading to significant compliance costs borne by the Company.

The activity, financial situation, results, development, and prospects of the Company in the medium and long term could be significantly affected by the realization of one or more of these risks.

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#### 1.4.5. Insurance and risk coverage

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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, 2020 and 2021.

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.



### 1.4.6. Extraordinary events and disputes

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During the 12-month period preceding the filing date of this universal 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 universal 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 all of the legal proceedings against Eli Lilly, the two arbitration proceedings launched by Adocia and the civil action proceedings launched by Eli Lilly, ended during the 2019 financial year (see section 1.2.8 of this universal registration document).

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02



# 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.

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#### 2.1.1. Definition of labor indicators

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**Workforce:** Number of employees on staff on 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 €7.6 million (French GAAP) for 2021.

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. To mark certain occasions, such as the Company's 10th anniversary or the signing of a partnership, Adocia's management may decide to allocate free shares to all staff. This was the case in December 2015, June 2018 and December 2019. In 2020 and 2021, the Company continued its internal promotion policy with the allocation of free shares to the employees in question.

Adocia is evolving in a very competitive sector, and thus decided in 2020 to hire an external firm, Deloitte, to identify the strengths and limitations of its current policy in terms of compensation. The first mission consisted in carrying out a compensation benchmark internally (equity) and externally (competitiveness).

This study enabled the acknowledgement of Adocia's compensation policy as fair and competitive. In the general market, the study shows that basic wages at Adocia are well above the average. We note a loss of competitiveness when we integrate the variable bonuses, profit-sharing and if we consider the total compensation. Despite this, total compensation remains globally above the general market. In the healthcare labor market, the trend is the same.

Following the study and in line with the market practices, Adocia adapted its compensation policy to introduce more variable part (bonus) starting in 2021 and work on long-term variable.

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### 2.2.1.2. Equity interests held by employees.

To the Company's knowledge, as of December 31, 2021, the Company's employees (including Olivier Soula) held 457,945 shares, i.e. 6.3% of equity and 8.5% 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 2.3% 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 on December 31, 2021, given the fiscal loss registered for fiscal year 2021.
- 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

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

- 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 2021, the Company had 112 employees (full-time and part-time), of which 111 work in France in the parent company and one is based in the US subsidiary Adocia Inc. On December 31, 2021, the breakdown of the workforce by socio-professional categories and gender is as follows:

Workforce by socio-professional categories and gender	12/31/2021	12/31/2020
<b>Executives</b>	59	70
of which permanent contracts	58	68
<b>Non executives</b>	53	56
of which permanent contracts	45	48
<b>Workforce (number)</b>	<b>112</b>	<b>126</b>
<b>Workforce breakdown by gender M/F (in %)</b>	<b>49/51</b>	<b>52/48</b>
Men (number)	55	66
Women (number)	57	60

At the end of December 2021, the company employed 39 researchers who hold a doctorate in science, medicine or pharmacy, or more than one-third of the total.

As of December 31, 2021, close to 75% 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. This ratio is down compared to last year (80% of the workforce last year in R&D), this is explained by the net decrease in the workforce, which was mainly in R&D positions in 2021.

	31/12/2021	31/12/2020
R&D workforce	85	99
SG&A workforce	27	27
<b>Total workforce</b>	<b>112</b>	<b>126</b>

On December 31, 2021, the average employee age was 39 years and the breakdown of the workforce by age bracket was as follows:

Age pyramid 2021	Men	Women	Total	Percentage
Younger than 25 years old	2	5	7	5%
25 to 34 years old	15	17	32	23%
35 to 44 years old	21	20	41	30%
Older than 44 years old	17	15	32	23%

## 2.2.4. Personnel movements in 2021

The table below presents the evolution of the workforce from January 1 to December 31, 2021:

	12/31/2021	12/31/2020	12/31/2019
<b>Number of hires</b>	<b>20</b>	<b>19</b>	<b>22</b>
<b>Number of Employee departures</b>	<b>34</b>	<b>31</b>	<b>16</b>
<b>Net increase of workforce</b>	<b>-14</b>	<b>-12</b>	<b>+6</b>
Of which permanent contracts	-15	-8	0
Of which short- term contracts for additional activity	1	0	2
Of which short- term contracts for replacement	-1	+2	2
Of which work study contracts	1	-6	2

The Company registered 34 departures during 2021, including:

- 8 departures at the end of fixed term contracts (including 3 work-study contracts)
- 4 amicable terminations by mutual consent
- 1 layoff for nonprofessional inability
- 3 at the end of their trial periods
- 18 resignations

2021 is marked by slightly more departures than last year (34 departures in 2021 compared to 31 in 2020) with a higher number of resignations. Since the sanitary crisis, Adocia seems to be confronted, on its own scale, with the changes that the work world is currently facing and with the unprecedented phenomenon of the "Great Resignation", which translates into resignations of employees seeking a better balance between their personal and professional lives.

### 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 the latter, effective working time is 36.15 hours per week, with allocation of compensatory days to result in an average working time of 35 hours per week.

In 2021, 13 employees worked part time. All these employees choose to work part time to deal with family responsibilities.

The main reasons for absences in 2021 were illness and maternity or paternity leaves.

The absenteeism rate was 3.17% in 2021 compared to 3.97% in 2019. The number of days of absence due to sickness, workplace accident and sick child for 2021 was 888 days, compared with 1226 days the previous year and at equivalent with 2019 (859 days).

Planned absences such as maternity leave or paternity leave are not included in this calculation.

Throughout the health crisis, Adocia has structured itself to maintain the continuity of its research activities and deal with the pandemic. Research activities continued at the site in Lyon and available resources were focused on priority activities and projects. The Company maintained a sustained level of activity despite the various epidemic peaks linked to Covid.

The Company continued to encourage the use of telecommuting for all employees for whom this was possible, and all operations were adapted, in particular the support functions for research activities and those related to administrative functions.

### 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. In November 2016, the single staff delegation was renewed.

Following the new legal provisions of article L2311-2 of the Labor Code and article 9 of Ordinance 2017-1386 of September 22, 2017, the company had the obligation to set up a Social and Economic Committee and before December 31, 2019.

In this context, the Management and the members of the current DUP have agreed to reduce the current mandates, as of December 31, 2020.

The elections for the new CSE were organized in advance, before the annual closure of the company, on December 05, 2019 and 12 members were elected (6 members, 6 alternates) including 5 women and 7 men.

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.

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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 (CSE).

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 29 accidents during the year. In relation to the average workforce in 2021, the rate of workplace accidents per employee is 0.26 compared with 0.16 the previous year, remaining at a rate that is considered as low. Six of these accidents resulted in medical leave, compared with 4 in 2020 for a maximal duration of 25 days, compared to 34days in 2020.

The frequency rate in 2021 was 35.24 and the 2021 severity rate was 0.15.

	31/12/2021	31/12/2020	31/12/2019
Frequency rate	35.24	22.54	26.86
Severity rate	0.15	0.19	0.5

No occupational or work-related illness was reported in 2021 or during the previous four 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. Being less exposed, administrative staff and some scientists are examined at least every five years as a result of not working in the laboratories.

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 2,180 hours of training were dispensed in 2021.

<i>Number of employees trained in 2021</i>	Men	Women	Total
Executives	38	31	69
Non executives	26	28	54
<b>Total workforce</b>	<b>64</b>	<b>59</b>	<b>123</b>
Breakdown by gender (in %)	52%	48%	

<i>Personnel in the Company as of 12/31/2021</i>	Men	Women	Average number
Average number of training actions taken per employee in 2021	3	2.95	2.98
Average number of training hours per employee in 2021	15.93	17.44	16.69

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To develop individual skills and maintain a high level of expertise, the company also encourages all researchers to attend international conferences and seminars. In 2021, Adocia participated in 11 conferences and scientific seminars (involving 12 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.

As of December 31, 2021, the breakdown of men and women in the workforce was perfectly balanced, with 57 women and 55 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).

The Company utilizes supported employment agencies for workers with disabilities (ESAT) for its supply of stationery, maintenance and cleaning. Since 2017, the Company outsources to 2 companies in the supported employment sector: ELISE specialized in paper recycling, and ALGED which intervenes monthly for the cleaning of green spaces.

## 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> was occupied by three companies to which Adocia had granted commercial leases until the end of 2019.

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 works were finalized in the first semester 2019.

In 2020, insulation work on part of the roof was carried out (500m<sup>2</sup> of the existing 1500m<sup>2</sup>).

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 employee based in the subsidiary Adocia Inc. has a low environmental impact due to his activity, limited to business travel. This employee is permanently excluded 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. with the objective of piloting the environmental aspects .

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

### 2.3.2. Pollution and waste management

---

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 2021, the quantity of hazardous laboratory waste sent to a specific center (soiled packaging and glass, chemical waste) totaled 25.04 metric tons versus 24.39 in 2020. 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 2021, the quantity of paper and cardboard removed totaled approximately 2.891 metric tons compared to 3.525 tons in 2020. Sorting and packaging are undertaken by the company ELISE for recycling in the paper industry, which generated in average 54 hours of work for employees with disabilities in 2021 as compared to 66 hours in 2020. All staff are made aware of waste management and this resulted in better control of this position in 2020, in particular with the organization of a specific operation aimed at sorting and eliminating paper archives. 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 38.961K€ in 2020 versus 41.4 M€ in 2019.
- 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 2019, a vegetable garden was also put in place and allows the employee to benefit from fruits and vegetables, which makes it possible to take advantage of a short circuit and reduce the specific packaging for the transport and conservation of these.

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. Furthermore, the new system was put into place to fit out the analysis department benefits from a very low noise level and meets the installation and regulatory standards.

### 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 and consumption.

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 cafeteria, 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.

Consumption en M <sup>3</sup>	31/12/2021	31/12/2020	31/12/2019
Bottled water	NS	NS	NS
Distilled water	NS	NS	7
Current consumption water (*)	2 251	3 024	3 986
<b>Water total</b>	<b>2 251</b>	<b>3 024</b>	<b>3 993</b>

(\*) prorated to the surface occupied by the Company

In 2021, there is a decrease in running water consumption, mainly due to better management. The Company is studying the possibility of recovering rainwater and, for this, returning to service an existing well that would be dedicated to watering.

2

### 2.3.3.2. Electricity

With respect to energy, the Company consumes electricity only.

Since November 2019, we have significantly reduced our electricity bill due to the departure of the tenants we had and who occupied approximately 1200m<sup>2</sup>. As a result, the electricity consumption bills for 2020 correspond to our own consumption:

Consumption 1n kWh	31/12/2021	31/12/2020	31/12/2019	31/12/2018
<b>Electricity total (*)</b>	<b>844 539</b>	<b>904 954</b>	<b>1 223 023</b>	<b>1 275 467</b>

(\*) prorated to the surface occupied by the Company

This decrease of the consumption is due also to the works **implemented in the Analytical service as follows:**

- Insulation of the walls,
- Performance of the CVC system
- Down regulation of the CVC system when the site is empty
- Led lighting with motion detection and light detection.

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 turn off lights automatically, have been installed in some locations. The Company also adopted and is gradually implementing a plan to replace older light bulbs with new generation of low consumption bulbs.

### 2.3.3.3. Climate change

After an initial analysis, the Company estimated that its greenhouse gas emissions are mainly related to its purchases of raw materials and consumables. In 2021, given the sanitary crisis, business travel was very low and emissions related to business travel very limited. In 2021, our travel provider reported a Co2 emission of 25.2 tons for business travel, down from 2019 (the baseline year prior to Covid, which had a Co2 emission of 1,376 tons).

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

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 15 years, the company hired over 130 people, most of them 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 (5 at the end of December 2021) and a certain number of trainees (14 during 2021). The Company is therefore attractive to and offers professional prospects for scientists, researchers, and technicians in the life sciences.

In 2021, the Company's payroll expenses, and social security contributions accounted for nearly 45% of operating expenses.

2

### 2.4.2. Relations with its shareholders and investors

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 2021, despite a context still marked by the sanitary crisis, the Company took part in conferences to meet its institutional investors at trade shows in France and abroad, both in person and remotely. Minority shareholders were also able to meet and discuss the Company's progress in 2021 with Management on several occasions: the Annual General Meeting, held in person at the Company's headquarters, and at meetings for shareholders and investors in Paris (Investir Day in November 2021, Investor Access in September 2021).

### 2.4.3. Subcontracting and suppliers

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 30% 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

## 2.4.5. Public health issues

---

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 universal registration document.



03





# Corporate governance

## Chapter 3

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# 3 CORPORATE GOVERNANCE

## REPORT ON THE CORPORATE GOVERNMENT

The present report of the board on the corporate governance was adopted by the board during the session of April 14, 2022.

### 3.1 Governance Code

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 per the revision published in September 2021 by MiddleNext (the "MiddleNext Code"). The Company has assessed its compliance with the new provisions of the MiddleNext Code and the first actions to be taken have been identified. This work will continue in 2022.

Code MiddleNext Recommendations	Compliance
<b>Supervisory power</b>	
R1 - Board members' ethics	Yes (3.1.3.4)
R2 - Conflicts of Interest	Yes (3.1.5)
R3 - Board composition - Presence of independent members	Yes (3.1.2)
R4 - Information for Board members	Yes (3.1.2.4)
R5 - Board member training	No - planned in 2022 <sup>(1)</sup>
R6 - Organization of Board and committee meetings	Yes (3.1.4)
R7 - Establishment of committees	No (3.1.4.3) <sup>(2)</sup>
R8 - Establishment of a specialized committee on corporate social/societal and environmental responsibility (CSR)	Non - planned in 2022 <sup>(3)</sup>
R9 - Establishment of internal rules of procedure for the Board	Yes (3.1.4.2)
R10 - Choice of each Board member	Yes (3.1.3.5)
R11 - Length of terms of Board members	Yes (3.1.3.3)
R12 - Compensation of Board members for their duties	Yes (3.2)
R13 - Implementation of an evaluation of the Board's work	Yes (3.1.4.2)
R14 - Shareholder relations	Yes (3.1.4.2)
<b>Executive Branch Powers</b>	
R15 - Diversity and equity policy within the company	Yes (3.2.1.3.8)
R16 - Definition and transparency regarding compensation of executive directors/corporate officers	Yes (3.1.3.4.2)
R17 - Executive succession plan	Yes (3.1.4.2)
R18 - Concurrent holding of an employment contract and corporate officer status	Yes
R19 - Severance pay	N/A, no severance pay provided
R20 - Supplementary pension schemes	N/A, no supplementary pension schemes provided

R21 - Stock-options and free share grants	Yes
R22 - Review of critical issues	Yes

<sup>(1)</sup> The internal rules of the Board of Directors will be amended at a forthcoming Board meeting to provide for a three-year training plan for directors.

<sup>(2)</sup> Chairmanship of the Compensation Committee has been entrusted to BP. It is planned to change the Chairmanship of the Remuneration Committee after the General Meeting scheduled in June 2022 to approve the financial statements for 2021.

<sup>(3)</sup> A specialized committee on corporate social responsibility (CSR) will be set up in 2022, chaired by an independent director. The internal rules of the Board of Directors will be amended accordingly to take account of the creation of this new committee.

### 3.1.1. Methods of corporate governance

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 3.1.4 'Operation of the governing and management bodies'.

### 3.1.2. Members of the Board of Directors

As of the filing date of this universal registration 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
Mr. Gérard Soula	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 May 28, 2020 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, 2022.
				Renewed as chairman and chief executive officer by the board of directors' meeting held on May 28, 2020 for the duration of his term of office as director.
Mr. Olivier Soula	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 May 16, 2019 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, 2021.
				Renewed as deputy chief executive officer by the board of directors' meeting held on May 28, 2020 for the duration of his term of office as director.

Mr. Olivier Martinez	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 May 16, 2019 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, 2021.
BPI France Investissement, represented by Mr. Laurent Arthaud	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 May 28, 2020 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, 2022.
Ms. Ekaterina Smirnyagina	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 May 16, 2019 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, 2021.
Dr. Katherine Bowdish	Independent Director	-	Chairman and Chief Executive Officer of Pics Therapeutics, Inc.	Appointed independent director by the shareholders' meeting held on May 20, 2021 for a three-year term which will expire at the conclusion of the shareholders' meeting convened to vote on the financial statements for the fiscal year ending December 31, 2023.
Dr. Claudia Mitchell	Independent Director	-	Senior Vice-President Strategy-Portfolio at Astellas Pharma	Appointed independent director by the shareholders' meeting held on May 20, 2021 for a three-year term which will expire at the conclusion of the shareholders' meeting convened to vote on the financial statements for the fiscal year ending December 31, 2023.
Monsieur Stéphane Boissel	Independent Director	-	Chairman of the Board and Chief Executive Officer of Sparing Vision	Appointed independent director by the shareholders' meeting held on May 20, 2021 for a three-year term which will expire at the conclusion of the shareholders' meeting convened to vote on the financial statements for the fiscal year ending December 31, 2023.

Ms. Dominique Takizawa resigned from her position as Company director with effect from May 20, 2021 and, at the date of this document, no longer holds any position within the Company.

### 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. Ekaterina Smirnyagina, c/o Capricorn Venture Partners, De Jonge Saint Jacob, Lei 19/1-B-3000 Leuven, Belgium.
- Ms. Claudia Mitchell, c/o Astellas Pharma, Nihonbashi-Honcho, Chuo-ku, Tokyo;
- Ms. Katherine Bowdish, c/o Pics Therapeutics, 22 Strathmore Rd, Natick, 01760, Massachusetts; and
- Mr. Stéphane Boissel, c/o SparingVision, 5/7 avenue Percier, CS40230, 75008 Paris.

## 3.1.2.2. Other corporate offices currently held by the directors

Name	Office held	Company
Mr. Gérard Soula	Director	Glowbl
Mr. Olivier Soula	Chairman of the board of directors	Glowbl
Mr. Olivier Martinez	Permanent representative of Bpifrance Investissement Board observer	Amolyt Pharma
	Permanent representative of Bpifrance Investissement Director	HalioDx
	Board observer	Innate Pharma
	Permanent representative of Bpifrance Investissement Board observer	Abionyx
	Member of the supervisory board	Emergence Therapeutics
Mr. Laurent Arthaud	Member of the supervisory board	Kurma Partners
	Director	Collectis SA
	Director	Sparingvision SA
	Director	Aledia SA
	Director	Calyxt Inc.
	Director	Enyo Pharma SA.
Ms. Ekaterina Smirnyagina	Director	Istar Medical SA (Belgique)
	Director	ConfoTherapeutics NV (Belgique)
	Director	InvestEurope (Belgique)
	Director	HalioDx (France)
Dr. Katherine Bowdish	President and Chief Executive Officer	Pics Therapeutics, Inc. (USA)
Dr. Claudia Mitchell	Chairman of the Board	Reaction
	Director	Alliance for regenerative Medicine
	Director	Chambre de commerce internationale France Japon
Monsieur Stéphane Boissel	Chairman of the Board and Chief Executive Officer	Sparing Vision
	Director	Eg427

In line with recommendation no. 1 of the MiddleNext Code, executive directors do not hold more than two other offices, including in foreign companies.

### 3.1.2.3. Other corporate offices, now expired, held by the directors during the last five fiscal years

Name	Office held	Company
Mr. Gérard Soula	Director	Life Cycle Pharma A/S
Mr. Olivier Soula	None	None
Mr. Olivier Martinez	Director	Cerenis Therapeutics
	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
	Board observer	Millendo Therapeutics Inc.
Mr. Laurent Arthaud	Director	Scynexis Inc.
	Member of the supervisory board	Emertec gestion SA
	Director	Calyxt Inc.
	Board observer	TxCeLL
Ms. Ekaterina Smirnyagina	Director	Nexstim plc (FINLANDE)
Madame Dominique Takizawa	Director, audit committee chairman and investment committee member	April Group
	Director and chairman	ElsaLys (*)
	Director and audit committee member	Theradiag
	Director and audit committee member	Mérieux Nutrisciences (USA) (*)
	Director and audit committee member, Permanent representative	Transgène (*)
	Permanent representative	Lyon Place Financière
Dr. Katherine Bowdish	Board observer	Dice Molecules (USA)
	Vice-President of the Board	Warp Drive Bio (USA)
	Director	Portal Instrument Inc. (USA)
	Director	Thermalin Inc. (USA)
Dr. Claudia Mitchell	Director	Universal Cells
	Director	Chambre de Commerce Franco-Americaine
Monsieur Stéphane Boissel	Chief Executive Officer	TxCeLL
	Chairman of the Board	Elsalys Biotech

### 3.1.2.4. Biographies of the directors

**Gérard Soula** PhD, 76 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, 51 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 over 40 patents.

**Olivier Martinez**, 50 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**, 58 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.

**Dominique Takizawa**, 64 years old, retired, has held the office of Secretary General of Institut Mérieux from 2006 to 2020. She joined Mérieux 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 Mérieux Connaught (since renamed Sanofi Pasteur), Rhône Mérieux/Mérial etc..

Dominique Takizawa is a graduate of the HEC Business School and holds a degree in Accounting and Financial Studies (DECF).

**Ekaterina Smirnyagina**, 54 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.

**Stéphane Boissel** is currently Chairman and CEO of SparingVision, a genomic medicine company in ophthalmology.

He was previously Executive Vice President of Corporate Strategy at Sangamo Therapeutics, based in San Francisco (USA). He joined Sangamo Therapeutics on the back of the acquisition by the latter of TxCell SA, a CAR-Treg company he was the CEO of. He is a seasoned biotech professional with over 25 years of leadership experience across corporate

finance, strategy and business development. He completed his undergraduate work in management and finance at the University of Lyon and Paris-Dauphine in France and received his MBA from the University of Chicago (IL, USA).

**Katherine Bowdish** is the President & CEO of PIC Therapeutics, a venture-backed precision-medicine company focused in oncology.

From 2013 to 2020, she worked for Sanofi to establish and lead Sanofi Sunrise, a venture investment/company co-creation and partnering vehicle focused on advancing pioneering science of strategic interest to Sanofi. Following a 5-year span leading Sunrise, Kathy accepted the role of Vice President and Head of R&D Strategy. Prior to Sanofi, she co-founded or led several early-stage life science companies focused on biological therapies. Past positions include Co-founder, President & CEO, Anaphore; President, Alexion Antibody Technologies and Senior Vice President, Alexion Pharmaceuticals; Founder, CEO & CSO, Prolifaron, prior to its acquisition by Alexion. She holds a Ph.D. in molecular genetics from Columbia University College of Physicians and Surgeons in the City of New York, and a B.S. degree in biology from the College of William and Mary.

**Claudia Mitchell** is the Senior VP, Head of Portfolio Strategy, at Astellas Pharma.

She was the CEO and co-founder of Universal Cells, a Seattle-based biotech company, until the company was acquired by Astellas. She has previously co-founded Halo-Bio RNAi Therapeutics and served as its Chief Scientific Officer. She received the EY Entrepreneur of the Year award in Life Sciences for the Pacific NW Region in 2018. Besides being a biotech entrepreneur, she has also held positions in the non-profit sector and in Academia. She worked as the Program Director at the LGMD2I Research Fund, a family non-profit foundation, and has held a tenured Academic research position at the French National Institute of Medical Research (INSERM). She has a PhD in Molecular Biology from the University of Paris and an MBA in International Management from the Ecole des Ponts Business School, Paris, France.

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### 3.1.3. Retained principles for composition of the board

#### 3.1.3.1. Gender balance

Three of the Board's eight 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.

#### 3.1.3.2. 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;

- be neither an employee or executive officer of the Company, nor an employee or executive officer of one of the companies in his group and have not been in the past 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.

The Board of Directors considered that four of its members, namely Ms. Ekaterina Smirnyagina, Ms. Katherine Bowdish, Ms. Claudia Mitchell and Mr. Stéphane Boissel, met all of these criteria and therefore qualified as independent members of the Board of Directors.



Annually, the Board of Directors reviews the situation of its members with respect to the above criteria on a case-by-case basis.

### 3.1.3.3. 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.

### 3.1.3.4. 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.

### 3.1.3.5. Choice of Directors

When a Director is appointed or reappointed, information on his or her experience, skills and offices held is published in the universal registration document and presented to the Shareholders' Meeting. This information is also published on the Company website, in line with recommendation no. 10 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 3.1.2.4 "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 not been called into question or be penalized by official public sanction pronounced by statutory or regulatory authorities (including designated professional bodies); and
- has been deprived by a court of the right to exercise the function of member of an administrative, management or supervisory body of an issuer or to intervene in the management or the conduct of the affairs of a transmitter

There are no service contracts between the members of the Company's Board of Directors or officers and the Company.

### 3.1.4. Operation of the governing and management bodies

#### 3.1.4.1. 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. 9. 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. An update is planned for 2022 during an upcoming meeting of the board in order to provide a three-year training plan for directors, in compliance with recommendation no.5 of the MiddleNext Code.

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.

#### 3.1.4.2. 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 five meetings (in line with recommendation no. 6 of the MiddleNext Code), on March 18, May 20, September 7, October 7, and December 16, 2021. The Chairman of the board chaired all 5 meetings, and the attendance rate was 100%.

The following main points were addressed at the meetings:

- impact of the health crisis on the Company's activity and its prospects;
- updates on Company financing;
- opportunity to a complementary financing and potential alternatives (discussion over a stock loan with IPF partners and conclusion of an agreement);
- follow up in regard to the legal proceedings against Eli Lilly (arbitrations and civil action);
- current negotiations with potential partners;
- progress reports on projects and main results;

- financial matters: quarterly reviews, 2021-2022 two-year plan, examination and closure of 2020 corporate financial statements and consolidated financial statements, presentation and approval of 2022 budget;
- convocation of the General Shareholders' Meeting: agenda and wording of resolutions.
- items relating to compensation, governance, review of the composition of the Audit Committee, issue of share warrants to new directors, determination of variable compensation for the Chairman and Chief Executive Officer and the Deputy Chief Executive Officer for fiscal year 2021, the compensation policy for non-executive directors, allocation of free shares to employees of the Company, determination of compensation allocated for a directorship; and
- 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;

In 2021, in line with recommendation no. 17 of the MiddleNext Code, discussions have taken place within the Compensation Committee on the succession plan for the Company's executives. Actions have been identified to ensure a successful succession and identify key people in the organization, and support them in their development to ensure the succession of Olivier Soula in his current position of R&D director. The summary of this work was reported to the Board of Directors.

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 fiscal year 2017, the Board carried out a self-assessment of its composition, organization, and operating procedures by sending and commenting on the questionnaire sent to the Board members. Another self-assessment is planned in 2022.

Lastly, it is noted that, following recommendation no. 14, despite a context still marked by the sanitary crisis, Management has given minority shareholders the opportunity to meet with them and discuss the Company's progress in 2021, on several occasions: the annual general meeting held in person at the Company's headquarters on May 20, 2021, and at the shareholders' and investors' meetings in Paris (Investir Day in November 2021, Investor Access in September 2021). The Board of Directors also pays particular attention to the votes cast by all its shareholders, in particular the majority of minority shareholders. Thus, at its meeting on April 14, 2022, the Board analyzed the negative votes cast on the various resolutions presented at the previous General Meeting.

### 3.1.4.3. Organization of committees

In line with recommendation no. 7 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. The Company plans to entrust the Chairmanship of the Compensation Committee to an independent director at the Board meeting to be held after the General Meeting scheduled for June 28, 2022

#### ▪ 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:

- Mr. Stéphane Boissel, independent member with financial and accounting expertise, and
- Mr. Olivier Martinez, Director.

Mr. Stéphane Boissel has chaired this committee since May 20, 2021, replacing Mrs. Takizawa who resigned from her position as director. Mr. Stéphane Boissel is the member of the Board "with specific financial or accounting skills", due to his experience of more than 20 years in the pharmaceutical industry and the general management and financial management positions he held at InnatePharma, Transgene and TxCell, and his role as Chairman and Chief Executive Officer at Sparing Vision.

The audit committee met twice during fiscal year 2021, on March 12 (under the chairmanship of Ms. Takizawa) and on September 2, 2021 (under the chairmanship of Mr. Stéphane Boissel). 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 once in 2021: on November 23, 2021.

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 allotted to the members of the Board of Directors as remuneration fees on the board and its committees and its distribution 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.

### 3.1.5. Conflicts of interest at the level of the governing and management bodies

The Chairman and the directors are direct or indirect shareholders of the Company (see section 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*) (see section 5.4.5 of the present universal registration document).

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.

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#### 3.1.6. Modalities of participation in the general meeting of shareholders or provision of the articles of association that provides for such modalities

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There are no specific provisions for the participation of shareholders to the shareholders' meeting other than those provided for in article 19 of the bylaws (see chapter 5.3.1 of this universal registration document).

#### 3.1.7. Information that is likely to have an impact in the event of a public offering

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Pursuant to Article L.22-10-11 of the French Commercial Code, the points likely to have an impact in the event of a public offer are specified below:

- Shareholder structure of the Company : See Chapter 5 of this universal registration document.
- 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.
- 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.
- 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.
- 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.
- Shareholder agreements of which the Company is aware that may impose restrictions on share transfers and exercising voting rights: none.
- 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.
- Powers of the Board of Directors, in particular the power to issue or redeem shares
- The general shareholders' meeting held on May 20, 2021 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 universal registration document) and,

- issue shares by capital increasing under the conditions defined below in paragraph 3.2.8.
- Agreements entered into by the Company that will be amended or terminated in the event of a change of control of the Company: none.
- 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.

### 3.1.8. Summary table of valid delegations granted by the shareholders' general meeting in matters of capital increase

Nature of the delegation or the authorisation	expiration date	Ceiling (nominal value)	Modalities of the price	Dates and modalities that may be used by the board of directors
<b>Date of the annual shareholder's meeting: May 16, 2019</b>				
Authorization given to the Board of Directors to grant options to subscribe or purchase shares of the Company	38 months July 15 2022	200,000 shares within the limit of 10% of the capital at the time of allocation (1)	n/a	The board made use of this authorization by issuing: 5,700 shares on December 16, 2021
<b>Date of the annual shareholder's meeting: May 28, 2020</b>				
Delegation of competence to the Board of Directors with a view to increasing the capital immediately or in the long term by issuing ordinary shares and/or transferable securities with the maintenance of the shareholders' preferential subscription right	26 months July 27 2022	383,000€ (3)	n/a	The board did not use this authorization
<b>Date of the annual shareholder's meeting: May 20, 2021</b>				
Authorization to be granted to the Board of Directors to reduce stated capital by cancelling shares pursuant to the authorization for the Company to purchase its own shares (16 <sup>th</sup> resolution)	18 months November 19 2022	within the limit of 10% of the capital at the time of allocation	n/a	The board did not use this authorization
Delegation of authority to be granted to the Board to increase capital by issuing common shares and/or equity securities without a preemptive subscription right for shareholders and offer to the public apart from the offers referred to in paragraph 1 ° of Article L. 411-2 of the Commercial Code (17 <sup>th</sup> resolution)	26 months July 19 2023	137,000 € (3)	(4)	The board did not use this authorization
Delegation of authority to be granted to the Board to increase capital by issuing common shares and/or equity securities without a preemptive subscription right for shareholders to be issued in regards to I of Article L. 411-2 of the French Monetary and Financial Code and offer to the public), (18 <sup>th</sup> resolution)	26 months July 19 2023	137,000 € (3)	(4)	The board did not use this authorization
Authorization to be granted to the Board to determine the issue price for up to 10% of stated capital, if shares or any equity securities are issued without a preemptive subscription right for shareholders, as set in the seventeenth and eighteenth resolutions (19 <sup>th</sup> resolution)	26 months July 19 2024	within the limit of 10% of the capital (3)	(5)	The board did not use this authorization
delegation of authority to be granted to the Board to increase capital immediately or in the future by issuing common shares	18 months Nov 19 2022	137 000€ (3)	(7) (3)	By decisions dated October 26, 2021, acting on delegation of the Board of Directors, made use of this delegation

Nature of the delegation or the authorisation	expiration date	Ceiling (nominal value)	Modalities of the price	Dates and modalities that may be used by the board of directors
and/or equity securities giving access to capital, without a preemptive subscription right for shareholders, in favor of certain categories of persons (20 <sup>th</sup> resolution)				and decided (i) to issue, at a unit price of 9.26 euros, 107,992 new shares, the subscription of which was reserved for Mr. Gérard Soula, representing a capital increase of a nominal amount of 10.10,799.20 and (iii) the issue of 6,568,422 convertible bonds (OC1023) to the benefit of 3 European investors, representing a total loan of EUR 6,240,000.90, convertible into a maximum number of 1,262,008 shares, representing a capital increase of a maximum nominal amount of EUR 126,200.80
delegation of authority to be granted to the Board to increase capital by issuing common shares and/or equity securities, without a preemptive subscription right for shareholders, in favor of a certain category of persons ensuring the underwriting of Company's equity securities within a specific equity or bond financing program (21 <sup>st</sup> resolution)	18 months Nov 19 2022	137,000€ (3)	n/a	The board did not use this authorization
delegation of authority granted to the Board of Directors to increase capital by issuing common shares with or without a preemptive subscription right (22 <sup>nd</sup> resolution)	26 months July 19 2023	15% of the initial issuance (3) (7)	Same price than the initial issuance	The board did not use this authorization
delegation of authority granted to the Board of Directors to issue common shares and/or equity securities as part of a public offer comprising an exchange component initiated by the company (23 <sup>th</sup> resolution)	26 months July 19 2023	68.000€ (3)	n/a	The board did not use this authorization
delegation of authority granted to the Board of Directors to decide to issue common shares and/or equity securities giving immediate or deferred access to shares or other equity securities of the Company, to remunerate shares or marketable securities (24 <sup>th</sup> resolution)	26 months July 19 2023	€68,000 in a limit of 10% of the capital /year (3)	n/a	The board did not use this authorization
delegation of authority granted to the Board of Directors to issue and attribute warrants for shares, without a preemptive subscription right for shareholders, to the profit of three types of persons, (26 <sup>th</sup> resolution)	18 months Nov 19 2022	200.000 BSA for the issuance of 100,000 shares (1)	(8)	The Board made use of this delegation on May 20, 2021 by granting 10,215 warrants to the new directors appointed on May 20, 2021
delegation of authority granted to the Board of Directors to grant options to subscribe for or purchase Company shares (27 <sup>th</sup> resolution)	38 months July 19 2024	200,000 shares (1)	(2)	The board did not use this authorization
delegation of authority granted to the Board of Directors to increase the share capital through the capitalization of share premiums, profits or other amounts (29 <sup>th</sup> resolution)	26 months July 19 2023	€100 000)	n/a	The board did not use this authorization



(1) The number of shares that may be allocated will be deducted from the ceiling of 250,000 shares referred to in the twentieth resolution of the General Meeting of May 17, 2028, it being specified that the sum of (i) the shares that may be issued or acquired on the exercise of options allocated, (ii) the shares that may be allocated free of charge, (iii) the shares that may be issued on the exercise of warrants to subscribe for business creator shares and (iv) the shares that may be issued on the exercise of warrants to subscribe for shares, shall not exceed 250,000 shares, it being specified that the additional amount of shares to be issued to preserve the rights of holders of securities and other rights giving access to shares, in accordance with the applicable contractual provisions, shall be added to this ceiling

(2) The maximum aggregate ceiling authorized for this capital increase in nominal value is set at € 210,000. The total nominal amount of issues of securities representing claims on the Company giving access to the Company's capital may not exceed €50,000,000; Compensation and benefits received by officers and directors

(3) These amounts are not cumulative. The maximum aggregate ceiling for capital increases in nominal value is set at €300,000. The total nominal amount of the issues of debt securities may not exceed € 50,000,000;

(4) The issue price will be set by the Board of Directors, in accordance with the provisions of Articles L. 22-10-52 and R. 22-10-32 of the Commercial Code (as an indication at the date of this universal registration document, the issue price of the shares must be at least equal to the weighted average of the prices of the last three stock exchange sessions preceding the beginning of the offer, possibly reduced by the discount authorized by the legislation (i.e., currently 10%)) and corrected in case of difference in the date of enjoyment, it being specified that the issue price of the securities giving access to the capital will be such that the amount received immediately by the Company, plus the amount that may be received subsequently by it, is, for each share issued as a result of the issue of these securities, at least equal to the issue price defined above;

(5) Within the limit of 10% of the Company's capital stock (as it exists on the date of the transaction) per 12-month period, the Board of Directors may derogate from the conditions for setting the price provided for above and set the issue price of the ordinary shares and/or securities giving immediate or future access to the capital issued, in accordance with the following terms and conditions

- the issue price of the ordinary shares shall be at least equal to the weighted average of the prices for the last three trading sessions preceding its setting, possibly reduced by a maximum discount of 20%, it being recalled that it may not in any event be less than the par value of a share in the Company on the date of issue of the shares concerned, it being specified that in the event of the issue of securities giving access to the capital, the issue price of the shares likely to result from their exercise their conversion or exchange may be set, at the discretion of the Board of Directors, by reference to a calculation formula defined by the Board and applicable after the issue of the said securities (for example on their exercise, conversion or exchange), in which case the maximum discount referred to above may be assessed, if the Board deems it appropriate, on the date of application of the said formula (and not on the date on which the issue price is set), and

- the issue price of the securities giving access to the capital shall be such that the amount received immediately by the Company, plus any amount that may be received subsequently by the Company, shall be, for each share issued as a result of the issue of such securities, at least equal to the issue price defined in the paragraph above,

(6) 15% or any other fraction that may be determined by decree.

(7) The issue price of the shares shall be at least equal to the volume-weighted average of the prices quoted for the shares over the three trading days preceding the setting of the issue price, less a maximum discount of 20%, if applicable, taking into account the date from which the shares carry dividend rights; it being specified that (i) in the event of the issue of securities giving access to the capital, the issue price of the shares likely to result from their exercise, conversion or exchange may, where appropriate, be set, at the discretion of the Board of Directors, by reference to a calculation formula defined by the latter and applicable after the issue of the said securities (for example when they are exercised, converted or exchanged), in which case the above-mentioned maximum discount may be assessed, if the Board deems this appropriate, (ii) the issue price of the securities giving access to the capital, if any, issued under this resolution shall be such that the amount received immediately by the Company, if any, plus the amount that may be received by the Company upon exercise or conversion of such securities, shall be, for each share issued as a result of the issue of such securities, at least equal to the minimum amount referred to above.

(8) The issue price of a warrant will be determined by the Board of Directors on the day of issue of the warrant, depending on the characteristics of the warrant, if necessary with the assistance of an independent expert, and will be at least equal to 15% of the average of the volume-weighted prices of the last five (5) trading sessions on the regulated market of Euronext Paris preceding the date of allocation of the warrant by the Board. The subscription price of an ordinary share of the Company upon exercise of a warrant will be determined by the Board of Directors at the time of the grant of the warrants and must be at least equal to the higher of the following two values

- the closing price of a share on the regulated market on the day preceding the Board's decision to grant the warrants; and

- the weighted average of the prices quoted on the twenty trading days preceding the day of the Board's decision to allocate the warrants;

(9) The purchase or subscription price per share will be set by the Board of Directors on the day the option is granted within the limits provided for by law and the resolution, without being less than ninety-five percent (95%) of the average of the prices quoted on the twenty trading days preceding the day of the Board's decision to grant the options, rounded down to the nearest euro, or, in the case of stock options, 80% of the average purchase price of the Company's own shares, rounded down to the nearest euro.

## 3.2 Compensation and benefits received by officers and directors

### 3.2.1. Compensation paid to corporate officers

All tables are made in reference to MiddleNext Code. Templates mentioned in appendix 2 of the AMF Recommendations n° 2021-02 are presented below.

### 3.2.1.1. Breakdown of compensation, stock options and bonus shares granted to each corporate officer

It is specified that all remunerations are in accordance with the remuneration policy approved by the shareholders in the *ex ante* vote.

<i>In € thousands IFRS</i>	<b>FY 2021</b>	<b>FY 2020</b>
<b>Gérard Soula - Chairman and chief executive officer</b>		
Compensation due in respect of the year <sup>(1)</sup>	485 620	372 518
Value of the multi-yearly variables compensation granted during the year	none	none
Value of the BSPCE founders' warrants granted during the year <sup>(2)</sup>	none	none
Value of the bonus shares granted during the year <sup>(2)</sup>	none	none
Value of the other long term compensation plans	none	none
<b>TOTAL</b>	<b>485 620</b>	<b>372 518</b>

<sup>(1)</sup> including benefits in kind (see section 3.2.1.2 "Summary table of the remuneration of each executive director" below).

<sup>(2)</sup> For more details, see section 3.2.1.3 "Stock Compensation Details (AGA, BSPCE, BSA and SO)" below

<i>In € thousands IFRS</i>	<b>FY 2021</b>	<b>FY 2020</b>
<b>Olivier Soula - Deputy chief executive officer</b>		
Compensation due in respect of the year <sup>(1)</sup>	344 043	283 990
Value of the multi-yearly variables compensation granted during the year	none	none
Value of the share subscription or purchase options granted during the year <sup>(2)</sup>	none	none
Value of the bonus shares granted during the year <sup>(2)</sup>	none	none
Value of the other long term compensation plans	none	none
<b>TOTAL</b>	<b>344 043</b>	<b>283 990</b>

<sup>(1)</sup> It is specified that all of the compensation elements paid to Mr. Olivier Soula are paid under his employment contract and in his capacity as R&D director. (see section 3.2.1.2 "Summary table of the remuneration of each executive director" below).

<sup>(2)</sup> For more details, see section 3.2.1.3 "Stock Compensation Details (AGA, BSPCE, BSA and SO)" below.

### 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, 2021 and December 31, 2020, as well as the compensation such persons received during those same fiscal years.

<i>In € thousands IFRS</i>	<b>FY 2021</b>		<b>FY 2020</b>	
	<b>Amounts owed (1)</b>	<b>Amounts paid (2)</b>	<b>Amounts owed (1)</b>	<b>Amounts paid (2)</b>
<b>Gérard Soula - Chairman and chief executive officer</b>				
Fixed compensation	364 130	364 130	364 130	364 130
Variable yearly compensation *	115 000	none	none	none
Variable multi year compensation*	none	none	none	none
Extraordinary compensation	none	none	none	none
Directors' fees	none	none	none	none
Non-cash benefits *	7 913	7 913	8 388	8 388
<b>TOTAL</b>	<b>487 043</b>	<b>372 043</b>	<b>372 518</b>	<b>372 518</b>

In € thousands IFRS	FY 2021		FY 2020	
	Amounts owed (1)	Amounts paid (2)	Amounts owed (1)	Amounts paid (2)
Olivier Soula - Deputy chief executive officer				
Fixed compensation (including paid vacation)	279 043	279 043	281 490	281 490
Variable yearly compensation *	65 000	none	none	none
Variable multi year compensation	none	none	none	none
Extraordinary compensation *	none	none	none	none
Invention premium	none	none	2 500	2 500
Directors' fees	none	none	none	none
Non-cash benefits *	none	none	none	none
<b>TOTAL</b>	<b>344 043</b>	<b>179 043</b>	<b>283 990</b>	<b>283 990</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.

M. Gérard Soula benefits from a single benefit in kind corresponding to a company car.

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. Details of the compensations in the form of shares

- **BSPCE, BSA or SO granted to each executive corporate officer during the fiscal years 2020 and 2021 to each executive corporate officer**

No profit-sharing instruments were granted to any of the Company's executive directors during fiscal years 2020 and 2021.

To be noted that, at its meeting on May 20, 2021, the Company's Board of Directors decided to issue 13,500 warrants to three of its independent directors, namely Mrs. Claudia Mitchell, Mrs. Katherine Bowdish and Mr. Stéphane Boissel (see in this respect section 3.2.4.2 of this Registration Document)

- **BSA or BSPCE or SO exercised during the fiscal years 2021 and 2020 by each executive corporate officer**

None.

- **Bonus shares granted to each executive corporate officer during the fiscal years 2021 and 2020**

None.

- Bonus shares that have become available to each corporate officer during the fiscal years 2020 and 2021

Full Year	Executive corporate officer name	Plan date and number	Number of available shares	Performing conditions	Vesting date
2020	Olivier SOULA	2016 Plan corporate Officers board as of 03/15/2016	2 000	no	March, 15 2020

The 2,000 AGMs were definitively acquired by the individual on March 5, 2020, but remain subject to a one-year retention period expiring on 15 March 2021. AGMs are not subject to any performance requirements or resale obligations.

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## 3.2.1.4. History of BSA stock warrants awarded to each corporate officer

	Plan 2015 Managers	Plan 2016 Managers		Plan 2018 N°2.2	Plan 2019 n°2.2
Date of the board meeting	12/16/2015	03/15/2016		05/17/2018	12/10/2019
Total Number of free granted shares	5 000	8 000	12 000	150	400
Beneficiary	Olivier Soula	Olivier Soula	Olivier Soula	Olivier Soula	Olivier Soula
Date of the definite acquisition of the 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 if achievement of performance criteria	05/17/2020	12/10/2020
Retention period end date	12/16/2017	2 000 : 15/03/2018 2 000 : 15/03/2019 2 000 : 15/03/2020 2 000 : 15/03/2021	15/03/2018	05/17/2020	12/10/2021
Number of shares acquired at the end of the financial year	5 000	8 000	4 000	150	400
Cumulative number of canceled or lapsed shares	none	None	8 000		
Free shares granted during the acquisition at the end of the financial year	0	0	0	0	0

- History of Warrants, BSPCE and/or SO founders' warrants awarded to each corporate officer

At the date of the present document, only BSPCE were attributed to each corporate officer.

	Plan 2014 Managers	BSPCE Managers 2015	BSPCE Managers 2016	BSPCE Managers 2017
AGM date	06/24/2014	12/11/2015	12/11/2015	12/11/2015
Board date	09/25/2014	16/12/2015	15/03/2016	08/09/2017
Nber of BSPCE authorized	100 000	40 000	40 000	150 000
Nber of BSPCE issued	100 000	40 000	40 000	150 000
Total nber of shares that can be subscribed	100 000	40 000	40 000	150 000
Of which by Gérard Soula	20 000	40 000	40 000	75 000
Of which by Olivier Soula	45 000	-	-	75 000

	achievement of performance criteria validated by the Board on 12/23/2014	achievement of performance criteria validated by the Board on 12/16/2015	achievement of performance criteria validated by the Board on 12/13/2016	achievement of performance criteria defined for 3 years
Starting date of exercise				
Expiry date	09/24/2024	12/16/2025	03/15/2026	09/08/2027
Issuance price	free	free	free	free
Exercise price (euros)	34.99	74.60	61.73	16.00
Conditions of exercise	Immediate vesting as soon as the criteria are met	Immediate vesting as soon as the criteria are met	Immediate vesting as soon as the criteria are met	Immediate vesting as soon as the criteria are met
Nber of shares subscribe at the end of year	0	0	0	0
Most recent date of subscription				
Nber of BSPCE caduc or cancelled	35 000	0	16 000	100 000
Most recent date of cancellation of BSPCE subscribed	october-19		december-16	december-20
BSPCE remaining at the end of the year	65 000	40 000	24 000	50 000
Total nber of shares that can be subscribed at 12/31/2021	65 000	40 000	24 000	50 000
Maximum total number of shares that may be subscribed upon exercise of all outstanding BSPCEs as of December 31, 2020, assuming fulfillment of all conditions for the exercise of said BSPCEs)	65 000	40 000	24 000	50 000

#### 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, then May 28, 2020 and as president & CEO on May 28, 2020							
Term of office end date	Ordinary general shareholders' meeting convened to vote on the financial statements for the fiscal year ending December 31, 2022							
<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, of June 27, 2017, and May 16, 2019 and as Deputy general director on May 28, 2020							
Term of office end date	Ordinary general shareholders' meeting convened to vote on the financial statements for the fiscal year ending December 31, 2021							

#### Equity ratio between the level of compensation of the two executive corporate officers and the average and median compensation of the employees of the Company

The Company complies with the provisions of Article L. 225-37-4 6° of the French Commercial Code relating to the diversity policy applied to members of the Board of Directors with regard to criteria such as age, gender or professional qualifications and experience. Consequently, the Company's directors come from a variety of backgrounds, both in terms of geographical origin (France, United States, Japan) and experience. They range in age from 50 to 65, with an average age of 58.

The Board of Directors ensures diversity of expertise and age not only among its members, but also within the Company. The Company's policy takes particular care to ensure gender balance, both overall (57 women and 55 men

as of December 31, 2021) and at each level of the company (Management Committee, Operational Committee and appointments to senior and/or expert positions).

In accordance with the terms of the article n ° 2019-486 of the French commercial Code the equity ratios were calculated on the basis of fixed, variable and exceptional compensation paid within of the Company during the fiscal years mentioned:

		2021 year	2020 Year	2019 Year
Gérard Soula CEO	Ratio with average compensation	6,3	6,0	6,0
	Ratio with median compensation	7,3	6,9	6,9
	Ratio with Minimum Growth Wage (SMIC) of the year in question	19,4	19,7	19,6
Olivier Soula Deputy general director	Ratio with average compensation	4,8	4,7	4,8
	Ratio with median compensation	5,6	5,4	5,5
	Ratio with Minimum Growth Wage (SMIC) of the year in question	14,9	15,4	15,6

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### 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, 2021, the Company recognized provisions of €181,997 for the payment of retirement benefits to Olivier Soula. (see note 11 appearing in appendix to the consolidated accounts established according to IFRS standards of the Company appearing chapter 4.1 of this document of universal registration) With the exception of the above, the Company has not provisioned sums for the purpose of payment of pensions, retirement and other benefits for the benefit of its members of the management and the board of directors.

The Company has not granted Mr. Soula any hiring or termination bonuses.

### 3.2.3. Compensation policy for corporate officers

#### 3.2.3.1. Compensation policy for corporate officers for the 2021 fiscal year

In accordance with Article L.22-10-8 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 2021 fiscal year the compensation policy for the corporate officers.

These principles and criteria, which were determined by the Board of Directors during the session of the board as of December 16, 2021, on the basis of recommendations by the Compensation Committee, are set out below:

- **For the members of the Board, excluding the Chief Executive Officer and the Deputy General Manager**

The members of the board of directors can receive:

- remunerations for specific missions which could be entrusted to them by the board of directors and would be the subject of regulated agreements which would be submitted to the vote of the general meeting of shareholders. The amount of this compensation will be set by the board of directors according to the nature of the specific mission entrusted to the administrator;
- a global annual fixed sum set by the general meeting of shareholders. The board of directors determines (within the limit of the envelope voted by the general meeting) the amount due to each director

according to the principles described below, it being specified that only independent directors receive compensation:

- participation in the Board of Directors: lump sum of 6,000 euros per meeting for a physical presence and 50% or 3,000 euros for a telephone or virtual participation. In the context of the Covid pandemic, and given the difficulties of travelling, the amount of virtual participation is increased to 4,500 euros,
- Chairing a committee: lump sum of 10,000 euros per meeting for a physical presence 50% or 5,000 euros for a telephone or virtual participation. Within the framework of the Covid pandemic, and taking into account the difficulties to travel, the amount of the virtual participation is raised to 7,500 euros.

The maximum amount of total compensation allocated annually to directors was set by the combined general meeting of May 20, 2021 at 200,000 euros.

Travel expenses are reimbursed for each actual presence on presentation of an expense report.

Finally, directors who are not employees or managers of the Company or one of its subsidiaries could be offered the option of subscribing, at market conditions, to share subscription warrants whose price issue date will be determined on the day of issue of the vouchers according to their characteristics, if necessary with the help of an independent expert.

▪ **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 €364,130 for 2022 (same amount than for 2021)
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.	
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. Olivier 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 €277,797 (impact of paid vacation excluded) for 2022, without any change compared to 2021.
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 bonuses on patents for which he is named 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, under certain conditions.

In accordance with Article L22-10-34 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 2022 fiscal year.

### 3.2.3.2. Approval of compensation owed or awarded to the Chairman and Chief Executive Officer and the Deputy General Manager for the 2021 fiscal year (ex-post vote)

In accordance with Article L22-10-34, sub-section II of the French Commercial Code, at the general shareholders' meeting called to vote on the financial statements for the 2021 fiscal year, the shareholders will be asked to approve the fixed, variable and extraordinary compensation awarded or to be awarded for the 2021 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 20, 2021 in the ninth and tenth resolutions, will be submitted to the approval of the shareholders' meeting that will be held on June 28, 2022, in order to validate the financial statements for the fiscal year 2021.

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## 3.2.4. Compensation and benefits of non- executive corporate officers

### 3.2.4.1. Compensation held by the non-executive corporate officers

The maximum amount of compensation allocated annually to directors was set by the combined general meeting of May 20, 2021 at 200,000 euros.

The total amount actually paid to all directors (non-executive corporate officers) for the 2021 financial year amounted to €68,000 in 2021 compared to € 52,000 in 2020.

Among the non-executive directors, only Ms. Dominique Takizawa and Ekaterina Smirnyagina received directors' fees insofar as the Board of Directors of the Company decided to grant directors' fees only to independent directors.

The amount of compensation paid to some members of the board was calculated in accordance with the compensation policy agreed by the board and approved by the general shareholders' meeting of May 28, 2020 and paid according to the scale contained in Article 3.2.3.1 above).

Travel expenses are reimbursed for each actual presence on presentation of an expense report.

The amounts thus paid to non-executive corporate officers were as follows:

<i>Non- executive corporate officers</i>	sums paid during fiscal year 2021	sums paid during fiscal year 2020
<b>M. Olivier Martinez</b> – Board Administrator		
Compensation for activities on the board and its committees (Article L. 225-45 of the Code of Commerce) (*)	-	-
Other compensation	-	-
<b>Bpifrance Investissement represented by Mr Laurent Arthaud</b> – Board Administrator		
Compensation for activities on the board and its committees (Article L. 225-45 of the Code of Commerce) (*)	-	-
Other compensation	-	-
<b>Mrs Dominique Takizawa</b> - Board Administrator		
Compensation for activities on the board and its committees (Article L. 225-45 of the Code of Commerce) (*)	10 000	30 000
Other compensation	-	-
<b>Mrs Ekaterina Smirnyagina</b> - Board Administrator		
Compensation for activities on the board and its committees (Article L. 225-45 of the Code of Commerce) (*)	29 500	-



Other compensation	-	-
<b>Mrs Katherine Bowdish - Board Administrator</b>		
Compensation for activities on the board and its committees (Article L. 225-45 of the Code of Commerce) (*)	18 000	-
Other compensation	-	-
<b>Mrs Claudia Mitchell - Board Administrator</b>		
Compensation for activities on the board and its committees (Article L. 225-45 of the Code of Commerce) (*)	13 500	-
Other compensation	-	-
<b>Mr Stéphane Boissel - Board Administrator</b>		
Compensation for activities on the board and its committees (Article L. 225-45 of the Code of Commerce) (*)	32 500	-
Other compensation	-	-
<b>TOTAL</b>	<b>103 500</b>	<b>52 000</b>

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### 3.2.4.2. BSA granted to non-executive corporate officers

	BSA 12-2013		BSA 05_2021		
	06/18/2013	18/06/2013	05/20/2021	05/20/2021	05/20/2021
AGM date	06/18/2013	18/06/2013	05/20/2021	05/20/2021	05/20/2021
Board date	12/13/2013	13/12/2013	05/20/2021	05/20/2021	05/20/2021
Nber of BSA authorized	10 000	10 000	200 000	200 000	200 000
Nber of BSA issued	10 000	10 000	4 500	4 500	1 215
Nber of new shares that can be subscribed	10 000	10 000	4 500	4 500	1 215
Name of the beneficiary	Dominique Takizawa	Ekaterina Smirnyagina	Stéphane Boissel	Katherine Bowdish	Claudia Mitchell
Starting point of the exercise	January 1st 2014	January 1st 2014	05/20/2021	05/20/2021	05/20/2021
Expiry date	12/13/2023	12/13/2023	05/19/2031	05/19/2031	05/19/2031
Issuance price (euros)	0.588	0.588	2.87	2.87	2.87
Exercise price (euros)	5.88	5.88	8.93	8.93	8.93
Conditions of exercise	Immediate vesting January 1st, 2014	Vesting on 3 years starting January 1st, 2014	Vesting on 3 years starting May 20, 2021	Vesting on 3 years starting May 20, 2021	Vesting on 3 years starting May 20, 2021
Nber of shares subscribe at the end of year	0	0	0	0	0
Nber of BSA caduc or cancelled	0	0	0	0	0
BSA remaining at the end of the year	10 000	10 000	4 500	4 500	1 215
Maximum total number of shares that may be subscribed	10 000	10 000	0	0	0

### 3.2.4.3. BSPCE and BSA granted and SO granted to the first 10 employees who are not corporate officers, powers and options exercised by them

Options for subscription or purchase of shares granted to the first ten employees who are not corporate officers and options exercised by them	Total number of options allocated / shares subscribed or purchased	Weighted average price (euros)	Plan SO 2018 n°2	Plan SO 2019
Total number of options accumulated at the start of the financial year	21 000	16.57	20 000	1 000
Stock subscription options granted during the financial year				
Options exercised during the fiscal year				
Total number of options canceled during the fiscal year				
Total number of options accumulated at the end of the financial fiscal year	21 000	16.57	20 000	1 000

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BSPCE granted to the first ten employees who are not corporate officers and options exercised by them	Total number of options allocated / shares subscribed or purchased	Weighted average price (euros)	Plan BSPCE 2013	Plan BSPCE 2014
Total number of options accumulated at the start of the financial year	51 000	10.56	42 700	8 400
Stock subscription options granted during the financial year				
Options exercised during the fiscal year	2 800	5.76	2 800	none
Total number of options canceled during the fiscal year	2 800	34.99		2 800
Total number of options accumulated at the end of the financial fiscal year	45 500	9.36	39 900	5 600

### 3.2.5. Summary of the operations of the directors and of the persons mentioned in article L.621-18-2 of the Monetary and Financial Code on the securities of the Company carried out during the past financial year

Persons	Nature of the operation	Date of the operation	Amount (in euros)
G�rard Soula	Subscription	10/28/2021	1 000 005.92
BpiFrance Investissement	Disposal	04/08/2021	36 231.13
BpiFrance Investissement	Disposal	04/02/2021	4 093.74
BpiFrance Investissement	Disposal	04/01/2021	806.4
BpiFrance Investissement	Disposal	03/30/2021	1 415.67
BpiFrance Investissement	Disposal	03/29/2021	43 300.71
BpiFrance Investissement	Disposal	03/26/2021	10 283.08

## 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

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#### 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>74</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 1.4 of the universal reference document.

### 3.3.2. Coordination of risk management with internal control

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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".

### 3.3.3. General principles of internal control

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#### 3.3.3.1. Definition

Adocia has adopted the definition of internal control proposed by the AMF<sup>75</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;

<sup>74</sup> Implementation guide for the reference framework on internal control adapted for midcaps and small-caps and updated on July 22, 2010

<sup>75</sup> Implementation guide for the reference framework on internal control adapted for midcaps and small-caps and updated on July 22, 2010

- 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:

- 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.

### 3.3.4. Limitations on risk management and internal control and areas of improvement

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.

04



# Annual financial statements as of December 31, 2021

## Chapter 4

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## 4 ANNUAL FINANCIAL STATEMENTS AS OF DECEMBER 31, 2021

### 4.1 Consolidated Financial Statements

#### 4.1.1. Consolidated Balance Sheet, IFRS

##### 4.1.1.1. Assets, IFRS

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<i>In (€) thousands</i>	Notes	<b>FY 2021 (12 months)</b>	<b>FY 2020 (12 months)</b>
<b>Current assets</b>		<b>22 084</b>	<b>36 446</b>
Inventories	5	517	569
Trade and similar receivables	6	207	0
Other current assets	7	6 197	7 763
Cash and cash equivalents	8	15 163	28 114
Goodwill amortization		0	0
<b>Non-current assets</b>		<b>1 073</b>	<b>8 720</b>
Other intangible assets	1	3	46
Land	2	0	2 032
Land development	2	0	322
Buildings and constructions	2	0	3 298
Laboratory equipment	2	325	378
Other property, plant and equipment	2	642	2 502
Non-current financial assets	3	102	142
Assets classified as held for sale	2	6 897	0
<b>TOTAL ASSETS</b>		<b>30 054</b>	<b>45 166</b>



## 4.1.1.2. Liabilities and Equity, IFRS

<i>In (€) thousands</i>	Notes	<b>FY 2021 (12 months)</b>	<b>FY 2020 (12 months)</b>
<b>Current liabilities</b>		<b>23 754</b>	<b>10 723</b>
Short-term financial debt	10	16 194	3 014
Trade and similar payables	12	3 835	4 943
Other current liabilities	12	3 724	2 766
<b>Non-current liabilities</b>		<b>20 115</b>	<b>28 110</b>
Long-term financial debt	10	18 285	25 180
Long-term provisions	11	1 521	2 214
Other non-current liabilities	13	309	715
<b>Equity</b>	<b>9</b>	<b>(13 815)</b>	<b>6 334</b>
Share capital		727	702
Share premium		80 562	78 731
Group translation gains and losses		1	(29)
Group reserves		(72 351)	(49 746)
Group net profit/loss		(22 754)	(23 324)
<b>TOTAL LIABILITIES</b>		<b>30 054</b>	<b>45 166</b>

4

## 4.1.2. Consolidated Income Statement, IFRS

<i>In (€) thousands</i>	Notes	<b>FY 2021 (12 months)</b>	<b>FY 2020 (12 months)</b>
<b>Operating revenue</b>		<b>6 055</b>	<b>6 833</b>
Revenue	15	1 444	841
Grants, research tax credits and others	16	4 611	5 992
<b>Operating expenses excluding additions and reversals</b>	<b>14</b>	<b>(24 262)</b>	<b>(26 848)</b>
<b>Additions to and reversals of depreciation, amortization and provisions</b>	<b>19</b>	<b>(1 158)</b>	<b>(1 133)</b>
<b>PROFIT (LOSS) FROM ORDINARY OPERATING ACTIVITIES</b>		<b>(19 366)</b>	<b>(21 148)</b>
Financial income		220	103
Financial expense		(3 608)	(2 250)
<b>FINANCIAL INCOME (LOSS)</b>	<b>20</b>	<b>(3 388)</b>	<b>(2 147)</b>
<b>PROFIT (LOSS) BEFORE TAX</b>		<b>(22 754)</b>	<b>(23 295)</b>
Tax expense	21	0	(29)
<b>NET PROFIT (LOSS)</b>		<b>(22 754)</b>	<b>(23 324)</b>
Base earnings per share (€)	22	(3,2)	(3,3)
Diluted earnings per share (€)	22	(3,2)	(3,3)
<b>GROUP NET PROFIT (LOSS)</b>		<b>(22 754)</b>	<b>(23 324)</b>
Actuarial adjustments on defined pension liabilities	11	363	1 382
<b>Unclassified elements in the Group net profit (loss)</b>		<b>363</b>	<b>1 382</b>
<b>TOTAL PROFIT (LOSS) FOR THE YEAR</b>		<b>(22 390)</b>	<b>(21 942)</b>

## 4.1.3. 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 12/31/2020</b>	<b>7 020 629</b>	<b>702</b>	<b>78 731</b>	<b>(49 901)</b>	<b>126</b>	<b>(23 324)</b>	<b>6 334</b>
Profit for the year 2021	0	0	0	0	0	(22 754)	(22 754)
Gain (losses) on actuarial adjustments on defined pension liabilities	0	0	0	0	363	0	363
Translation adjustment	0	0	0	31	0	0	31
<b>Comprehensive income for the period</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>31</b>	<b>363</b>	<b>(22 754)</b>	<b>(22 359)</b>
Allocation of profit for the year 2019	0	0	0	(23 324)	0	23 324	0
Increase in capital	107 992	11	989	0	0	0	1 000
Increase in capital cost	0	0	0	0	0	0	0
Exercise of equity instruments (OCA 1023)	123 960	12	911	85	0	0	1 009
Exercise of equity instruments (warrants)	18 375	2	14	29	0	0	45
Share-based payment	0	0	0	197	0	0	197
Liquidity Contract - Elimination of treasury shares	0	0	(84)	44	0	0	(40)
Others	0	0	0	0	0	0	0
Total shareholder relations	250 327	25	1 831	(22 968)	0	23 324	2 212
<b>BALANCE AT 12/31/2021</b>	<b>7 270 956</b>	<b>727</b>	<b>80 562</b>	<b>(72 839)</b>	<b>489</b>	<b>(22 754)</b>	<b>(13 815)</b>

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## 4.1.4. Cash Flow Statement, IFRS

<i>In (€) thousands</i>	<b>FY 2021 (12 months)</b>	<b>FY 2020 (12 months)</b>
Net profit	(22 754)	(23 324)
Net depreciation, amortization & provisions (excl. current assets)	1 158	1 198
Capital gains and losses on non-current assets	27	53
Calculated income and expenses	4 791	2 650
Tax paid	0	0
<b>Cash flow from operations before cost of net financial debt and tax</b>	<b>(16 777)</b>	<b>(19 423)</b>
Cost of gross financial debt	(3 303)	(1 423)
<b>Change in deferred revenues</b>	<b>(451)</b>	<b>(736)</b>
<b>Change in working capital requirement (including employee benefits)</b>	<b>1 297</b>	<b>(272)</b>
<b>NET CASH FLOW RELATED TO OPERATING ACTIVITIES</b>	<b>(19 234)</b>	<b>(21 854)</b>
Acquisitions of property, plant and equipment & intangible assets	(361)	(205)
Disposals of property, plant and equipment & intangible assets	0	0
Acquisitions of non-current financial assets	0	0
Disposals of non-current financial assets	0	0
Other cash flows related to investing activities	0	0
<b>NET CASH FLOW RELATED TO INVESTING ACTIVITIES</b>	<b>(361)</b>	<b>(204)</b>
Capital increase	1 042	0
New loans and reimbursable advances	6 000	7 000
Repayments of loans and reimbursable advances	(398)	(488)
Other cash flows related to financing activities	0	0
<b>NET CASH FLOW RELATED TO FINANCING ACTIVITIES</b>	<b>6 644</b>	<b>6 512</b>
	<b>0</b>	<b>0</b>
<b>CHANGE IN NET CASH AND EQUIVALENTS</b>	<b>(12 951)</b>	<b>(15 547)</b>
Opening cash	28 114	43 661

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### 4.1.4.1. Detailed Analysis of WCR:

<i>In (€) thousands</i>	<b>Change 2021 / 2020</b>
Inventories	(9)
Trade and similar receivables	207
Other receivables and advances	(1 518)
Pre-paid expenses / other receivables	(52)
Trade and similar payables	1 049
Other debt	(974)
<b>CHANGE IN WORKING CAPITAL REQUIREMENT</b>	<b>(1 297)</b>

**Components of consolidated net cash and cash equivalents analyzed by type and reconciliation with the balance sheet:**

<i>In (€) thousands</i>	<b>FY 2021 (12 months)</b>	<b>FY 2020 (12 months)</b>
Short-term investment securities (due in < 3 months)	4 104	4 103
Cash on hand	11 059	24 011
<b>NET CASH AND CASH EQUIVALENTS</b>	<b>15 163</b>	<b>28 114</b>

## 4

## 4.1.5. Notes to the Consolidated Financial Statements

Unless specified otherwise, the amounts indicated in these notes are in thousands of euros.

### 4.1.5.1. Information about the company

Adocia is a clinical stage biopharmaceutical company specialized in the development of innovative formulations of proteins and peptides for the treatment of diabetes and other metabolic diseases.

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, 2021, 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 April 14, 2022 and authorized for publication.

### 4.1.5.2. Main events of 2021

2021 was marked by major advances in our insulin portfolio and by the achievement of important proofs of concept on new technological platforms in cell therapy and oral delivery of peptides. In addition, the financial operation carried out in the last quarter strengthened the resources available to support the company's growth.

#### Significant progress made on mature projects in our pipeline:

- BioChaperone® Lispro: approved to enter Phase 3 in China

In October 2021, Tonghua Dongba received approval from the CDE (Center for Drug Evaluation) to start the Phase 3 program of BC Lispro ultra-fast insulin for the treatment of type 1 and type 2 diabetes in China. The operational start of Phase 3 in China should trigger a milestone payment to Adocia, expected in the second quarter of 2022.

In parallel, the preparatory work for the Phase 3 studies in the United States and Europe has successfully been completed. Our commercial activities are aimed at finding a partner capable of financing the pivotal program until marketing authorization is obtained in these regions.

- M1Pram and BioChaperone® LisPram: intensified clinical development efforts

Adocia has intensified the clinical development of its two product candidates, M1Pram and BC LisPram, positioned respectively for the auto-injector pen and pump markets. These fixed combinations of insulin and amylin analogs are expected to provide an improvement in medical service, as compared to rapid insulins administered alone, through weight loss in obese or overweight diabetic patients. These rapid insulins are essential to the survival of many patients

and generate more than \$9 billion in revenue each year. These combinations are intended to improve glycemic control whilst generating weight loss in overweight or obese diabetic patients. In the United States, 65% of type 1 diabetic patients and 85% of type 2 diabetic patients are overweight or obese<sup>76,77</sup>.

A Phase 2 study (CT041) was initiated in March 2021 with M1Pram as an auto-injector pen. This comes after the establishment of proof of concept in humans in a study from 2020 that demonstrated improved glycemic control and very significant weight loss, as compared to the reference rapid insulin aspart, in just 3 weeks of treatment. The CT041 study, which aims to confirm these results over a 4-month period in type 1 diabetic patients, has been designed to define all of the parameters of a future Phase 3 program. The results will be communicated in the second quarter of 2022.

Concurrently, a proof-of-concept study in humans has been initiated with BC LisPram. This combination has been specifically designed for automated pump administration using an algorithm. This study is being conducted in collaboration with Dr. Ahmad Haidar of McGill University (Canada) and results are expected in Q3 2022.

### New proprietary technology platforms in new growth markets

- Revolutionizing islet transplantation (AdoShell® technology)

In January 2021, Adocia announced the filing of patents on a hydrogel matrix designed to improve islet transplantation cell therapy techniques. The function of this matrix is to maintain transplanted cells' secretory activity, while protecting them from the immune system. Adocia's objective is to create an organoid capable of secreting insulin in response to glycemic variations, thus avoiding the use of immunosuppressive drugs. An academic collaboration has been established with several teams, including Inserm with Professor François Pattou, a world specialist in islet transplantation. Animal trials are underway, prior to human implantation trials.

- Combining hormones to treat obesity

In 2021, Adocia also initiated new projects in the field of obesity. Patient management is undergoing major changes, due, on the one hand, to gradual recognition of obesity as a pandemic requiring drug treatment, and, on the other hand, to the discovery of the efficacy of certain hormones - which are also involved in diabetes - in controlling weight. These treatments make it possible to avoid recourse to bariatric surgery.

Adocia has succeeded in combining hormones with synergistic effects and in formulating two hormonal combinations to address the different profiles of obese patients.

These products are intended to be administered on pump so that the patient can set up, with the support of a doctor, a personalized treatment adapted to lifestyle.

Patents have been filed by Adocia on these pump-administered hormone combinations. The objective is to prepare a proof-of-concept study in humans by 2022/2023.

These products could also be developed in other medical indications such as NASH (Non-Alcoholic Steatohepatitis) and type 2 diabetes.

- Delivering peptides in oral form that were previously administered by injection (AdOral® technology)

Adocia has developed a technology that can enable oral delivery of peptides by limiting their natural degradation in the digestive tract before reaching the bloodstream. Initial results obtained in preclinical studies have shown an increase in the absorption efficiency of peptides by the gastrointestinal tract, which would allow for a switch from injectable to oral forms.

This new technological platform opens up numerous applications for oral forms of molecules intended, in particular, for the treatment of diabetes and obesity.

<sup>76</sup> Conway et al, *Diabetes Med* 2010 April; 27(4):398-404. BMI>25, Data for 2004-2007 period

<sup>77</sup> *Epidemiology of Obesity and Diabetes and Their Cardiovascular Complications*

### The company's cash position was strengthened in October 2021 by a financing transaction and in March 2022 by a real estate transaction:

- The financing transaction carried out in October was for 7 million euros

In October 2021, the Company carried out a financing transaction through (i) the issue of 6,568,422 bonds convertible into shares with a par value of one euro each for a total amount of 6 million Euros net subscribed by Vester Finance and two other European investors and (ii) a capital increase of 1 million Euros, the subscription of which was reserved for the benefit of Gérard Soula, the Company's Chairman and CEO and a shareholder, by way of the issue of new ordinary shares.

- Governance reinforcement

In June 2021, Adocia strengthened its Board of Directors with the appointment of three new independent members: Dr. Claudia Mitchell, Senior Vice President in charge of Portfolio Strategy at Astellas Pharma; Dr. Katherine Bowdish, President and CEO of PIC Therapeutics; and Stéphane Boissel, CEO of SparingVision

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#### 4.1.5.3. 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, 2021 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:

[https://ec.europa.eu/info/index\\_fr](https://ec.europa.eu/info/index_fr)

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 used are the same as those used for the preparation of the consolidated IFRS financial statements for the year ended December 31, 2020, except for the implementation of new standards, amendments to standards and interpretation adopted by the European Union whose implementation was mandatory for the Company as of January 1, 2021:

##### Standards, amendments to standards and interpretations applicable as of January 1, 2021:

- Amendments to IFRS 4 - deferral of IFRS 9
- Amendments to IFRS 4, 7, 9, 16, 39 - Benchmark interest rate reform - Phase 2
- Amendments to IFRS 16 on rent concessions applicable for rent concessions obtained after June 30, 2021

These new texts adopted by the European Union did not have a significant impact on the Company's financial statements.

##### Standards, amendments to standards and interpretations not yet adopted by the Company

There are no significant standards, amendments, or interpretations, adopted or not yet adopted by the European Union, which could have been implemented early or that would come into effect after June 30, 2021.

Standards, Amendments, or interpretations adopted by IASB that will come into effect after the fiscal year opened on January 1, 2021, and are currently in the process of being adopted by the European Union are the following ones:

- Annual improvement of standards - 2018-2020 (amendments to standards IFRS 1, IFRS 9, IFRS 16 and IAS 41 published by IASB in May 2020) (a),
- Amendments to IFRS 3 - reference to the conceptual framework, published by the IASB in May 2020 (a),
- Amendments to IAS 37 - onerous contracts - contract performance costs, issued by the IASB in May 2020 (a),

- Amendments to IAS 16 - property, plant and equipment - revenue in advance of intended use, issued by the IASB in May 2020 (b),
  - Amendments to IAS 1 - disclosure of accounting policies, published by the IASB in February 2021 (b),
  - Amendments to IAS 8 - definition of accounting estimates, published by the IASB in February 2021 (b),
  - Amendments to IAS 12 - deferred taxes related to assets and liabilities arising from a single transaction (b),
  - IFRS 17 – insurance contract (b),
- (a) applicable for fiscal years beginning on or after January, 1, 2022,
- (b) applicable for fiscal years beginning on or after January, 1, 2023.

The Company is currently revising the consecutive impacts of the first implementation of these new texts and does not anticipate any significant on its financial statements.

#### ▪ Application of the IAS 32 standard for the loan contract signed with IPF Fund II

On October 3, 2019, the Company's board of directors, acting under delegation from the general meeting of shareholders of May 16, 2019, authorized the issue of a bond loan with attached warrants (BSA) for a maximum amount of €15 million. The loan was subscribed with IPF Partners through two tranches of €7.5 million each, respectively on October 11, 2019, and December 10, 2019.

The bonds issued by the Company contain a contractual commitment to pay principal and interest repayments in the form of cash flows. In accordance with IAS 32, these bonds are considered as financial liabilities and must be recognized as debt at the date of each drawdown.

The exercise price of the warrants is contractually fixed at €8.57. It may, however, be revised downwards in the event of a new share issue at a lower price. The warrants issued will therefore be settled by the exchange of a variable number of shares for a fixed amount of cash (€1,125,000 per tranche) and are qualified, in accordance with IAS 32, as derivative liabilities.

The valuation of these warrants on the subscription date was entrusted to an independent actuary. In view of this valuation and the expenses incurred by the Company and directly related to this bond issue, an effective interest rate calculation (EIR) was performed and will be used, at each balance sheet date, to discount the amount of the debt recognized in the Company's consolidated financial statements.

In July 2020, in a context marked by the Covid-19 pandemic, the Company obtained a debt restructuring with a new deferral of payment of the maturities of 12 additional months, with the final maturity dates of the two tranches remaining unchanged.

In consideration for this arrangement, the Company's Board of Directors granted a total of 35,005 share warrants (BSAs) to the IPF Fund II SCA SICAV FIAR fund free of charge, under terms and conditions similar to those of the BSAs granted to IPF Fund II SCA SICAV FIAR under the main agreement, with an exercise price of the BSAs of €7.70. The number of warrants corresponds to 15% of the deferred capital amount, i.e. EUR 300,000. As of the date of this document, and excluding any adjustment to the exercise price of the BSAs, the number of shares that could be issued would be 38,961 shares, i.e. approximately 0.5% of the Company's share capital. The fair value of the warrants has been recognized in P&L as of 31 December 2021.

#### ▪ IFRS 9 application for the recognition of the State-guaranteed loan (PGE) contracts:

In August 2020, a €7 million non-dilutive financing was approved by BNP, HSBC, LCL and Bpifrance in the form of a state-guaranteed bank loan (PGE).

These bank loans are guaranteed by the French government up to 90% of the due amounts and are not subject to payment in the first year. In June 2021, the Company chose to differ payment for another year, the first reimbursements in cash being planned for August 2022 with an unchanged maturity in August 2026.

- **IAS 32 and IFRS 9 application for the accounting of the bond issue contract signed with Vester Finance :**

On October 26, 2021, the Company made a financing of €6 million net with the issuance of 6.568.422 bonds convertible into shares of a par value of €1 each (the "OC") subscribed by Vester Finance and two other European investors.

Part of these bonds (970 000) was converted at the end of December, the balance being recorded as a liability and measured at fair value in its entirety in compliance with IG+FRS 9 and IAS 32.

- **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.

In order to meet the financial commitments made to its lenders (see §.10 financial liabilities) and given (i) the cash position of €15.2 million at 31 December 2021, (ii) the receipt of €19 million in March 2022 related to the sale of the headquarters (iii) the expected receipt in the second quarter of 2022 of the milestone payment from Tonghua Dongbao following the start of phase 3 of the BC Lispro and (iv) the forecasts made, the Company will have to conclude a partnership agreement or a capital raising operation during the fourth quarter of 2022. Management is confident that it will be able to obtain new sources of financing or, failing that, obtain a new temporary arrangement of its financial ratios to be respected in the context of the loans granted to the Company. The Company's financial statements as of December 31, 2021, have been closed on a going concern basis.

To prepare the financial statements in accordance with IFRS, some 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, 2020. These assumptions mainly relate to IFRS 2 ("Share-based Payment"), IFRS 15 ("Revenue from Contracts with Customers") and, to IAS 32 ("Financial Instruments: Presentation").

- **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 2020.

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 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 to 10 years
Laboratory equipment	3 to 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)**

According to IFRS 16 ("Leases"), 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.

As of December 31, 2021, only lease contracts fall within the scope of IFRS 16. As the accounting treatment is identical to that made under IAS 17, the application of IFRS 16 has no impact on the Company's consolidated financial statements.

- **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, 2021, 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.

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## ▪ 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 has received a certain amount of government assistance in the form of repayable advances.

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 (independent directors and consultants).

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 on December 31, 2021 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.

The licenses sold by the Company correspond to rights of use. As a consequence, the revenue generated from these licenses is recognized immediately from the date the customer can start using the license.

When the payment of a license 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 license 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 then 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 (MA). 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 as the ratio of the costs incurred by the Company for research and development services performed under the contract to the total estimated budget for the duration of the contract.

If the license 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.

#### ▪ Other income

##### Grants:

Due to its innovative nature, the company has received since its creation a certain amount of assistance and grants from the French government and public authorities to help finance its operation or recruit specific individuals.

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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 research expenditures (in particular salaries and wages, depreciation of research equipment, services outsourced to approved research organizations and intellectual property costs) 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.

Foreign-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).

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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.



## 4.1.5.4. Notes to the financial statements

## Summary of notes

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- NOTE 1 Intangible assets

<i>In (€) thousands</i>	12/31/2020	Acquisitions / Additions	Disposals / reversals	12/31/2021
Gross amount	191	0	(23)	169
Depreciation and impairment	146	20	0	165
<b>NET AMOUNT</b>	<b>46</b>	<b>(20)</b>	<b>(23)</b>	<b>3</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>	12/31/2020	Acquisitions / Additions	Disposals / reversals	Reclassement IFRS 5 Actifs destinés à être vendu	12/31/2021
Lands	2 032	0	0	(2 032)	(0)
Land development	409	0	0	(409)	0
Buildings	4 276	6	0	(4 282)	(0)

Laboratory equipment	3 630	159	(18)	0	3 771
Fixtures and facilities	3 753	109	(4)	(3 194)	665
Furniture, office equipment	1 573	57	0	0	1 630
Assets classified as held for sale	0	0	0	9 917	9 917
<b>GROSS AMOUNT</b>	<b>15 673</b>	<b>332</b>	<b>22</b>	<b>-</b>	<b>15 983</b>
Lands	0	0	0	0	0
Land development	87	41	0	(127)	0
Buildings	978	214	0	(1 192)	(0)
Laboratory equipment	3 252	212	(18)	0	3 447
Fixtures and facilities	1 512	388	0	(1 700)	201
Furniture, office equipment	1 308	139	0	0	1 447
Assets classified as held for sale	0	0	0	3 019	3 019
<b>DEPRECIATION AND IMPAIRMENT</b>	<b>7 136</b>	<b>995</b>	<b>18</b>	<b>-</b>	<b>8 114</b>
Lands	2 032	0	0	(2 032)	(0)
Land development	322	(41)	0	(282)	0
Buildings	3 298	(208)	0	(3 090)	0
Laboratory equipment	378	(53)	0	0	325
Fixtures and facilities	2 239	(279)	(4)	(1 494)	462
Furniture, office equipment	263	(82)	0	0	181
Assets classified as held for sale	0	0	0	6 897	6 897
<b>NET AMOUNT</b>	<b>8 532</b>	<b>663</b>	<b>4</b>	<b>-</b>	<b>7 864</b>

Net property, plant and equipment decreased by €0.7 million between 2020 and 2021, due mainly to the depreciation of the net property, plant, and equipment over the period partially compensated by some investments made in 2021.

In a favorable real estate context, Adocia made an operation to sell its building in March 2022. The building's sale on March 28, 2022, for an amount of €23.3 million was carried out within the framework of a sale and leaseback transaction enabling Adocia to sustain its growth while securing the occupation of its historic site. Indeed, the lease contract is for a fixed term of 12 years (renewable for another 9 years) without option to buy.

The sale of the building resulted in a net cashing of €19 million (after repayment of the loans).

#### IFRS 5 application for the accounting of Assets and Liabilities classified as held for sale

In order to be classified as held for sale, the non-current asset or group of assets must meet the following cumulative criteria (IFRS 5.6 and .7):

- it is available for immediate sale in its current condition, subject only to the usual and customary conditions for the sale of such assets,
- the sale is highly probable,
- its book value is recovered principally through its sale rather than through its continuing use.

A sale agreement was signed on December 22, 2021. After the lifting of the conditions precedent, the final deed of sale was signed in March 2022. At the end of December 2021, it was thus considered that the sale was "highly probable" according to the accounting standard of IFRS 5 at the time of the signature of the sale agreement.

In consequence, the criteria classifying non-current assets as held for sale were met at the end of December 2021. The date of classification as non-current assets or group of assets held for sale is the first date on which the criteria are met, namely **December 22, 2021**.

As a reminder, this is a sale and leaseback operation of the building located in Lyon, France.

Still according to IFRS 5.15, these assets or group of assets must be evaluated at the lowest amount:

- of their net accounting value, after accounting for the adjustments identified in the first step, and
- of the fair net value of the sale cost.

In the present case, it is the **net accounting value** that has the lowest amount.

Thus, the whole group of assets held for sale are evaluated as of December 31, 2021, at their net accounting value.

A breakdown in main categories of the “non-current asset or group of assets held for sale” and “liabilities associated with a group of assets held for sale” sections must be included, either in the balance sheet or in the notes ([IFRS 5.38 and .39](#)).

Comment: the IFRS 5 standard does not require a **retrospective** presentation change or restatement in the balance sheets for previous financial years as comparative information concerning assets or groups of assets held for sale, identified and classified as such during the year ([IFRS 5.40](#)).

Consequently, in compliance with [IFRS standard 5](#), €6.9 M of net assets have been reclassified among the current items, in a separate sub-heading after the other current items.

#### ▪ NOTE 3 Non-current financial assets

The company's non-current financial assets are as follows:

<i>In (€) thousands</i>	12/31/2020	Acquisitions / Additions	Disposals / reversals	12/31/2021
Gross amount	142	0	(40)	102
Amortization and impairment	0	0	0	0
<b>NET AMOUNT</b>	<b>142</b>	<b>0</b>	<b>(40)</b>	<b>102</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 €190.7 million on December 31, 2021. This loss carry forward is not limited in time.

#### ▪ NOTE 5 Inventories

<i>In (€) thousands</i>	12/31/2021	12/31/2020
Raw materials	517	569
Semi-finished products	0	0
Finished products	0	0
<b>TOTAL NET VALUE</b>	<b>517</b>	<b>569</b>

The net value of inventories was €569 thousand on December 31, 2020 and €517 thousand on December 31, 2021. The item does not call for any particular comment.

Impairment was recorded for the inventory, mainly for products related to a project which the company recognized as a failure.

- NOTE 6 Trade receivables

<i>In (€) thousands</i>	12/31/2021	12/31/2020
Gross amount	207	0
Impairment	0	0
<b>TOTAL NET VALUE</b>	<b>207</b>	<b>0</b>

- NOTE 7 Other current assets

<i>In (€) thousands</i>	12/31/2021	12/31/2020
Research tax credit	4 611	5 992
VAT claims	542	618
Receivables from suppliers	496	513
Pre-paid expenses	500	551
Carry-back	0	0
Others	49	90
<b>TOTAL NET VALUE</b>	<b>6 197</b>	<b>7 763</b>

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 tax credit calculated for the eligible expenses during the year. In 2020 and 2021, the Company cannot apply its CIR 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 €4.6 million and €6 million, respectively, under current assets. Please note that the CIR 2020 research tax credit for an amount of €6 million was received in April 2021 (government measures related to the COVID-19 pandemic).

Prepaid expenses relate to current expenses.

In addition to social security claims and other creditors, the miscellaneous item includes grants receivable.

- 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>	12/31/2021 Balance sheet value	Value on the balance sheet under IAS 39				12/31/2021 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	11 059	11 059	0	0	0	11 059
Cash equivalents (UCITS)	4 104	4 104	0	0	0	4 104
<b>TOTAL ASSETS</b>	<b>15 163</b>	<b>15 163</b>				<b>15 163</b>

## NOTE 9 Equity

For easier cross-reference between the periods, the number of shares in the 2011 fiscal year has been restated to reflect the decision taken 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. The table below presents the capital over the period:

	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

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12/16/2018 - Grant of bonus shares	2 700	2 700			270
02/08/2019 - Grant of bonus shares	675	675			68
03/15/2019 - Grant of bonus shares	2 000	2 000			200
05/17/2019 - Grant of bonus shares	5 400	5 400			540
09/25/2019 - Grant of bonus shares	1 400	1 400			140
10/03/2019 - Grant of bonus shares	5 000	5 000			500
12/05/2019 - Grant of bonus shares	2 900	2 900			290
12/13/2019 - Grant of bonus shares	6 375	6 375			638
12/14/2019 - Grant of bonus shares	2 375	2 375			238
12/16/2019 - Grant of bonus shares	2 700	2 700			270
02/08/2020 - Grant of bonus shares	225	225			23
15/03/2020 - Grant of bonus shares	2 000	2 000			200
17/05/2020 - Grant of bonus shares	12 760	12 760			1 276
17/05/2020 - Grant of bonus shares	1 400	1 400			140
25/09/2020 - Grant of bonus shares	1 400	1 400			140
03/10/2020 - Grant of bonus shares	900	900			90
05/12/2020 - Grant of bonus shares	2 675	2 675			268
10/12/2020 - Grant of bonus shares	29 450	29 450			2 945
10/12/2020 - Grant of bonus shares	1 825	1 825			183
13/12/2020 - Grant of bonus shares	5 775	5 775			578
14/12/2020 - Grant of bonus shares	2 150	2 150			215
02/08/2021 - Grant of bonus shares	225	225			23
03/15/2021 - Grant of bonus shares	900	900			90
09/30/2021 - Grant of bonus shares	2 900	2 900			290
09/30/2021 - Grant of bonus shares	675	675			68
09/30/2021 - Grant of bonus shares	1 400	1 400			140
07/23/2021 - Exercice of BSPCE	2 800	2 800			280
10/27/2021 - Issue of IPO Shares by private placement	107 992	107 992			10 799
10/28/2021 - Issue of shares following conversion of bonds OCA1023	14 303	14 303			1 430
11/03/2021 - Issue of shares following conversion of bonds OCA1023	23 256	23 256			2 326
11/08/2021 - Issue of shares following conversion of bonds OCA1023	31 980	31 980			3 198
11/30/2021 - Issue of shares following conversion of bonds OCA1023	17 241	17 241			1 724
12/16/2021 - Issue of shares following conversion of bonds OCA1023	12 212	12 212			1 221
12/20/2021 - Issue of shares following conversion of bonds OCA1023	8 231	8 231			823
12/27/2020 - Issue of shares following conversion of bonds OCA1023	16 737	16 737			1 674
12/31/2021 - Grant of bonus shares	9 475	9 475			948
<b>AT DECEMBER 31, 2021</b>	<b>7 270 956</b>	<b>7 270 956</b>	<b>0</b>	<b>0</b>	<b>727 096</b>

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## 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 in February 2012, preferred shares were converted into ordinary shares and the Ratchet stock warrants became null and void.

On October 26, 2021, the Company did a financing of €7 million net through (i) the issuance of 6.568.422 bonds convertible into shares with a par value of EUR 1 each (the "Convertible Bonds") subscribed by Vester Finance and two other European investors and (ii) a share capital increase of EUR 1 million (the "Capital Increase"), the subscription of which has been reserved for the benefit of Gérard Soula, Chairman, Chief Executive Officer and shareholder of the Company, through the issuance of new ordinary shares.

The increase in the "share capital" and "issue premium" lines is mainly due to the issuance of ordinary shares subscribed by Gérard Soula (+€1 M) and the partial conversion of the Convertible Bonds issued in October 2021 (+€0.9 M).

The issuance of 6.568.422 convertible bonds and the fair value treatment of the conversions in share of convertible bonds (Bonds OCA1023) are detailed in note 10.

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## Stock warrants

**Stock options** were granted to (i) certain employees and managers 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"), (iv) to the investment company IPF in the context of the bond issue financing in October 2019 and related to the rescheduling of the loan debt in July 2020.

The main characteristics of these share-based compensation plans are described in detail in section 4.3.3.7 of this registration document.

The issuance of 6.568.422 **convertible bonds** and the fair value treatment of the conversions in share of convertible bonds (Bonds OCA1023) are detailed in note 10.

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, according to IFRS 2. This expense amounted to €0.05 million in 2021 compared to €0.2 million in 2020.

The **BSAs** granted to IPF are treated differently as they are an integral part of the €15 million financing that the Company has received. The cost of BSAs at the date of attribution has been included in the calculation of the amortized cost of debt, in accordance with IAS 32 (see dedicated paragraph 4.1.5.3). The revaluation of the fair value of BSAs on the closing date of the BSAs affects the financial result of the period. For the record, the exercise price of the BSA is contractually set at 8.57 euros. However, it may be revised downwards in the case of a new share issue at a lower price. The issued BSAs will therefore be resolved by exchanging a variable number of shares against a fixed amount of cash (€1,125,000 per tranche) and are qualified, in accordance with IAS 32, as passive derivatives. In July 2020, the Company obtained a debt restructuring with a further deferral of payment of the maturities of an additional 12 months, with the final maturities of the two tranches remaining unchanged. In return for this development, the Company's Board of Directors awarded a total of 35,005 share warrants (BSA) free of charge to the IPF Fund II SCA SICAV FIAR fund, with a BSA exercise price of €7.70. The fair value of the BSAs was recorded in LP on 31/12/2021.

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	Independant 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	74,60
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	19,00
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
BSA IPF 2019 - Tranche A	IPF Partners	No	Immediate vesting upon fulfillment of relevant performance criteria	8,57
BSA IPF 2019 - Tranche B	IPF Partners	No	Immediate vesting upon fulfillment of relevant performance criteria	8,57
SO 2019	Employees	No	Until 12/10/2021	8,00
BSA IPF 2020	IPF Partners	No	immédiate 07/20/2020	7,70
BSA 2021	Independant directors	No	Until 05/19/2024	8,93
OCA 2021	Vester finance	No	immediate 10/26/2021	0,12

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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	35 000		65 000		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	13 000				375
SO 2017 N°2	40 000	39 909	91			375
BSPCE 2017	150 000	100 000		50 000		579
SO 2018	23 000	3 000		12 000	8 000	217
BSA IPF 2019 - Tranche A (*)	131 271			131 271		478
BSA IPF 2019 - Tranche B (*)	131 271			131 271		442
SO 2019	2 000	1 000		500	500	8
BSA IPF 2020	35 005			35 005		128
BSA 2021	10 215				10 215	91
OCA 2021	6 568 422		970 000	5 598 422		6 322
<b>TOTAL</b>	<b>7 438 184</b>	<b>248 009</b>	<b>978 491</b>	<b>6 172 469</b>	<b>39 215</b>	<b>17 637</b>

(\*) The Company has issued BSA 7,500,000 per tranche of loans, which are convertible into shares for a total amount of EUR 1,125,000 per tranche. The exercise of the BSAs at a contractually determined price of 8.57 euros would lead to the issuance of 131,271 shares per tranche. It is specified that in the event that the Company issues new shares (excluding employees and managers' interest) at a price below this amount during the exercise period of the BSAs, their exercise price will be reduced to 95% of the lowest of those issue prices.

### 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
Plan 2008 N°1	42 000	2 100	39 900	
Plan 2008 N°2	5 600		5 600	
Plan 2009	5 600		5 600	
Plan 2010 N°1	5 600		5 600	
Plan 2010 N°1	5 600		5 600	
Plan 2015 N°1 - 10 ans	39 150	2 860	36 290	
Plan 2015 N°2.1	5 000		5 000	
Plan 2015 N°2.2	12 600	1 800	10 800	
Plan 2015 Dirigeant	5 000		5 000	
Plan 2016 Dirigeant	20 000	8 000	12 000	
Plan 2016 N°2	40 000	3 525	36 475	
Plan 2017	9 500	900	8 600	
Plan 2018 N°1	2 700	1 350	1 125	225
Plan 2018 N°2	19 050	2 290	16 760	
Plan 2018 N°3	5 600	2 800	2 800	
Plan 2018 N°4	5 600		4 200	1 400
Plan 2018 N°5	11 600	1 125	8 025	2 450
Plan 2019 N°1	3 600	2 700	900	
Plan 2019 N°2	33 300	3 850	29 450	
Plan 2019 N°3	7 300	975	3 325	3 000
Plan 2020 N°1	9 600	6 000	900	2 700
Plan 2020 N°2	11 600		2 900	8 700
Plan 2020 N°3	2 700		675	2 025
Plan 2020 N°4	4 800		1 200	3 600
Plan 2020 N°5	22 000	2 000	2 625	17 375
Plan 2021 N°1	5 700			5 700
<b>TOTAL</b>	<b>340 800</b>	<b>42 275</b>	<b>251 350</b>	<b>47 175</b>

Movements in bonus shares are as follows:

Number of shares	FY 2021	FY 2020
Number of shares with ongoing vesting at the beginning of the year	63 400	89 770
Shares granted during the year	5 700	50 700
Shares vested during the year	15 350	60 785
Shares cancelled during the year	6 575	16 285
<b>NUMBER OF SHARES WITH ONGOING VESTING AT THE END OF THE YEAR</b>	<b>47 175</b>	<b>63 400</b>

The cost of services rendered is recognized as a payroll expense over the vesting period. This expense amounted to €0.2 million in 2021 compared to €0.4 million in 2020.

#### 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. The resources made available under the liquidity agreement with Kepler Capital Markets S.A. were increased by €200,000 on September 10, 2015 and by €250,000 on February 12, 2018.

Over the course of 2021, 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.

As of December 31, 2021, the company had 39,816 shares and €65,112.35 allocated to the liquidity account under this agreement.

#### ▪ NOTE 10 Short and long-term financial debt

Financial debt includes bank loans and repayable advances.

A **bond loan** was contracted in October 2021. On October 26, 2021, the Company issued 6.568.422 bonds convertible into shares with a par value of EUR 1 each (the "Convertible Bonds") for a total amount of EUR 6 million net subscribed by Vester Finance and two other European investors.

These Convertible Bonds were issued at a price equal to 95% of their nominal value. The Convertible Bonds will not bear interest and may be converted into ordinary shares at the request of the holder, at any time and at a subscription price per share (the "Conversion Price") equal to the lower of (i) EUR 11.87 and (ii) 93% of the lowest of the daily VWAPs over a period of 15 days preceding each conversion request, in compliance with the limit set by the General Meeting, that is 80% of the volume-weighted average price of the last three trading sessions preceding the conversion request.

Convertible Bonds may also be converted or redeemed (in cash or in convertible bonds) at the request of the holder should an event of default occur.

In the event that the Convertible Bonds have not been fully converted and/or redeemed at the end of the initial duration of 24 months (extendable under certain conditions), they will be fully redeemed by the Company at 100% of their nominal value.

As of December 31, 2021, part of these bonds has been converted (970 000 bonds corresponding to 14.77% of the total amount issued) and resulted in the issuance of 123.960 shares.

The bond loan includes a 5% premium for an amount of €315.790 and fixed costs of 4% for an amount of € 252.632. This loan that was part of a contract has a duration of 24 months. The 5% redemption premium has been recorded as an asset on the balance sheet. The latter is written back as conversions are made, and is also amortized over the term of the contract (24 months). The redemption premium amounts to €244 thousand as of December 31, 2021.

Part of the bonds (970 000) have been converted as of the end of December, the balance has been recorded as a liability and measured **at fair value through profit or loss** in its entirety in accordance with IFRS 9 and IAS 32 without making use of the "split accounting" method.

The "split accounting" method is not applicable in the present case for the following reasons:

- The redemption periods are uncertain,
- The convertible bonds have a variable parity.

The costs related to the issuance of the loan (banks, lawyer, etc.) have been directly expensed in the year 2021.

The valuation of these convertible bonds at the subscription date and at the closing of accounts was entrusted to an independent actuary. The convertible bonds not bearing interest rates, they are similar to a call option with a variable exercise price. In order to reflect the characteristics of the convertible bonds (variable conversion price, depending on the share price at the time of conversion), our actuary used the so-called "Monte-Carlo" approach.

On the basis of this approach, the fair value of the convertible bonds amounts to €7.5 million as of October 26, 2021, and to €6.3 million as of December 31, 2021.

**Bank loans** amounting to €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. Between March and May 2019, the Company contracted a loan of €1.2 million to finance the development of two 450 m<sup>2</sup> floors for the analysis department, one composed of offices, the other of laboratories.

These loans were entirely repaid during the sale of the building that happened in March 2022 (see note 2 of the present document). As of December 31, 2021, the loans were reclassified as short-term financial debt on the liabilities side of the balance sheet for a total amount of €4.4 million.

The Company also subscribed to a **bond loan**, with attached warrants (BSA), for a total amount of €15 million from IPF Fund II, through two tranches of €7.5 million each, respectively on 11 October 2019 and 10 December 2019. The exercise price of the warrants is contractually fixed at €8.57. However, it may be revised downwards in the event of a new issue of shares at a lower price. In July 2020, the Company obtained a debt restructuring from IPF Partners. In return for this development, the Company's Board of Directors awarded a free grant to the BSA IPF Fund, under terms and conditions similar to those of the BSAs awarded under the main contract, with a BSA exercise price of 7.70 euros.

The valuation of these warrants on the subscription date was entrusted to an independent actuary. In view of this valuation and the costs incurred by the Company, directly related to this bond issue, an interest rate calculation (EIR) has been carried out and will be used, at each balance sheet date, to discount the amount of the debt recognized in the Company's consolidated financial statements.

Under the terms of the bank loan obtained from IPF Partners and following its rescheduling in July 2020, the Company has, among other things, committed to meet the following obligations:

- not to take on a new debt (beyond a threshold by type of debt and a global ceiling of € 6.5 million of debt)
- do not grant new security or guarantees,
- maintain a minimum cash position equivalent to \$16 million;
- have a cash amount to cover 7 months of operating cash flow including debt service (cash covenant),
- not to change activity substantially,
- do not proceed with asset disposals other than in the normal course of business, acquisitions or joint ventures without the prior approval of IPF Fund II,
- comply with all legal and regulatory obligations applying to the Company,

In September 2021, the Company obtained a temporary accommodation from its lenders of its cash covenants in anticipation of (i) an additional financing to be completed by October 31, 2021 at the latest and (ii) the sale of the building to be completed by March 31, 2022 at the latest. The cash flow threshold initially fixed at \$16 million was lowered to €10 million.

In this context, the minimum cash amount of operating cash flow that must be available was temporarily lowered to €10 million (initially \$16 million), this accommodation being accompanied by a raise of 1% of the IPF interest rates (cash margin and PIK margin) over the period in question.

IPF authorizes the Company to sell its real estate asset, but in return asks for the possibility of using part of the sale price to the early repayment of its loan up to the amount of 2 million from August 31, 2022.

Failure to comply with these commitments, which would not be remedied within 10 working days of the occurrence or notification by IPF Fund II (or immediately with respect to non-compliance with the covenant cash) could lead IPF Fund II to declare the loan's anticipated due date and to proceed with the implementation of the security detailed above.

As of December 31, 2021, the Group was in compliance with the commitments described above.

Finally, in August 2020, Adocia was granted a bank loan of € 7 million by BNP, HSBC, LCL and Bpifrance in the form of a State Guaranteed Loan (PGE). These loans do not require any repayment in the first year. In June 2021, the Company chose to differ for another year, the first repayments in capital being planned for August 2022 with an unchanged maturity in August 2026.

At the end of December 2021, the amount of financial debt was €34.5 million, €18.3 million of which was long-term.

At the end of 2021, the classification as current and non-current was as follows:

<i>In (€) thousands</i>	Current	Non-current	Total
Reimbursable advances	520	0	520
Bank Loans	4 429	(0)	4 429
State-guaranteed bank loan	440	6 615	7 055
IPF loan	3 270	11 670	14 940
Fair value of share subscription warrants granted to IPF	1 156	0	1 156
Fair value of OCA 1023	6 322	0	6 322
Other financial debts	57	0	57
<b>TOTAL FINANCIAL DEBT</b>	<b>16 194</b>	<b>18 285</b>	<b>34 479</b>

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<i>In (€) thousands</i>	12/31/2021		
	Balance sheet value	Breakdown by category of instrument	
		Fair value through the income statement	Debt at amortized cost
Reimbursable advances	520		520
Banks loans	4 429		4 429
State-guaranteed bank loan	7 055		7 055
IPF loan	14 940		14 940
Fair value of share subscription warrants granted to IPF	1 156	1 156	
Fair value of OCA 1023	6 322	6 322	
Other financial debts	57		57
<b>TOTAL FINANCIAL DEBT</b>	<b>34 479</b>	<b>7 478</b>	<b>27 001</b>

Ci-après, le détail des variations en normes IFRS de la juste valeur des OCA1023 sur l'exercice 2021 :

<b>VALUE AT DECEMBER 31, 2020</b>	<b>0</b>
Fair Value at Subscription Date (10/26/2021)	7 455
Share conversions	(1 101)
Change in fair value	(32)
<b>VALUE AT DECEMBER 31, 2021</b>	<b>6 322</b>

Details about advances granted and repaid in 2021:

<i>In (€) thousands</i>	Amount	Historical cost
<b>VALUE AT DECEMBER 31, 2020</b>	<b>0</b>	<b>0</b>
Long term portion	0	0
Short term portion	520	0
Grant during the year	0	0
Repayment during the year	0	0
Discount on grant during the year	0	0
Financial expenses	0	0
<b>VALUE AT DECEMBER 31, 2021</b>	<b>520</b>	<b>0 (*)</b>
Long term portion	0	0
Short term portion	520	0

<i>(*) in € thousands</i>	12/31/2021	Less than 1 year	1 to 5 years	More than 5 years
Avance Insuline (2012)	520	520	0	0
<b>TOTAL</b>	<b>520</b>	<b>520</b>	<b>0</b>	<b>0</b>

In 2015, the Company recognized the end of the program and made the scheduled repayments in the event of commercial failure of the program over the years 2017 and 2018. An expertise commissioned by BpiFrance is planned for 2020 and should make it possible to close this file in the coming months.

#### 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, 2020</b>	<b>2 214</b>	<b>0</b>	<b>0</b>	<b>2 214</b>
Additions	247	0	78	325
Reversal of used provisions	0	0	0	0
Reversal of unused provisions	(1 018)	0	0	(1 018)
<b>VALUE AT DECEMBER 31, 2021</b>	<b>1 444</b>	<b>0</b>	<b>78</b>	<b>1 521</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.

The main actuarial assumptions used to value retirement benefits are as follows:

<i>In (€) thousands</i>	12/31/2021	12/31/2020
<b>Economic assumptions</b>	<b>0</b>	<b>0</b>
Discount rate	1,00%	0,40%
Rate of annual salary increase	3% pour les cadres et 2% pour les non cadres	3% pour les cadres et 2% pour les non cadres
<b>Demographic assumptions</b>	<b>0</b>	<b>0</b>
Retirement age	entre 62 et 67 ans	entre 62 et 67 ans
Type of retirement	Initiative du salarié	Initiative du salarié
Mortality table	INSEE 15 - 17	INSEE 14 - 16
Rate of tax and social security charges	44,50%	44,50%
Annual mobility	Moyen ou Fort selon catégories	Moyen ou Fort selon catégories
Present value of obligations	1 444	2 214
Payments to a fund	0	0
<b>Provision recorded on the balance sheet</b>	<b>1 444</b>	<b>2 214</b>
Past service costs for the period	240	450
Financial expense	7	25
Actuarial gains and losses and change in accounting method (1)	(1 018)	(1 382)
Annual expense	247	475

(1) Includes the impact due to the implementation of the IFRIC decision of May 2021 relating to the calculation of end-of-career allowances

#### NOTE 12 Trade payables and other current liabilities

<i>In (€) thousands</i>	12/31/2021	12/31/2020
<b>Trade payables</b>	<b>3 835</b>	<b>4 943</b>
Subsidiary accounts	1 092	2 433
Notes payable	0	0
Invoices pending	2 743	2 510
<b>Other current liabilities</b>	<b>3 724</b>	<b>2 766</b>
Customer credit balances	0	0
Tax and social security liabilities	3 314	2 321
Other debt	37	27
Unearned income	373	418
<b>TOTAL CURRENT OPERATING LIABILITIES</b>	<b>7 560</b>	<b>7 709</b>

Trade payables reached €3.8 million as of December 31, 2021 compared to €4.9 million as of December 31, 2020. The variation of this item (-€1.1 million) is a reflection of the decrease in R&D activities (external expenses) over the period.

The expenses related to “the non-received invoices from suppliers” are recognized as related expenses.

Unearned income accounted for at the end of 2021, for €0.4 million, corresponds to the short-term part of the revenue as upfront payment from Tonhua Dongbao’s Pharmaceuticals Co. Ltd, not recognized as revenue as of December 31, 2021.

The tax and social security liabilities amounted to €3.3 million at the end of 2021, an increase of 1 million euros compared to 2020. The increase in this item is mostly due to the provisioned bonuses for the year 2021 (+€1.1 million compared to 2020).

All trade payables and other current liabilities have a maturity of less than one year.

Tax and social security liabilities are as follows:

<i>In (€) thousands</i>	12/31/2021	12/31/2020
Compensation owed	1 678	967
Debt owed to social welfare agencies	1 410	1 147
Other tax and social security liabilities	226	207
<b>TOTAL TAX AND SOCIAL DEBTS</b>	<b>3 314</b>	<b>2 321</b>

- NOTE 13 Other non-current liabilities

Other non-current liabilities amounted to €0.3 million on December 31, 2021 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	FY 2021 (12 months)	FY 2020 (12 months)
<b>Operating revenue</b>		<b>6 055</b>	<b>6 833</b>
Revenue	15	1 444	841
Grants, research tax credits and others	16	4 611	5 992
<b>Operating expenses</b>		<b>(25 421)</b>	<b>(27 981)</b>
Purchases used in operations		(1 264)	(1 457)
Payroll expense	18	(11 631)	(12 124)
External expenses	17	(11 102)	(13 010)
Taxes and contributions		(265)	(257)
Dotation aux amortissements et provisions	19	(1 158)	(1 133)
Other current operating income and expenses		0	0
<b>PROFIT (LOSS) FROM ORDINARY OPERATING ACTIVITIES</b>		<b>(19 366)</b>	<b>(21 148)</b>

Breakdown of expenses by function:

<i>In (€) thousands</i>	FY 2021 (12 months)	Exercice 2020 (12 mois)
Research and development expenses	(20 016)	(22 547)
General and administrative expenses	(5 404)	(5 434)
<b>OPERATING EXPENSES</b>	<b>(25 421)</b>	<b>(27 981)</b>

General and administrative expenses amounted to €5.4 million in 2021 and are stable compared to 2020.



Research and development costs were as follows:

<i>In (€) thousands</i>	<b>FY 2021 (12 months)</b>	<b>FY 2020 (12 months)</b>
Purchases used in operations	(1 264)	(1 457)
Payroll expense	(8 322)	(8 632)
Share-based payments	(115)	(267)
External expenses	(9 249)	(11 197)
Taxes and contributions	(137)	(135)
Depreciation, amortization & provisions	(930)	(859)
<b>OPERATING EXPENSES</b>	<b>(20 016)</b>	<b>(22 547)</b>

#### ▪ NOTE 15 Revenue

<i>In (€) thousands</i>	<b>FY 2021 (12 months)</b>	<b>FY 2020 (12 months)</b>
Research and collaborative agreements	983	0
Licencing revenues	461	841
<b>REVENUE</b>	<b>1 444</b>	<b>841</b>

The Company's revenue is mainly due to the licensing agreements signed with Tonghua Dongbao for the BioChaperone® Lispro and BioChaperone® Combo combinations in China and other territories.

This revenue concerning research and development services provided by Adocia to Tonghua Dongbao are recognized for advancement in compliance with IFRS 15, in comparison with the costs incurred by Adocia and the total budget estimated to date during the duration of the contract.

These agreements anticipate that the Company:

- benefits from upfront payments of \$40 million (BC Combo) and \$10 million (BC Lispro), paying for the licenses and exclusive rights granted to Tonghua Dongbao as well as the transfer of know-how and related services, these payments were received by the Company in April 2018;
- could benefit from reimbursement of certain research and development costs incurred at the request of Tonghua Dongbao during the duration of the contract;
- is eligible to receive milestone payments of up to \$50 million for BC Combo and \$35 million for BC Lispro;
- could collect royalties on sales of these two products in the relevant territories.

As of December 31, 2021, the Company's revenue of €1.4 million is mostly coming from :

- licensing agreements signed with Tonghua Dongbao Pharmaceuticals Co. Ltd in April 2018 for an amount €0.4 million;
- the rebilling to Tonghua Dongbao, for the 2021 fiscal year, of complementary services made on their demand, in particular for BC Combo project. These services amounted to close €1 million.

The part of the initial payment still to be recognized as revenue as of December 31, 2021 amounts to €0.7 million and is accounted for as deferred income.

In 2020, the Company had recognized a revenue of €0.8 million for the licensing agreements and €0.1 for additional research services.

- NOTE 16 Other income

<i>In (€) thousands</i>	<b>FY 2021 (12 months)</b>	<b>FY 2020 (12 months)</b>
Research tax credit	4 611	5 992
Other	0	0
<b>OTHER INCOME</b>	<b>4 611</b>	<b>5 992</b>

The Research Tax Credit amounted to €4.6 million as of December 31, 2021. The decrease compared to the previous year reflects the decrease in expenses eligible to the Research Tax Credit in 2021.

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- NOTE 17 Other purchases and external charges

Purchases and external charges mainly consist of the company's preclinical and clinical studies, subcontracting expenses, intellectual property costs, fees general expenses.

These expenses amounted to € 11 million as of December 31, 2021, decreased by €1.9 million compared to 2020. This decrease is mainly related to the decrease in external R& expenses linked to less activities in preclinical and clinical studies.

- NOTE 18 Payroll expense

Payroll expense was as follows:

<i>In (€) thousands</i>	<b>FY 2021 (12 months)</b>	<b>FY 2020 (12 months)</b>
Wages and salaries	7 830	8 419
Social contributions	3 604	3 437
Share-based payment	197	267
<b>PAYROLL EXPENSE</b>	<b>11 631</b>	<b>12 124</b>

	<b>12/31/2021</b>	<b>12/31/2020</b>
Technicians	53	56
Management personnel	59	70
<b>STAFF</b>	<b>112</b>	<b>126</b>

On December 31, 2021, the Company had 39 postdoctoral researchers in science, medicine or pharmacy, i.e. nearly 35% of the whole staff. Nearly 77% of employees are directly assigned to research and development activities.

Staff expenses, excluding equity-based payments, amounted to €11.4 million as of December 31, 2021 compared to €11.9 million in 2020. The variation of this item is mostly linked to the decrease in the workforce from 133 Full-Time Equivalent (FTEs) in 2020 to 122 FTEs as of December 31, 2021.

- NOTE 19 Depreciation, amortization and impairment

Net depreciation, amortization and provisions were as follows:

<i>In (€) thousands</i>	<b>FY 2021 (12 months)</b>	<b>FY 2020 (12 months)</b>
<b>Depreciation, amortization and provisions for fixed assets</b>	<b>1 015</b>	<b>1 198</b>
Depreciation of property, plant and equipment	863	946
Amortization of intangible assets	20	25
Depreciation of leased assets	132	228
<b>Depreciation, amortization and provisions for fixed assets</b>	<b>143</b>	<b>(65)</b>
Provisions pour risques et charges (dotations)	101	0
Provisions for current assets (additions)	42	0
Reprises	0	(65)
<b>DEPRECIATION, AMOTIZATION AND IMPAIRMENT</b>	<b>1 158</b>	<b>1 133</b>

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- NOTE 20 Financial income/expense

The cost of net financial debt was as follows:

<i>In (€) thousands</i>	<b>FY 2021 (12 months)</b>	<b>FY 2020 (12 months)</b>
<b>Cost of net financial debt</b>	<b>(3 553)</b>	<b>(1 852)</b>
Cash and cash equivalents income	1	(14)
Interest on conditional advances	(2 249)	(2 052)
Fair value revaluation of OCA 1023	(1 078)	0
Fair value revaluation of IPF's share subscription warrants	(227)	214
<b>Foreign exchange gains and losses</b>	<b>176</b>	<b>(304)</b>
<b>Other financial income and expenses</b>	<b>(11)</b>	<b>10</b>
<b>FINANCIAL INCOME (LOSS)</b>	<b>(3 388)</b>	<b>(2 147)</b>

The negative financial income of €3.4 million as of December 31, 2021, is mainly due to the interests generated by the bond loan contracted with IPF Fund II in October 2019 (€2.9 million) and the revaluation of the fair value of the bond loan subscribed in October 2021 (€1.1 million).

It is to be noted that, as of December 31, 2021, the revaluation of the BSA stock warrants granted to IPF in the bond loan subscribed in October then December 2019, amounts to a financial income of €0.2 million.

Some change variations are also recognized for a net amount of €0.2 million.

- NOTE 21 Corporate tax

In 2021, the Company recognized a tax loss of €25.9 million.

The amount of carryforward tax losses amounted to €190.7 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 2021 (12 months)</b>	<b>FY 2020 (12 months)</b>
<b>PROFIT (LOSS) BEFORE TAX</b>	<b>(22 754)</b>	<b>(23 295)</b>
National tax at the period standard rate	6 371	6 523
Permanent differences	1 231	1 605
Uncapitalized tax loss adjusted for deferred tax	(7 615)	(8 140)
<b>ACTUAL TAX EXPENSE</b>	<b>(13)</b>	<b>(13)</b>

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- NOTE 22 Earnings per share

	<b>FY 2021 (12 months)</b>	<b>FY 2020 (12 months)</b>
<b>CONSOLIDATED NET PROFIT / LOSS (in euros thousands)</b>	<b>(22 754)</b>	<b>(23 324)</b>
Average number of shares	7 057 600	6 973 639
<b>NET EARNINGS (LOSS) PER SHARE (in euros)</b>	<b>(3,2)</b>	<b>(3,3)</b>
<b>NET EARNINGS (LOSS) PER SHARE FULLY DILUTED (in euros)</b>	<b>(3,2)</b>	<b>(3,3)</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 2021 (12 months)</b>	<b>FY 2020 (12 months)</b>
Short-term benefits	762	709
Posterior employment benefits	182	122
Other long term benefits	0	0
Termination benefits employment contract	0	0
Share-based payment	0	(208)
<b>TOTAL COMPENSATION PAID TO CORPORATE OFFICERS</b>	<b>944</b>	<b>622</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.

If the Company were to enter into additional licensing and collaboration agreements with U.S. pharmaceutical groups, it could be exposed to additional Euro-US dollar exchange rate risk.

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. Between March and May 2019, the Company contracted a bank loan of €1.2 million to finance the development of two 450 m<sup>2</sup> floors, one consisting of offices and the other of laboratories.

These loan contracts were negotiated at a fixed rate.

The bond loan contracted with IPF Fund II generates two types of interest: interest to be repaid quarterly and capitalized interest to be repaid *in fine*. The applicable interest rates are indexed to Euribor (with a minimum set at 0%).

The State guaranteed loans have fixed interest rates between 0.25% and 1.75% as the first year's payment. For the record, these loans do not require payment in the first two years.

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 €28.1 million as of December 31, 2020 and close to €15.2 million as of December 31, 2021. 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.

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,
- a mortgage on the building

In order to guarantee the repayment of the bonds issued by the Company for the benefit of IPF Fund II, the latter has granted a pledge on some of its assets and in particular:

- a pledge under French law of the Company's bank accounts and securities accounts,
- a pledge of the Company's main intellectual property rights (Core IP) registered in France, Europe, the United States and China secured by the conclusion of a deed of pledge of patents under French law, a deed of pledge under New York State law and a deed of pledge under Chinese law on the following patent families:
  - FAST Insulin (BC lispro and HinsBet): WO2014076423
  - Combination of basal insulin, especially insulin glargine, and prandial insulin: WO2019110773
  - Combination of prandial insulin and prandial glucagon suppressor: WO2019020820
- a pledge of the Company's trade receivables secured by the conclusion of a deed of pledge of Receivables under French law,

being specified that the creation of additional securities may in the future be required by IPF Fund II, in particular on inventory with a value of more than €250,000 and intellectual property rights developed or acquired in the future.

These securities may be enforced by IPF Fund II in the event of default by the Company or at the request of IPF Fund II in the event of the occurrence of any event of default stipulated in the contract of issue. The implementation of such security interests would result in the judicial attribution, forced sale or, as the case may be, transfer of ownership of the pledged assets to IPF Fund II.

▪ **NOTE 26 Events subsequent to year end**

In March 2022, the Company completed a sale and leaseback transaction resulting in the sale of its building, acquired in 2016, and the signature of a 12-year renewable lease. This transaction resulted in a net cash inflow of €19 million. As of March 28, 2022, the Company's cash position thus amounted to €28 million.

## 4.2 Statutory auditors' report on the consolidated financial statements

ODICEO

ERNST & YOUNG et Autres

*This is a translation into English of the statutory auditors' report on the consolidated financial statements of the Company issued in French and it is provided solely for the convenience of English speaking users. This statutory auditors' report includes information required by European regulation and French law, such as information about the appointment of the statutory auditors or verification of the information concerning the Group presented in the management report and other documents provided to shareholders. This report should be read in conjunction with, and construed in accordance with, French law and professional auditing standards applicable in France.*

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Adocia

Year ended December 31, 2021

Statutory auditors' report on the consolidated financial statements

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Commissaire aux Comptes  
Membre de la compagnie  
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Commissaire aux Comptes  
Membre de la compagnie  
régionale de Versailles

Adocia

Year ended December 31, 2021

## Statutory auditors' report on the consolidated financial statements

To the Annual General Meeting of Adocia,

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### 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, 2021.

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, 2021 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 requirements of the French Commercial Code (*Code de commerce*) and the French Code of Ethics (*Code de déontologie*) for statutory auditors for the period from January 1, 2021 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.

### Emphasis of Matters

We draw your attention to the following matter described in Note "Basis for preparation of the financial statements" to the consolidated financial statements relating to the assumptions retained to ensure going concern basis. Our opinion is not modified in respect of this matter.



## Justification of Assessments - Key Audit Matters

Due to the global crisis related to the COVID-19 pandemic, the financial statements for this period have been prepared and audited under special circumstances. Indeed, this crisis and the exceptional measures taken in the context of the health emergency have had numerous consequences for companies, particularly on their operations and their financing, and have led to greater uncertainties regarding their future prospects. Some of these measures, such as travel restrictions and remote working, have also had an impact on companies' internal organization and on the performance of audits.

It is in this complex and evolving context that, 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.

### ■ Accounting treatment and valuation of convertibles bonds

Risk identified	Our response
<p>On October 26, 2021, the company entered into an agreement for the issuance of convertible bonds for a total amount of € million 6. Your company issued a total number of 6 568 422 convertible bonds with nominal value equal to €1 ("les OCA"), which have been subscribed by Vester Finance and two other European investors as described in the note 10 to the accompanying consolidated financial statements.</p> <p>These bonds ("OCA") have been issued at 95% of their nominal value. They do not hold interests and can be converted into ordinary shares, upon holder's request, at any time and using a variable subscription price.</p> <p>If these bonds ("OCA") would not have been reimbursed or converted at the end of the initial 24-month period, they would be full reimbursed by the company at 100% of their nominal value.</p> <p>At the end of December 31, 2021, a portion of these bonds has been converted and the remaining bonds have been classified as financial liabilities and measured at the fair value, as a whole.</p> <p>To perform this fair value measurement, your company has been assisted by an independent actuary, who measured these bonds as call options with variable exercise price and used a "Monte-Carlo" valuation approach.</p> <p>As disclosed in the note 10 in the accompanying consolidated financial statements, under IFRS 9 and IAS 32 rules, your company qualified these bonds as debt</p>	<p>As part of our audit of the consolidated financial statements, Our procedures consisted in:</p> <ul style="list-style-type: none"> <li>▶ Obtaining an understanding of the bond contract and the analysis performed by the company.</li> <li>▶ Evaluating the assumptions and the documentation related to the accounting treatment (under IFRS 9 and IAS 32) retained by the company</li> <li>▶ Obtain an understanding of the reports prepared by the independent actuary to assess the fair value of these bonds ("OCA") on the issuance date (October 2021) and the remaining not converted bonds at the closing date and also to examine the assumptions retained in connection with the bond contract specificities and the company's analysis.</li> <li>▶ Examine the appropriateness of the information provided about this risk in the disclosures.</li> </ul>

instruments with a fair value measurement through profit and loss at the end of each reporting period.

We considered the topic as a key audit matter as it requires judgmental basis to assess the accounting treatment and the fair value of these bonds.

#### 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 relating to the Group given in the Board of Directors management report.

We have no matters to report as to their fair presentation and their consistency with the consolidated financial statements.

#### Report on Other Legal and Regulatory Requirements

##### ■ Format of preparation of the consolidated financial statements included in the annual financial report

We have also verified, in accordance with the professional standard applicable in France relating to the procedures performed by statutory auditor regarding the annual and consolidated financial statements prepared in the European single electronic format, that the preparation of the consolidated financial statements included in the annual financial report mentioned in Article L. 451-1-2, I of the French Monetary and Financial Code (*Code monétaire et financier*), prepared under the CEO's responsibility, complies with the single electronic format defined in Commission Delegated Regulation (EU) No. 2019/815 of 17 December 2018. Regarding consolidated financial statements, our work includes verifying that the tagging thereof complies with the format defined in the above-mentioned regulation.

On the basis of our work, we conclude that the preparation of the consolidated financial statements included in the annual financial report complies, in all material respects, with the European single electronic format.

##### ■ Appointment of the Statutory Auditors

We were appointed as statutory auditors of Adocia by Decision of the Sole Shareholder of July 31, 2006 for ODICEO and by your Annual General Meeting held on October 24, 2011 for ERNST & YOUNG et Autres.

As at December 31, 2021, ODICEO was in the sixteenth year of uninterrupted engagement and ERNST & YOUNG et Autres was in the eleventh year of total uninterrupted engagement, which is the tenth year since securities of the Company were admitted to trading on a regulated market, respectively.

#### 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.

4

Villeurbanne and Lyon, April 21, 2022

The Statutory Auditors  
*French original signed by*

ODICEO

ERNST & YOUNG et Autres

Agnès Lamoine

Mohamed Mabrouk

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## 4.3 Corporate annual financial statements

### 4.3.1. Balance sheet, French GAAP

<i>In € thousands French gaap</i>	12/31/2021	12/31/2020
Intangible assets - Gross amount	169	169
(Cumulated depreciation and amortization)	(165)	(146)
<b>Intangible assets - Net amount</b>	<b>3</b>	<b>23</b>
<b>Tangible fixed assets</b>		
Lands	2 441	2 441
Constructions	4 281	4 275
Fixtures & fittings, industrial equipment	2 489	2 347
Other tangible fixed assets	5 408	5 212
Construction work in progress	0	56
Total tangible fixed assets	14 619	14 332
(Cumulated depreciation and amortization)	(6 772)	(5 926)
<b>Total tangible fixed assets - Net amount</b>	<b>7 847</b>	<b>8 406</b>
<b>Fiancial assets - Net amount</b>	<b>422</b>	<b>378</b>
<b>Long term assets</b>	<b>8 273</b>	<b>8 807</b>
<b>Inventory and work in progress</b>	<b>517</b>	<b>569</b>
<b>Receivables</b>		
Advance payments made on orders	124	74
Trade and similar receivables	207	0
Other receivables	5 574	7 138
<b>Total receivables</b>	<b>5 904</b>	<b>7 212</b>
<b>Cash assets and miscellaneous</b>		
Short-term investment securities	4 077	4 077
Cash assets	11 037	23 958
Pre-paid expenses	490	539
<b>Total Cash assets and Miscellaneousm</b>	<b>15 604</b>	<b>28 575</b>
<b>Current assets</b>	<b>22 026</b>	<b>36 356</b>
Bond redemption premium	245	
Translation losses	29	6
<b>TOTAL ASSETS</b>	<b>30 573</b>	<b>45 168</b>

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<i>In € thousands French gaap</i>	12/31/2021	12/31/2020
Paid-up capital	727,096	702,063
Additional paid-in capital	81 559	79 615
Balance brought forward	(72 076)	(49 683)
Profit/loss for the year	(21 383)	(22 393)
<b>Equity</b>	<b>- 11 172</b>	<b>8 242</b>
<b>Conditional advances</b>	<b>520</b>	<b>520</b>
<b>Provisions for risks and charges</b>	<b>107</b>	<b>6</b>
Loans and debt with credit institutions	32 862	27 673
Misc.loans and financial debt	-	0
<b>Total financial debt</b>	<b>32 862</b>	<b>27 673</b>
Trade and similar payables	4 248	5 213
Tax and social security liabilities	3 283	2 308
Debt on fixed assets and similar accounts	7	36
Other debt	37	27
<b>Total miscellaneous debt</b>	<b>7 574</b>	<b>7 584</b>
<b>Unearned income</b>	<b>682</b>	<b>1 133</b>
<b>Translation gain</b>	<b>0</b>	<b>11</b>
<b>TOTAL LIABILITIES</b>	<b>30 573</b>	<b>45 168</b>

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### 4.3.2. Income statement, French GAAP

<i>In € thousands French gaap</i>	FY 2021 (12 months)	FY 2020 (12 months)
Net revenue	1 450	842
Reversals of depr./amort.and prov., transfers of charges	180	334
Other income	11	48
<b>Operating income</b>	<b>1 641</b>	<b>1 225</b>
Purchase of raw materials ans other supplies (incl. change in inventory)	(1 264)	(1 457)
Other purchases and external charges	(11 455)	(13 577)
Taxes and similar payments	(265)	(257)
Wages and salaries	(8 236)	(7 933)
Social contributions	(3 553)	(3 372)
Depreciation and provisions for fixed assets	(1 051)	(970)
Provisions for current assets	0	0
Other operating expenses	(83)	(58)
<b>Operating expenses</b>	<b>(25 906)</b>	<b>(27 626)</b>
<b>Operating profit / loss</b>	<b>(24 265)</b>	<b>(26 401)</b>
<b>Financial profit / loss</b>	<b>(1 810)</b>	<b>(2 016)</b>
<b>Profit / loss from ordinary activities before tax</b>	<b>(26 075)</b>	<b>(28 417)</b>

<b>Extraordinary profit / loss</b>	<b>82</b>	<b>32</b>
Income tax	4 611	5 992
<b>PROFIT / LOSS</b>	<b>(21 383)</b>	<b>(22 393)</b>

## 4.3.3. Notes to the corporate annual financial statements

### 4.3.3.1. 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, 2021 was €30.6 million.

The net accounting loss was €21.4 million.

The following notes and tables form an integral part of the annual financial statements, which were approved by the Board of Directors on April 14, 2022.

The financial statements were prepared in accordance with:

- the General Chart of Accounts approved by the ANC regulation n° 2014-03 of 5 June 2014 updated by ANC regulation n° 2016-07 of 4 November 2016:

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.

In order to meet the financial commitments made to its lenders (see §.10 financial liabilities) and given (i) the cash position of €15.2 million at 31 December 2021, (ii) the receipt of €19 million in March 2022 related to the sale of the headquarters (iii) the expected receipt in the second quarter of 2022 of the milestone payment from Tonghua Dongbao following the start of phase 3 of the BC Lispro and (iv) the forecasts made, the Company will have to conclude a partnership agreement or a capital raising operation during the fourth quarter of 2022.

Management is confident that it will be able to obtain new sources of financing or, failing that, obtain a new temporary arrangement of its financial ratios to be respected in the context of the loans granted to the Company.

To prepare its financial statements, the Company has adopted the going concern assumption.

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 one employee: a Director Business Development.

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 2021, the unrealized capital gain on these investments was €27 thousand.

- **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.

- **Revenue**

The Company's revenue is mainly due to the licensing agreements signed with Tonghua Dongbao for the BioChaperone® Lispro and BioChaperone® Combo combinations in China and other territories.

In 2020, revenue resulted in €0.7 million from the initial upfront payment of \$50 million (€41.1 million) in April 2018 at the signature of the two partnership and licensing agreement with Tonghua Dongbao. These revenues related to R&D services provided by Adocia to Tonghua Dongbao, are recognized based on progress, by comparison between the costs incurred by Adocia and the total budget estimated to date over the term of the contract. The Company had also rebilled Tonghua Dongbao a PK/PD study for the 2020 financial year that amounted to €0.1 million.

Revenue for the year 2021 of €0.4 million reflects the progress of research and development services provided by Adocia in the context of the transfer and development of the products as contracted in 2018. At the request of the partner, additional services were provided by Adocia's teams, notably on the BC combo project and represent an amount of nearly 1 million euros.

The portion of the initial payment yet to be recognized as revenue, as of December 31, 2021, amounts to €0.7 million and is recognized as deferred income.

- **Change in methods**

None.

### 4.3.3.2. Highlights of the fiscal year

2021 has been marked by important advances in our insulin portfolio and the launch of new projects in the field of diabetes and obesity. The financing operation done in the last quarter enabled the reinforcement of available financial means to support the Company's growth.

#### Significant progress has been made on the more mature projects of our pipeline.

- Phase 3 of BioChaperone® Lispro was authorized by the CDE

In October 2021, Tonghua Dongbao received the authorization to start the phase 3 program of ultrarapid insulin BioChaperone Lispro for the treatment of type 1 and 2 diabetes in China. The operational start of phase 3 in China must trigger a milestone payment to Adocia. At the same time, the preparation work for phase 3 studies in the United States and in Europe has been completed successfully and our business activities are aimed at finding a partner able to finance the pivotal program until marketing authorization is obtained for these territories.

- M1Pram and BioChaperone® LisPram: strong value added first-in-classes

Adocia intensified the clinical development of its two candidates, M1 Pram and BC LisPram, respectively positioned for the auto-injector pen and pump markets. These fixed combinations of analog insulin and amylin are intended to replace rapid insulins, essential to the survival of many patients, and whose revenue amount to more than \$9 billion a year. These combinations' aim is to improve glycemia control, as well as to generate weight loss for obese diabetes patients. In the United States, 65% of type-1 diabetic patients and 85% of type-2 diabetics are overweight or obese<sup>78,79</sup>.

A Phase 2 study (CT041) was initiated with M1Pram in auto-injector pens. It follows the establishment of proof of concept in humans, for which results were published in September 2020 (CT038 – part B). M1Pram demonstrated an improvement in glycemia control and significant weight loss compared to the aspart reference rapid insulin in only 3 weeks of treatment. The Phase 2 study CT041 which objective is to confirm these results over a 4-month period in type-1 diabetes patients, was created to define all the parameters for an upcoming Phase 3 program. Results are expected in the first quarter of 2022.

#### New projects were launched capitalizing on the team's skills and the expertise gained in the field of diabetes.

- Revolutionize the transplant of Langerhans islets

In January 2021, Adocia announced the filing of patents on a hydrogel matrix that aims to improve cell therapy techniques for the transplant of Langerhans islets. This matrix's function is to maintain secretory activity of transplanted cells while protecting them from the immune system. Adocia's objective is to create an organoid able to secrete insulin in response to glycemic variations while avoiding the use of immunosuppressive medicines. An academic collaboration is established with the Inserm team of Professor Pattou, world leader in the transplant of Langerhans islets. Trials on animals are ongoing before human implantation trials.

- Associate hormones to treat obesity

These last months, Adocia also initiated new projects in the obesity field. Patient care is changing: on the one hand, due to the progressive recognition of obesity as a pandemic requiring medical treatment and, on the other hand, due to the discovery of the efficiency of some hormones – also involved in diabetes – in weight control. These treatments make it possible to avoid bariatric surgery.

Adocia succeeded in associating hormones with synergistic effects and in formulating two hormonal combinations to address the different types of obese patients.

These products are for pump administration so that the patient can implement a personalized treatment adapted to their lifestyle with the help of their doctor.

Patents have been filed by Adocia for these pump-administered hormone combinations. A human proof-of-concept study will be initiated in 2022.

<sup>78</sup> Conway et al, *Diabetes Med* 2010 April; 27(4):398-404. BMI>25, Data for 2004-2007 period

<sup>79</sup> *Epidemiology of Obesity and Diabetes and Their Cardiovascular Complications*

These products could also be developed for other conditions such as NASH (Non-Alcoholic Steatohepatitis) and type 2 diabetes.

#### The financing operation done in October reinforces the Company's cash flow

In October 2021, the Company did a financing operation by (i) the issuance of 6.568.422 bonds convertible into shares with a par value of €1 each for a total net amount of €6 million subscribed by Vester Finance and two other European investors and (ii) a share capital increase of €1 million, the subscription of which has been reserved for the benefit of Gérard Soula, Chief Executive Officer and shareholder through the issuance of new ordinary shares.

To conclude, in terms of governance, Adocia reinforced its Board of Directors with the appointment of three new independent members: Dr Claudia Mitchell, Senior Vice-President and Head of Portfolio Strategy at Astellas Pharma; Dr Katherine Bowdish, President and CEO of PIC Therapeutics; and Stéphane Boissel, CEO of SparingVision.

### 4.3.3.3. 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

#### NOTE 1 Intangible assets

	12/31/2020	Acquisitions, contributions, creation, transfers	Decreases	12/31/2021
Start-up and development costs	11			11
Other intangible assets	157	0	0	157
<b>GROSS AMOUNT</b>	<b>169</b>	<b>0</b>	<b>0</b>	<b>169</b>
Start-up and development costs	(11)			(11)
Other intangible assets	(135)	(20)	0	(154)
<b>DEPRECIATION / AMORTIZATION</b>	<b>(146)</b>	<b>(20)</b>	<b>0</b>	<b>(165)</b>
Start-up and development costs	0			0
Other intangible assets	23	(20)		3
<b>NET AMOUNT</b>	<b>23</b>	<b>(20)</b>	<b>0</b>	<b>3</b>

▪ NOTE 2 Property, plant and equipment

	12/31/2020	Acquisitions, contributions, creation, transfers	Decreases	12/31/2021
Lands	2 032	0	0	2 032
Land development	409	0	0	409
Buildings	4 275	6	0	4 281
Laboratory equipment	2 347	159	(18)	2 489
Fixtures and facilities	3 679	134	0	3 813
Furniture, office equipment	1 533	61	0	1 595
Advances and payment on account	56	(29)	(27)	(0)
<b>GROSS AMOUNT</b>	<b>14 332</b>	<b>332</b>	<b>(45)</b>	<b>14 619</b>
Lands	0	0	0	0
Land development	87	41	0	127
Buildings	978	214		1 192
Laboratory equipment	2 090	109	(18)	2 181
Fixtures and facilities	1 489	375	0	1 864
Furniture, office equipment	1 283	125	0	1 408
<b>DEPRECIATION / AMORTIZATION</b>	<b>5 926</b>	<b>863</b>	<b>(18)</b>	<b>6 772</b>
Lands	2 032	0	0	2 032
Land development	322	(41)	0	282
Buildings	3 298	(208)	0	3 090
Laboratory equipment	258	51	0	308
Fixtures and facilities	2 190	(241)	0	1 949
Furniture, office equipment	250	(64)	0	187
Advances and payment on account	56	(29)	(27)	(0)
<b>NET AMOUNT</b>	<b>8 406</b>	<b>(532)</b>	<b>(27)</b>	<b>7 847</b>

▪ NOTE 3 Receivables and debts

Receivables <i>In € thousands French gaap</i>	Gross amount	Up to 1 year	1 year or more
Long-term financials assets	422		422
Other trade receivables	207	207	
Social security and other social agencies	23	23	
Government - Income tax (including CICE et CIR)	4 636	4 636	
Government - Value added tax	542	542	
Miscellaneous debtors	496	496	
<b>Current assets</b>	<b>5 904</b>	<b>5 904</b>	
Pre-paid expenses	490	490	
<b>TOTAL</b>	<b>6 817</b>	<b>6 395</b>	<b>422</b>

<i>Debts In € thousands French gaap</i>	Gross amount	Up to 1 year	1 year or more
Loans and debt with credit institutions	33 382	15 096	18 286
Miscellaneous loans and financial debt	-	-	
<b>Financial debts</b>	<b>33 382</b>	<b>15 096</b>	<b>18 286</b>
Trade and similar payables (*)	3 826	3 826	
Staff and similar accounts	1 646	1 646	
Social security and other agencies	1 410	1 410	
Value added tax	-	-	
Other taxes and similar	226	226	
Debt on fixed assets and similar accounts*	7	7	
Group and partners	422	422	
Other debt	37	37	
<b>Miscellaneous debt</b>	<b>7 574</b>	<b>7 574</b>	
<b>Unearned income</b>	<b>682</b>	<b>373</b>	<b>309</b>
<b>TOTAL GENERAL</b>	<b>41 638</b>	<b>23 043</b>	<b>18 595</b>

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(\*) including accrued expenses and accrued income

- NOTE 4 Accrued expenses

<i>In € thousands French gaap</i>	12/31/2021	12/31/2020
Trade and similar payables	2 743	2 510
Tax and social security liabilities	2 418	1 443
<b>TOTAL</b>	<b>5 161</b>	<b>3 953</b>

- NOTE 5 Revenue accruals

<i>In € thousands French gaap</i>	12/31/2021	12/31/2020
Trade and similar receivables	207	0
Government	25	25
Other receivables	519	562
Cash assets	0	0
<b>TOTAL</b>	<b>751</b>	<b>587</b>

▪ **NOTE 6 Prepaid expenses and unearned income**

<i>In € thousands French gaap</i>	12/31/2021	12/31/2020
Operating income or expense	(192)	(594)
Financial income or expense		
Extraordinary income or expense		
<b>TOTAL</b>	<b>(192)</b>	<b>(594)</b>

▪ **NOTE 7 Share capital structure**

	As of January 1st, 2020	Capital increase (in euros)	As of December 31st, 2021	Share capital (in euros)
Common shares	7 020 629	250 327	7 270 956	727 096

▪ **NOTE 8 Workforce**

	12/31/2021	12/31/2020
Technicians	53	56
Management personnel	58	69
<b>Total employees</b>	<b>111</b>	<b>125</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 the event of commercial failure of the program, even partial, given the nature of the work carried out as part of the Rapid Human Insulin project, the Company has committed to reimburse OSEO a minimum sum of €280,000, corresponding to the 2017 and 2018 deadlines.

In 2015, the Company recognized the end of the program and made the scheduled repayments in the event of commercial failure of the program over the years 2017 and 2018. An expertise commissioned by BpiFrance was realized in 2020 and should make it possible to close this file in the next few months.

▪ **NOTE 10 Income statement**

The Company's revenue of €1.4 million mostly results from:

- the licensing agreements signed in April 2018 with the company Tonghua Dongbao Pharmaceuticals for an amount of €0.4 million
- the rebilling of Tonghua Dongbao for additional services provided at the request of the partner for the 2021 financial year, particularly for the BC Combo project. These services amounted to close to €1 million.

<i>In € thousands French gaap</i>	<b>FY 2021 (12 months)</b>	<b>FY 2020 (12 months)</b>
Net revenue	1 450	842
Reversals of depr./amort.and prov., transfers of charges	180	334
Other income	11	48
<b>Operating income</b>	<b>1 641</b>	<b>1 225</b>

In 2021, operating expenses totaled €25.9 million compared to €27.6 million in 2020 and included the following items:

<i>In € thousands French gaap</i>	<b>FY 2021 (12 months)</b>	<b>FY 2020 (12 months)</b>
Purchase of raw materials and other supplies	(1 264)	(1 457)
Other purchases and external charges	(11 455)	(13 577)
Taxes and similar payments	(265)	(257)
Payroll expense	(11 788)	(11 305)
Depreciation and provisions	(1 051)	(970)
Other operating expenses	(83)	(58)
<b>Operating expenses</b>	<b>(25 906)</b>	<b>(27 626)</b>

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There was an operating loss of €24.3 million versus a loss of €26.4 million the previous year.

A net financial loss of €1,8 million was recorded in 2021 compared to a loss of €2 million the previous year. It is mainly due the interest rates generated by the bond loan subscribed with IPF Fund II in October 2019.

As a result, there was a pre-tax loss on ordinary activities of €26.1 million versus a loss of €28.4 million the previous year.

After taking into account the Research Tax Credit of €4,6 million, fiscal year 2021 ended with a net loss after tax of €21.4 million compared to a net loss of €22.4 million the previous year.

- **NOTE 11 Balance sheet**

### Assets

Non-current assets amounted to €8.3 million on December 31, 2020 compared to €8.8 million on December 31, 2020. This decrease reflects the amortization of the assets of the period as well as a low investment level in 2021.

Current assets totaled €22 million compared to €36.4 million a year earlier. They consisted of the following items:

"Cash and cash equivalents" decreased from €28 million on December 31, 2020 to €15,1 million on December 31, 2021. The change in the line item (€-12.9 million) mainly results from the cash outflow totaling €19,9 million over the year 2021 and an increase in cash of €7 million as a result of € 7 million financing operation carried out through the issue of (i) convertible bonds subscribed by European investors and (ii) ordinary shares subscribed by Gérard Soula.

The "other receivables" item amounted to €5.6 million on December 31, 2021, down by €1.5 million compared to €7.1 million in 2020. It includes receivables from the government, such as the Research Tax Credit (CIR) of €4,6 million, the VAT credit and credit notes receivable from suppliers. The decrease compared to last year reflects the decrease in expenses eligible for the Research Tax Credit in 2021.

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 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	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 term : upon invoice reception				

**Prepaid expenses** amounted to €0.5 million in 2021, stable compared to 2020.

## Liabilities

The company's **equity** totaled €-11.2million compared to €8.2 million a year earlier.

The equity is negative and therefore less than half the share capital for the first time. Share capital amounted to €727 096 on December 31, 2021 versus €702,063 at the end of the previous year. The share premium of €81.6 million at the end of 2021 is up compared to 2020 (+€1.9m). The increase in the "share capital" and "share premium" lines is mainly due to the issue of ordinary shares subscribed by Gérard Soula (+€1m) and the partial conversion of bonds issued in October 2021 (+€0.9m).

Indeed, on October 26, 2021, the Company issued 6.568.422 bonds convertible into shares with a par value of EUR 1 each (the "Convertible Bonds") for a total amount of EUR 6 million net subscribed by Vester Finance and two other European investors.

These Convertible Bonds were issued at a price equal to 95% of their nominal value. The Convertible Bonds will not bear interest and may be converted into ordinary shares at the request of the holder, at any time and at a subscription price per share (the "Conversion Price") equal to the lower of (i) EUR 11.87 and (ii) 93% of the lowest of the daily VWAPs over a period of 15 days preceding each conversion request, in compliance with the limit set by the General Meeting, that is 80% of the volume-weighted average price of the last three trading sessions preceding the conversion request.

Convertible Bonds may also be converted or redeemed (in cash or in convertible bonds) at the request of the holder should an event of default occur.

In the event that the Convertible Bonds have not been fully converted and/or redeemed at the end of the initial duration of 24 months (extendable under certain conditions), they will be fully redeemed by the Company at 100% of their nominal value.

As of December 31, 2021, part of these bonds has been converted (970 000 bonds corresponding to 14.77% of the total amount issued) and resulted in the issuance of 123.960 shares.

At the end of 2021, carryforward losses totaled €72,1 million compared to €49,7 million at the end of 2020, with the difference coming from the allocation of the €22.4 million profit of the fiscal year closed end of 2020.

The conditional advances were stable at €0.5 million on December 31, 2021 (see note 9 on repayable advances).

## The company's debt position based on business volume and complexity

**Financial debt** totaled €32.9 million at the end of December 2021, increasing by €5.2 million compared to the end of December 2020. This increase mostly results from the convertible bond financing operation done in October 2021



that resulted in a net receipt of €6 million. A part of these bonds (€ 1 million) was converted at the end of December, 2021, the balance being recorded as liabilities (€ 5,6 million).

In September 2021, the Company obtained a temporary accommodation from its lenders of its cash covenants in anticipation of (i) an additional financing to be completed by October 31, 2021 at the latest and (ii) the sale of the building to be completed by March 31, 2022 at the latest. The cash flow threshold initially fixed at \$16 million was lowered to €10 million.

In this context, the minimum amount of cash required to be available has been temporarily reduced to 10 million euros, with a 1% increase in interest rates (cash margin and PIK margin) over the relevant period.

IPF authorizes the Company to sell its real estate assets but asks in return for the possibility of allocating part of the sale price to the early repayment of its loan, up to a maximum of 2 million euros as of August 31, 2022.

Failure to comply with these commitments, which would not be remedied within 10 working days of the occurrence or notification by IPF Fund II (or immediately with respect to non-compliance with the covenant cash) could lead IPF Fund II to declare the loan's anticipated due date and to proceed with the implementation of the security detailed above.

As of December 31, 2021, the Group was in compliance with the commitments described above.

"**Tax and staff cost liabilities**" amounted to €3.3 million at the end of 2021, one million euros more than in 2020. The increase in this line item is mainly due to the premiums provisioned for 2021 (+ €1.1 million compared to 2020).

"**Trade payables**" totaled €4.2 million compared to €5.2 million at the end of December 2020, this variation is related to the decrease in R&D activities (external expenses) over the period compared to the previous year.

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	4	5	4	1	14
Total amount of concerned invoices, tax included	127	6	18	12	163
Percentage of total purchases amount for the year, tax included	0,87%	0,04%	0,12%	0,08%	1,12%
<b>(B) Invoices excluded from (A) due to contentious or unrecognized debts and receivables</b>					
Number of invoices excluded			10		
Total amount of invoices excluded, tax included			47		
<b>(C) Standard payment delay used</b>					
Payment term used to calculate the payment delay	Contract term : depending on the supplier, upon invoice reception, within 30 days, within 45 days, etc.				

#### 4.3.3.4. Proposed allocation of losses for fiscal year 2021

A proposal is made to allocate the loss for the fiscal year ended December 31, 2021 amounting to €21,382,669.19 to retained earnings.

As a reminder, the company did not pay out dividends over the last three years.

#### 4.3.3.5. 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, 2021.

### 4.3.3.6. 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 €1.4 million on December 31, 2021 compared to €2.2 million at December 31, 2020. (See note 11 about the consolidated financial statements prepared under IFRS in section 4.1.6 of this registration document).

#### Signing of financial leases

The Company owns several assets financed through leasing. At the end of December 2021, it had two agreements. These agreements cover equipment for which the total acquisition cost is €0.2 million. The two agreements have a financing term of three years. These two contracts will expire in 2022.

It should be noted that in 2020 the leases were extended for a period of 6 months, as a result of measures taken by the banking sector to support businesses in the context of the COVID-19 pandemic.

#### Guarantees provided

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,
- a mortgage on the building

In order to guarantee the repayment of the bonds issued by the Company for the benefit of IPF Fund II, the latter has granted a pledge on some of its assets and in particular:

- a pledge under French law of the Company's bank accounts and securities accounts,
- a pledge of the Company's main intellectual property rights (Core IP) registered in France, Europe, the United States and China secured by the conclusion of a deed of pledge of patents under French law, a deed of pledge under New York State law and a deed of pledge under Chinese law on the following patent families:
  - FAST Insulin (BC lispro and HinsBet): WO2014076423
  - Combination of basal insulin, especially insulin glargine, and prandial insulin: WO2019110773
  - Combination of prandial insulin and prandial glucagon suppressor: WO2019020820
- a pledge of the Company's trade receivables secured by the conclusion of a deed of pledge of Receivables under French law,

being specified that the creation of additional securities may in the future be required by IPF Fund II, in particular on inventory with a value of more than €250,000 and intellectual property rights developed or acquired in the future.

These securities may be enforced by IPF Fund II in the event of default by the Company or at the request of IPF Fund II in the event of the occurrence of any event of default stipulated in the contract of issue. The implementation of such security interests would result in the judicial attribution, forced sale or, as the case may be, transfer of ownership of the pledged assets to IPF Fund II.

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### 4.3.3.7. Bonus shares, stock subscription warrants, BSA, bonds convertible into shares and BSPCE

As of the date of this universal reference document, there were four types of shares conferring equity rights.

#### BSA stock warrants plan

	BSA 06-2011	BSA 12-2013	BSA 03-2017	BSA 2019	BSA 2020 <sup>IPF</sup>
Date of shareholders' meeting	06/17/2011	06/18/2013	11/12/2015	05/16/2019	05/28/2020
Date of Board of directors' decision	06/17/2011	12/13/2013	03/07/2017	10/03/2019	07/20/2020
Number of BSA stock warrants authorized	140	20 000	40 000	15 000 000	35 005
Number of BSA stock warrants issued	140	20 000	40 000	15 000 000	35 005
Total number of shares that may be subscribed	1 400	20 000	40 000	262 542 <sup>(5)</sup>	38 961
Of which, number that may be subscribed by corporate officers	-	20 000	-	-	-
Earliest exercise date	06/17/2011	1/1/2014	03/07/2017	10/11/2019	07/20/2020
Expiration date	06/17/2021	12/13/2023	03/07/2027	12/11/2026	07/19/2027
Issue price (Euros)	free	0.588	1	free	free
Exercise price (Euros)	8.571 <sup>(1)</sup>	5.88	20.65	8.57 <sup>(6)</sup>	7.70 <sup>(8)</sup>
Exercise conditions	(2)	(2)	(3)	(7)	(7)
Number of subscribed shares at the filing date of this registration document	0	0	0	0	0
Number of lapsed or cancelled warrants at the filing date of this registration document	0	0	0	0	0
Remaining warrants at the filing date of this registration document	140	20 000	40 000	15 000 000	35 005
Total number of shares that may be subscribed at the filing date of this registration document	1 400	20 000	40 000	262 542 <sup>(5)</sup>	38 961 <sup>(5)</sup>
Maximum total number of shares that may be subscribed upon exercise of all outstanding BSA stocks warrants as of December 31, 2020 (assuming fulfilment of all conditions for the exercise of said BSPCEs)	1 400	20 000	40 000	262 542 <sup>(5)</sup>	38 961 <sup>(5)</sup>

<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 that 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 universal registration document, the remaining balance, ie 25,000 BSA 03-2017, 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.

<sup>(5)</sup> Not including adjustment of the BSA stock warrants exercise price.

<sup>(6)</sup> The exercise price of the warrants is set at 8.57 euros, it being specified that in the event of the issue by the Company of new shares (excluding employee and manager profit-sharing) at a price below this amount for the duration of the 'exercise of the BSA, their exercise price will be reduced to 95% of the lowest of the said issue prices, and may not, in any event, be less than the par value of one share of the Company (i.e. €0.10) or less than the floor price set under the terms of the eighteenth resolution of the shareholders' meeting of May 16, 2019.

<sup>(7)</sup> The BSA stock warrants may be exercised in total or in part, for a minimum total exercise share of €100,000, in one or more times, at any moment from their issue date to their expiration date.

<sup>(8)</sup> The exercise price of the warrant is set at 7.70 euros, it being specified that in the event of the issue by the Company of new shares (excluding employee and manager profit-sharing) at a price below this amount for the duration of the 'exercise of the BSA, their

exercise price will be reduced to 95% of the lowest of the said issue prices, and may not, in any event, be less than the par value of one share of the Company (i.e. €0.10) or less than the floor price set under the terms of the eighteenth resolution of the shareholders' meeting of May 20, 2020.

<sup>(9)</sup> The warrants are redeemable in one-third installments on each anniversary date of their allocation, and at the latest within 10 years of their allocation.

As of the date of the present universal registration document, 15,105,220 BSA may be exercised (subject to the achievement of performance objectives) and the full exercise of the BSA could result in the creation of 371,718 shares with a par value of € 0.10.

## Bonds convertible into shares at variable price

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	CB 2021
Date of shareholders' meeting	20/05/2021
Date of Board of directors' decision	07/10/2021
Date of decision by the Chief Executive Officer (subject to the abovementioned sub-delegation)	26/10/2021
Number of bonds issued	6,568,422
Total number of shares that may be subscribed <sup>(1)</sup>	782,887
Start date for conversions	26/10/2021
Maturity date <sup>(2)</sup>	19/05/2031
Bond par value	1 €
Bond issue price	95% of the nominal value
Share issue price	<sup>(3)</sup>
Issuance terms	<sup>(4)</sup>
Number of shares issued	123,960
Cumulative number of bonds lapsed or cancelled as of the date of this registration document	0
Bonds remaining at the date of this universal registration document	3,123,922
Total number of shares that may be issued at the date of this Universal Registration Document <sup>(1)</sup>	372,339
Maximum total number of shares that may be issued upon exercise of all outstanding bonds as of the date of this Universal Registration Document <sup>(1)</sup>	372,339

- (1) on the basis of a Conversion Price (as this term is defined in note (2) below) equal to €8.39, as calculated on the assumption of a request for conversion on the date of signature of the contract on October 26, 2021
- (2) the CBs have a maturity of 24 months, renewable under certain conditions. In the event that the CBs have not been fully converted and/or reimbursed at maturity, they will be fully reimbursed by the Company at 100% of their nominal value
- (3) the CBs may be converted into ordinary shares at a issue price per share (the "Conversion Price") equal to the lesser of (i) 11.87 Euros and (ii) 93% of the lesser of the daily volume-weighted average share price over a period of 15 days preceding each conversion request, without, in any event, being less than 80% of the volume-weighted average share price over the last 3 trading sessions preceding the conversion request
- (4) the convertible bonds may be converted at any time upon request from the holder. They may also be converted or redeemed (in cash or in convertible bonds) at the request of their holder in the event of a default

## Bonus shares

	Plans 2017	Plans 2018		
	employees	n°1 employees	n°4 employees	n°5 employees
Date of shareholders' meeting	12/14/2017	02/08/2018	09/25/2018	12/05/2018
Recipients	employees	employees	employees	employees
Vesting date	12/15/2021 <sup>(1)</sup>	02/08/2022 <sup>(1)</sup>	09/25/2022 <sup>(1)</sup>	12/05/2022 <sup>(1)</sup>
End of retention period	12/15/2022 <sup>(2)</sup>	02/08/2023 <sup>(6)</sup>	09/25/2023 <sup>(6)</sup>	12/05/2023 <sup>(6)</sup>
Total number of bonus shares	9,500	2,700	5,600	11,600
Number of cancelled bonus shares at the end of the year	450	1,350	0	1,125
Number of shares with ongoing vesting at the end of the year	2,150	225	2,800	5,350

	Plan 2019	Plans 2020					
	n°3 employees	n°1 employees	n°2 employees	n°3 employees	n°4 employees	n°5.1 employees	n°5.2 employees
Date of shareholders' meeting	10/12/2019	12/03/2020	20/07/2020	29/09/2020	17/12/2020	17/12/2020	17/12/2020
Recipients	employees	employees	employees	employees	employees	employees	employees
Vesting date	10/12/2023 <sup>(1)</sup>	12/03/2024 <sup>(1)</sup>	20/07/2024 <sup>(1)</sup>	29/09/2024 <sup>(1)</sup>	17/12/2024 <sup>(1)</sup>	17/12/2024 <sup>(1)</sup>	17/12/2022 <sup>(7)</sup>
End of retention period	10/12/2024 <sup>(6)</sup>	12/03/2025 <sup>(6)</sup>	20/07/2025 <sup>(6)</sup>	29/09/2025 <sup>(6)</sup>	17/12/2025 <sup>(6)</sup>	17/12/2025 <sup>(6)</sup>	17/12/2025 <sup>(7)</sup>
Total number of bonus shares	7,300	9,600	11,600	2,700	4,800	11,500	10,500
Number of cancelled bonus shares at the end of the year	975	6,000				1,000	1,000
Number of shares with ongoing vesting at the end of the year	3,000	2,700	8,700	2,025	3,600	7,875	9,500

	Plan 2021
Date of shareholders' meeting	16/12/2021
Recipients	employees
Vesting date	16/12/2025 <sup>(1)</sup>
End of retention period	16/12/2026 <sup>(6)</sup>
Total number of bonus shares	5,700
Number of cancelled bonus shares at the end of the year	0
Number of shares with ongoing vesting at the end of the year	5,700

(1) The vesting period is four years, with one-quarter vesting on each anniversary date. The date stated is the latest date for the last one-quarter.

(2) The retention period is two years from the vesting date.

(3) The vesting period is five years, with one-quarter vesting on each anniversary date starting from the second anniversary. The date stated is the latest date for the last one-quarter.

(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 of the shares in question. The date mentioned corresponds to the end of retention period date of the last actions vested.

(7) The final acquisition of bonus shares is subject to the achievement of performance objectives defined at the earliest on 12/2022 and at the latest on 12/2024, with no retention period.

As of the date of the present universal registration document, 47,175 bonus shares were in the process of being acquired, which may result in the creation of 47,175 shares with a par value of €0.10.

## BSPCE founders' warrants

	2013 Plans		2014 Plans	
	n°1 managers	n°2 managers	n°1 managers	corporate officers
Date of shareholders' meeting	06/18/2013	06/18/2013	06/24/2014	06/24/2014
Date of Board of directors' decision	12/13/2013	12/13/2013	09/25/2014	09/25/2014
Number of BSPCE stock warrants authorized	28,000	22,400	14,000	100,000
Number of BSPCE stock warrants issued	28,000	22,400	14,000	100,000
Total number of shares that may be issued	28,000	22,400	14,000	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)	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	09/24/2024
BSPCE stock warrant issue price (euros)	free	free	free	free
BSPCE stock warrant strike price (euros)	5.76	5.76	34.99	34.99
Exercise conditions	4-year vesting	4-year vesting	4-year vesting	Immediate vesting upon fulfillment of relevant performance criteria
Number of issued shares at the end of the year	4,900	700	0	0
Most recent issue date	June -16	March-15		
Number of lapsed or cancelled warrants at the end of the year	0	2,100	5,600	35,000
Most recent BSPCE subscription cancellation		May-20	July-20	October-19
Remaining warrants at the end of the year	23,100	19,600	8,400	65,000
Total number of shares that may be issued as of 12/31/2020	23,100	19,600	8,400	65,000
Maximum total number of shares that may be issued on exercise of all outstanding BSPCEs as of December 31, 2020 (assuming all exercise conditions of aforementioned BSPCEs are met)	23,100	19,600	8,400	65,000

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	<b>BSPCE Corporate officers 2015</b>	<b>BSPCE Corporate officers 2016</b>	<b>BSPCE Corporate officers 2017</b>
Date of shareholders' meeting	11/12/2015	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 issued	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 criteria approved by the Board of directors meeting of 12/16/2015	Fulfillment of performance criteria approved by the Board of directors meeting of 12/13/2016	Upon achievement of performance criteria defined for 3 years
BSPCE stock warrant expiration date	12/16/2025	15/03/2026	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
Number of shares issued at the end of the year	0	0	0
Most recent issue date			
Number of lapsed or cancelled warrants at the end of the year	0	16,000	100,000
Most recent BSPCE subscription cancellation		December-16	December-2020
Remaining warrants at the end of the year	40,000	24,000	50,000
Total number of shares that may be issued as of 12/31/2020	40,000	24,000	50,000
Maximum total number of shares that may be issued on exercise of all outstanding BSPCEs as of December 31, 2020 (assuming all exercise conditions of aforementioned BSPCEs are met)	40,000	24,000	50,000

As of the date of the present universal registration document, 224,500 BSPCE founders' warrants would be exercisable (provided the performance objectives are met), and the exercise of all these BSPCE founders' warrants could lead to the creation of 224,500 shares of €0.10 par value.

## Stock options

	Plan SO 2018	Plan SO 2019
Date of shareholders' meeting	05/17/2018	05/17/2018
Granting date	05/17/2018	05/17/2019
Total number of stock options granted	23,000 <sup>(1)</sup>	2,000 <sup>(2)</sup>
Total number of stock options that may be subscribed	23,000	2,000
Of which corporate officers	-	-
Earliest stock option exercise date	05/17/2018	12/10/2020
Stock option expiration date	05/17/2028	10/09/2029
Stock option strike price (euros)	17.00	8.00
Number of issued shares at the end of the year		
Number of lapsed or cancelled stock options at the end of the year	3,000	1,000
Most recent cancellation date	mars-20	mars-20
Number of remaining stock options at the end of the year	20,000	1,000
Maximum total number of stock options that may be issued as of 12/31/2020	8,000	500
Maximum total number of stock options that may be issued upon exercise of all outstanding SOs as of December 31, 2020 (assuming all exercise conditions of aforementioned SOs are met)	20,000	1,000

(1) The stock options granted on May 17, 2018 can be exercised per quarter by their beneficiary according to the following exercising agenda:

- 20% of the stock options starting August 3<sup>rd</sup>, 2018;
- 20% of the stock options starting May 2<sup>nd</sup>, 2019;
- 20% of the stock options starting May 2<sup>nd</sup>, 2020;
- 20% of the stock options starting May 2<sup>nd</sup>, 2021; and
- The remaining balance, i.e. 20% of the stock options starting May 2<sup>nd</sup>, 2022.

Therefore, as of the date of the present universal registration document, 60% of the stock options can be exercised.

(2) The 16,000 stock options granted on December 10, 2019 can be exercised on 2 years.

As of the filing date of the present universal registration document, 21,000 stock options are exercisable, which, if fully exercised, would result in the creation of 21,000 shares with a par value of €0.10.

### Summary of dilutive instruments

As of the filing date of the present universal registration 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 1,331,666 shares, i.e. a maximum dilution of 15.48% based on fully diluted capital. Dilution in voting rights stands at 11.73% on the basis of fully diluted voting rights.

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#### 4.3.3.8. 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	
	FY 2021 (12 months)	FY 2020 (12 months)	FY 2021 (12 months)	FY 2020 (12 months)
Statutory auditor services, certification, review of individual and consolidated financial statements	50	49	40	39
Other services and due diligence directly related to the statutory audit assignment				
<b>Subtotal audit services</b>	<b>50</b>	<b>49</b>	<b>40</b>	<b>39</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>50</b>	<b>49</b>	<b>40</b>	<b>39</b>

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#### 4.3.3.9. Events subsequent to year end

In March 2022, the Company completed a sale and leaseback transaction resulting in the sale of its building, acquired in 2016, and the signature of a 12-year renewable lease. This transaction resulted in a net cash inflow of €19 million. As of March 28, 2022, the Company's cash position thus amounted to €28 million.

## 4.3.3.10. Table showing results over the last five fiscal years

<i>In € thousands French gaap</i>	<b>12/31/2021</b>	<b>12/31/2020</b>	<b>12/31/2019</b>	<b>12/31/2018</b>	<b>12/31/2017</b>
<b>Capital during the fiscal year (in euros)</b>					
Share capital	727 096	702 063	696 007	693 124	691 075
Number of existing ordinary shares	7 270 956	7 020 629	6 960 069	6 931 244	6 910 753
Number of existing ordinary shares cum dividend	7 270 956	7 020 629	6 960 069	6 931 244	6 910 753
Maximum number of future shares to be created					
by bond conversion	667 273				
by exercise of subscription rights	47 175	63 400	89 770	75 695	62 900
<b>Transactions and results for the fiscal year</b>					
Pre-tax revenue	1 450	842	2 622	47 562	938
Profit/loss before tax, employee profit-sharing, depreciation, amortization and provisions	(24 943)	(27 415)	(25 629)	7 976	(31 424)
Income tax	(4 611)	(5 992)	(8 840)	(2 242)	(7 535)
Employee profit-sharing owed for the year					
Profit/loss after tax, employee profit-sharing, depreciation, amortization and provisions	(21 383)	(22 393)	(17 652)	9 423	(24 667)
Distributed profit					
<b>Earnings per share (in euros per share)</b>					
Profit/loss after tax and employee profit-sharing, but before depreciation, amortization and provisions	(3)	(3)	(2)	1	(3)
Profit/loss after tax, employee profit-sharing, depreciation, amortization and provisions	(3)	(3)	(3)	1	(4)
Dividend per share					
<b>Staff (in thousands of euros)</b>					
Average number of employees during the year	121	132	136	131	126
Total payroll for the year	8 236	7 933	8 659	8 682	7 372
Total employee benefits paid for the year (social security, social agencies, etc.)	3 552	3 392	3 638	3 732	3 593

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## 4.4 Statutory auditors' report on the corporate financial statements

ODICÉO

ERNST & YOUNG et Autres

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*This is a translation into English of the statutory auditors' report on the financial statements of the Company issued in French and it is provided solely for the convenience of English-speaking users.*

*This statutory auditors' report includes information required by European regulations and French law, such as information about the appointment of the statutory auditors or verification of the management report and other documents provided to the shareholders.*

*This report should be read in conjunction with, and construed in accordance with, French law and professional auditing standards applicable in France.*

Adocia

Year ended December 31, 2021

**Statutory auditors' report on the financial statements**

**ODICEO**  
115, boulevard de Stalingrad  
CS 52038  
69616 Villeurbanne  
S.A. au capital de € 275 000  
430 130 393 R.C.S. Lyon

Commissaire aux Comptes  
Membre de la compagnie  
régionale de Lyon-Riom

**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 et du Centre

Adocia

Year ended December 31, 2021

## Statutory auditors' report on the financial statements

To the Annual General Meeting of Adocia,

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### Opinion

In compliance with the engagement entrusted to us by your Annual General Meeting, we have audited the accompanying financial statements of Adocia for the year ended December 31, 2021.

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, 2021 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 the independence requirements of the French Commercial Code (*Code de commerce*) and the French Code of Ethics for Statutory Auditors (*Code de déontologie de la profession de commissaire aux comptes*) for the period from January 1, 2021 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.

### Emphasis of Matter(s)

We draw your attention to the following matter described in Note "4.3.3.1 Accounting rules and methods" to the annual financial statements relating to the assumptions retained to ensure going concern basis. Our opinion is not modified in respect of this matter.

## Justification of Assessments - Key Audit Matters

Due to the global crisis related to the COVID-19 pandemic, the financial statements for this period have been prepared and audited under special circumstances. Indeed, this crisis and the exceptional measures taken in the context of the health emergency have had numerous consequences for companies, particularly on their operations and their financing, and have led to greater uncertainties regarding their future prospects. Some of these measures, such as travel restrictions and remote working, have also had an impact on companies' internal organization and on the performance of audits.

It is in this complex, evolving context that, 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.

We determined that there were no key audit matters to communicate in our report.

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## 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 the fair presentation and the consistency with the financial statements of the information relating to payment deadlines mentioned in Article D. 441-6 of the French Commercial Code (*Code de commerce*).

### ■ Report on Corporate Governance

We attest that the Board of Directors' Report on Corporate Governance sets out the information required by Articles L. 225-37-4 and L. 22-10-10 and L. 22-10-9 of the French Commercial Code (*Code de commerce*).

Concerning the information given in accordance with the requirements of Article L. 22-10-9 of the French Commercial Code (*Code de commerce*) relating to the remuneration and benefits received by, or allocated to the members of the Executive Board 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 companies controlled thereby, included in the consolidation scope. 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 takeover bid or exchange offer, provided pursuant to Article L. 22-10-11 of the French Commercial Code (*Code de commerce*), we have agreed this information to the source documents communicated to us. Based on these procedures, 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 purchase of investments and controlling interests and the identity of the shareholders and holders of voting rights has been properly disclosed in the management report.

### Report on Other Legal and Regulatory Requirements

#### ■ Format of preparation of the financial statements included in the annual financial report

We have also verified, in accordance with the professional standard applicable in France relating to the procedures performed by statutory auditors regarding the annual and consolidated financial statements prepared in the European single electronic format, that the preparation of the financial statements included in the annual financial report mentioned in Article L. 451-1-2, I of the French Monetary and Financial Code (*Code monétaire et financier*), prepared under the CEO's responsibility, complies with the single electronic format defined in Commission Delegated Regulation (EU) No. 2019/815 of 17 December 2018. Regarding annual financial statements, our work includes verifying that the tagging thereof complies with the format defined in the above-mentioned regulation.

On the basis of our work, we conclude that the preparation of the financial statements included in the annual financial report complies, in all material respects, with the European single electronic format.

#### ■ Appointment of the Statutory Auditors

We were appointed as statutory auditors of Adocia by Decision of the Sole Shareholder of July 31, 2006 for ODICEO and by your Annual General Meeting held on October 24, 2011 for ERNST & YOUNG et Autres.

As at December 31, 2021, ODICEO was in the sixteenth year of uninterrupted engagement and ERNST & YOUNG et Autres was in the eleventh year of total uninterrupted engagement, which is the tenth year since securities of the Company were admitted to trading on a regulated market, respectively.

### 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 risk 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 made 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 significant deficiencies, if any, 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 as set out in particular in Articles L. 822-10 to L. 822-14 of the French Commercial Code (*Code de commerce*) and in the French Code of Ethics for Statutory Auditors (*Code de déontologie de la profession de commissaire aux comptes*). 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 21, 2022

The Statutory Auditors  
*French original signed by*

ODICEO

ERNST & YOUNG et Autres

Agnès Lamoine

Mohamed Mabrouk

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# 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, 2021, the Company's capital was €727.095.60, divided into 7.270.956 fully paid-in common shares, with a par value of €0.10 each.

#### 5.1.2. Shares not representing capital

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On October 14, 2019, the Company obtained a bond financing line from IPF Fund II. This bond loan is divided into two tranches, each with a principal amount of 7.5 million euros. All of these, for a total amount of € 15 million, were subscribed by IPF Fund II SCA, SICAV FIAR (for more details on the characteristics of these bonds, see section 1.2.8.5 of this universal registration document).

On October 26, 2021, the Company did a financing operation by the issuance of bonds convertible into shares. The characteristics of the 6.568.422 issued are detailed in sections 1.2.8.7 and 4.3.3.7 of this universal registration document.

#### 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' shareholders held on May 20, 2021, 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. 22-10-62 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 for the same purpose on May 28, 2020 .

**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 service provider, in compliance with the market practice authorized by the *Autorité des marchés financiers* (AMF) in relation to share liquidity agreements
- 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 any potential external growth transactions particularly in compliance with stock market regulations

- To cancel all or some of the repurchased shares, in accordance with the reduction of the share capital and,
- More generally, to operate for any purpose that might be authorized by law or any market practice that might 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:** €50 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 occur during the current 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 of the total number of shares that make up its capital.

**Maximum amount of funds that may be used for share buybacks:** €2,500,000.

As of the date of the current universal reference document, this stock option purchase program was exclusively used in the context of the Liquidity agreement with Kepler Cheuvreux- concluded May 19, 2014 - see below.

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#### 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 on December 31, 2021, 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 managers of the Company or its affiliates associated thereof.

#### 5.1.4.3. Report on the liquidity contract with Kepler Cheuvreux

	FY 2021	FY 2020
Number of shares purchased	142 891	157 381
Average price of the purchases (euros)	9,51	9,05
Number of shares sold	132 114	151 657
Average price of the sales (euros))	9,89	9,67
Number of shares used during the year	none	none
Number of shares owned at year end and percentage of control	39 816 0,55% of capital	30 533 0,43% of capital
Value estimated at the average price of the purchases (euros)	357 432,88	236 258,77
Total trading fees (euros)	22 500	22 500

As of December 31, 2021, in connection with this contract, the Company held 39,816 shares, i.e. 0.55% of its capital and € 65,112.35 euros in cash.

## 5.2 Authorized capital

### 5.2.1. 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.

### 5.2.2. History of the corporate capital

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#### 5.2.2.1. Historical evolution since January 1<sup>st</sup>, 2019

Date	Nature of Operations	Capital	Number of shares created	Number of shares comprising the corporate capital	Nominal value	Corporate capital
déc.-18	Acquisition of AGA	1,440.00€	14 400	6 931 244	0.1€	693,124,40€
mars-19	Acquisition of AGA	267.50€	2 675	6 933 919	0.1€	693,391.90€
juin-19	Acquisition of AGA	540.00€	5 400	6 939 319	0.1€	693,931.90€
oct.-19	Acquisition of AGA	640.00€	6 400	6 945 719	0.1€	694,571.90€
déc.-19	Acquisition of AGA	1,435.00€	14 350	6 960 069	0.1€	696,006.90€
mars-20	Acquisition of AGA	225.50€	2 225	6 962 294	0.1€	696,229.40€
juin-20	Acquisition of AGA	1,416.00€	14 160	6 976 454	0.1€	697,645.40€
sept.-20	Acquisition of AGA	230.00€	2 300	6 978 754	0.1€	697,875.40€
déc.-20	Acquisition of AGA	4,417.00€	41 875	7 020 629	0.1€	702,062.90€
mars-21	Acquisition of AGA	112.50€	1 125	7 021 754	0.1€	702,175.40€
juil.-21	Subscription BSPCE	280.00€	2 800	7 024 554	0.1€	702,455.40€
sept.-21	Acquisition of AGA	497.50€	4 975	7 029 529	0.1€	702,952.90€
oct.-21	Shares issuance	10,799.20€	107 992	7 137 521	0.1€	713,752.10€
oct.-21	Conversion of bonds	1,430.30€	14 303	7 151 824	0.1€	715,182.40€
nov.-21	Conversion of bonds	7,247.70€	72 477	7 224 301	0.1€	722,430.10€
déc.-21	Conversion of bonds	3,718.00€	37 180	7 261 481	0.1€	726,148.10€
déc.-21	Acquisition of AGA	947.50€	9 475	7 270 956	0.1€	727,095.60€

- **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.

During the 2021 financial year, the stock market price reached its highest level on January 21, 2021 at 12.10 euros and its lowest level on December 22, 2021, at 7.74 euros. At the end of December 2021, the price stood at 8.10 euros, leading to a market capitalization of 58.9 million euros.

In the early months of 2022, the share price went from €8.26 on January 3, 2022 to €4.9 on April 12, 2022, giving the Company a market capitalization of almost €38.3 million.

## 5.3 Articles of incorporation and statutes

### 5.3.1. Corporate purposes

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;
- The 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.

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### 5.3.2. Rights, privileges and restrictions pertaining to the Company's shares

None.

### 5.3.3. Requirements for amending shareholders' rights

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.

### 5.3.4. General shareholder's meetings

#### 5.3.4.1. 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, 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, internet included, 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 who use the electronic voting form offered on the website set up by the meeting's centralizing agent are deemed to be present. The electronic form can be entered and signed directly on this site by means of an identification code and a password. The proxy or the vote thus expressed before the meeting by this electronic means, as well as the acknowledgement of receipt given, will be considered as non-revocable writings and opposable to all.

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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. The votes cast do not include those attached to shares for which the shareholder has not taken part in the vote, has abstained, or has voted blank or null.

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. The votes cast do not include those attached to shares for which the shareholder has not taken part in the vote, has abstained, or has voted blank or null.

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.

#### 5.3.4.2. Powers of shareholders' meetings

Ordinary and extraordinary general shareholders' meetings shall exercise their respective powers in accordance with the requirements prescribed by law.

#### 5.3.5. 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, with the exception of the double voting rights conferred on shares for which proof of registration in the name of the same shareholder for at least two years is provided (see in this respect section 5.4.4 of this universal registration document).



## 5.4 Major shareholders

### 5.4.1. Change in the Company's capital structure over the past three years on an undiluted basis

	Situation as of December 31, 2021			Situation as of December 31, 2020			Situation as of December 31, 2019		
	Nber of shares	% of capital	% of voting rights <sup>(1)</sup>	Nber of shares	% of capital	% of voting rights	Nber of shares	% of capital	% of voting rights
<b>Soula family</b>	<b>1 622 675</b>	<b>22,3%</b>	<b>31,3%</b>	<b>1 519 683</b>	<b>21,6%</b>	<b>31,0%</b>	<b>1 536 983</b>	<b>22,1%</b>	<b>31,5%</b>
Gérard Soula (*)	1 006 455	13,8%	19,0%	898 463	12,8%	18,4%	898 463	12,9%	18,5%
Olivier Soula (*)	310 040	4,3%	6,2%	310 040	4,4%	6,3%	307 490	4,4%	6,3%
Rémi Soula	288 690	4,0%	5,8%	293 690	4,2%	5,9%	313 540	4,5%	6,4%
Laure Soula	17 490	0,2%	0,3%	17 490	0,2%	0,4%	17 490	0,3%	0,4%
<b>Financial investors</b>	<b>1 172 106</b>	<b>16,1%</b>	<b>23,2%</b>	<b>1 155 922</b>	<b>16,5%</b>	<b>23,7%</b>	<b>1 178 856</b>	<b>16,9%</b>	<b>23,9%</b>
Innobio (a)	671 641	9,2%	13,4%	671 641	9,6%	13,8%	671 641	9,6%	13,4%
Fund BioAM (b)	112 716	1,6%	2,3%	112 716	1,6%	2,3%	112 716	1,6%	2,3%
<i>Sub total (a)+(b)</i>	<i>784 357</i>	<i>10,8%</i>	<i>15,7%</i>	<i>784 357</i>	<i>11,2%</i>	<i>16,1%</i>	<i>784 357</i>	<i>11,3%</i>	<i>15,7%</i>
Fund Amundi	1 570	0,0%	0,0%	1 570	0,0%	0,0%	1 570	0,0%	0,0%
Fund Viveris	25 618	0,4%	0,3%	9 434	0,1%	0,2%	32 368	0,5%	0,7%
Oréo Finance	40 561	0,6%	0,8%	40 561	0,6%	0,8%	40 561	0,6%	0,8%
SHAM <sup>(2)</sup>	320 000	4,4%	6,4%	320 000	4,6%	6,6%	320 000	4,6%	6,6%
<b>Employees</b>	<b>147 905</b>	<b>2,0%</b>	<b>2,3%</b>	<b>151 830</b>	<b>2,2%</b>	<b>2,4%</b>	<b>118 415</b>	<b>1,7%</b>	<b>2,2%</b>
Scientific committee (BSA)	700	0,0%	0,0%	700	0,0%	0,0%	700	0,0%	0,0%
Non-executive corporate officer (*)	0	0,0%	0,0%	0	0,0%	0,0%	0	0,0%	0,0%
Auto-control <sup>(3)</sup>	39 816	0,5%	0,0%	30 533	0,4%	0,0%	21 544	0,3%	0,0%
<b>Others shareholders <sup>(4)</sup></b>	<b>4 287 754</b>	<b>59,0%</b>	<b>43,1%</b>	<b>4 161 961</b>	<b>59,3%</b>	<b>42,9%</b>	<b>4 103 571</b>	<b>59,0%</b>	<b>42,4%</b>
<b>TOTAL</b>	<b>7 270 956</b>	<b>100,0%</b>	<b>100,0%</b>	<b>7 020 629</b>	<b>100,0%</b>	<b>100,0%</b>	<b>6 960 069</b>	<b>100,0%</b>	<b>100,0%</b>

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(\*) Directors of the Company

(1) A voting right double that conferred on other shares, with regard to the percentage of the share capital they represent, is allocated to all fully paid-up shares (whatever their category) for which proof is provided of having been registered for at least two years in the name of the same shareholder.

(2) SHAM : Hospital Mutual Insurance Company

(3) Self-owned shares under the liquidity contract with Kepler Cheuvreux

(4) Including bearer shares, if any, held by the Company's historic financial investors

As of the date of this universal reference document, the Company is not aware of any significant changes in its shareholding structure since December 31, 2021. It is not aware of any thresholds being crossed either during the year ended December 31, 2021 or between December 31, 2021 and the date of this universal registration document.

## 5.4.2. Distribution of capital and voting rights as of December 31, 2021 on a fully diluted basis

	Situation as of December 31, 2021 (non diluted)			Situation as of December 31, 2021 (diluted)		
	Nbre d'actions	% du capital	% des droits de vote <sup>(1)</sup>	Nbre d'actions	% du capital	% des droits de vote <sup>(1)</sup>
<b>Soula family</b>	1 622 675	22,3%	31,3%	1 801 675	20,9%	29,2%
Gérard Soula (*)	1 006 455	13,8%	19,0%	1 115 455	13,0%	17,7%
Olivier Soula (*)	310 040	4,3%	6,2%	380 040	4,4%	6,1%
Rémi Soula	288 690	4,0%	5,8%	288 690	3,4%	5,1%
Laure Soula	17 490	0,2%	0,3%	17 490	0,2%	0,3%
<b>Financial investors</b>	1 172 106	16,1%	23,2%	1 839 379	21,4%	26,4%
Innobio (a)	671 641	9,2%	13,4%	671 641	7,8%	11,8%
Fund BioAM (b)	112 716	1,6%	2,3%	112 716	1,3%	2,0%
<b>Sub total (a)+(b)</b>	784 357	10,8%	15,7%	784 357	9,1%	13,8%
Vester Finance	0	0,0%	0,0%	667 273	7,8%	5,9%
Fund Amundi	1 570	0,0%	0,0%	1 570	0,0%	0,0%
Fund Viveris	25 618	0,4%	0,3%	25 618	0,3%	0,3%
Oréo Finance	40 561	0,6%	0,8%	40 561	0,5%	0,7%
SHAM <sup>(2)</sup>	320 000	4,4%	6,4%	320 000	3,7%	5,6%
<b>Employees</b>	147 905	2,0%	2,3%	261 580	3,0%	3,1%
Scientific committee (BSA)	700	0,0%	0,0%	40 700	0,5%	0,4%
Non-executive corporate officer (*)	0	0,0%	0,0%	30 215	0,4%	0,3%
Auto-control <sup>(3)</sup>	39 816	0,5%	0,0%	39 816	0,5%	0,0%
<b>Others shareholders <sup>(4)</sup></b>	4 287 754	59,0%	43,1%	4 589 257	53,3%	40,7%
<b>TOTAL</b>	<b>7 270 956</b>	<b>100,0%</b>	<b>100,0%</b>	<b>8 602 622</b>	<b>100,0%</b>	<b>100,0%</b>

(\*) Directors of the Company

(1) A voting right double that conferred on other shares, with regard to the percentage of the share capital they represent, is granted to all fully paid-up shares (whatever their category) for which proof is provided of having been registered for at least two years in the name of the same shareholder.

(2) SHAM : Hospital Mutual Insurance Company

(3) Self-owned shares under the liquidity contract with Kepler Cheuvreux

(4) Including bearer shares, if any, held by the Company's historic financial investors

## 5.4.3. Major shareholders not represented on the board of directors

The Innobio and Bioam Funds are major shareholders of the Company, holding 10.8% of the capital and 15.7% of the voting rights as of December 31, 2021. They are represented on the board of directors by their management company Bpifrance Investments.

Société Hospitalière d'Assurance Mutuelles (SHAM) holds 4.4% of the Company's capital and 6.4% 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 double that conferred on other shares, with regard to the percentage of the corporate capital they represent, is granted to all fully paid-up shares (whatever their category) for which proof is provided of having been registered for at least two years in the name of the same shareholder.

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 universal registration 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 universal registration document, other than the collective undertaking to retain their securities in the Company (known as a "Dutreil" 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 six other directors (Olivier Martinez, Laurent Arthaud representing Bpifrance Investment, Ekaterina Smirnyagina, Katherine Bowdish, Claudia Mitchell and Stéphane Boissel).

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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The Company is not aware of any agreement of which the implementation could result in a change in control.

#### 5.4.7. Pledges of the Company's shares

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None.

## 5.5 Regulated agreements

No agreement was entered into during the past fiscal year, either directly or by proxy, 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) a Company's subsidiary as defined by article L.233-3 of the French Commercial Code.

### 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 company on the financial statements as of December 31, 2021, is limited. The expenses totaling €0.4 million are for the payroll costs of the employee and their travel and entertainment expenses.

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### 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, 2021

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ODICEO

ERNST & YOUNG et Autres

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*This is a translation into English of a report issued in French and it is provided solely for the convenience of English-speaking users. This report should be read in conjunction with, and construed in accordance with, French law and professional standards applicable in France.*

Adocia

Annual General Meeting held to approve the financial statements for the year ended December 31, 2021

Statutory auditors' report on related party agreements

**ODICEO**

115, boulevard de Stalingrad  
CS 52038  
69616 Villeurbanne  
S.A. au capital de € 275 000  
430 130 393 R.C.S. Lyon

Commissaire aux Comptes  
Membre de la compagnie  
régionale de Lyon-Riom

**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 et du Centre

Adocia

Annual General Meeting held to approve the financial statements for the year ended December 31, 2021

**Statutory auditors' report on related party agreements**

To the Shareholders,

In our capacity as statutory auditors of your Company, we hereby present to you our report on related party agreements.

We are required to inform you, on the basis of the information provided to us, of the terms and conditions of those agreements 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. 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 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, 2021, of the agreements 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 submitted for approval to the Annual General Meeting**

We hereby inform you that we have not been notified of any agreements authorized during the year ended December 31, 2021 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 previously approved by the Annual General Meeting**

We hereby inform you that we have not been notified of any agreements previously approved by the Annual General Meeting, whose implementation continued during the year ended December 31, 2021.

Villeurbanne and Lyon, April 21, 2022

The Statutory Auditors  
*French original signed by*

ODICEO

ERNST & YOUNG et Autres

Angès Lamoine

Mohamed Mabrouk

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# Complementary information

## Chapter 6

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## 6 COMPLEMENTARY INFORMATION

### 6.1 Persons responsible

#### 6.1.1. Person responsible for the registration document

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Gérard Soula, Chairman and Chief Executive Officer

#### 6.1.2. Responsibility statement

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“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, to the best of my knowledge, that the accounts have been drawn up in accordance with the applicable accounting standards and give a true picture of the assets, the financial situation and the result of the company and of all the companies included in the consolidation, and that the management report included in this registration document presents a true picture of the development of the business, results and financial situation of the company and of all the companies included in the consolidation and that it describes the main risks and uncertainties they face.”

April 21, 2022,

Gérard Soula

Chairman and Chief Executive Officer

#### 6.1.3. Person responsible for financial information

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Ms. Valérie 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

#### 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

Tour Oxygène, 10-12 boulevard Marius Vivier Merle, 69 393 Lyon Cedex 03,

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.

### 6.2.2. Attestation of the fees of the statutory auditors

<i>In thousands of € (French GAAP)</i>	Ernst & Young		Odicéo	
	Fiscal year 2021 (12 months)	Fiscal year 2020 (12 months)	Fiscal year 2021 (12 months)	Fiscal year 2020 (12 months)
Statutory auditor, certification, examination of individual accounts and consolidated accounts	50	49	40	39
Other services and diligence directly related to the mission of the statutory auditor				
<b>Sub-total Audit</b>	<b>50</b>	<b>49</b>	<b>40</b>	<b>39</b>
Other fiscal services				
Other services and diligence directly related to the mission of the statutory auditor				
<b>Sub-total Other services</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>
<b>TOTAL</b>	<b>50</b>	<b>49</b>	<b>40</b>	<b>39</b>

These are the fees that have been billed during the year, excluding tax.

## 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 headquarters.

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)):

- The last version of the bylaws of the Company
- And more generally, the regulated information within the meaning of the provisions of the AMF general regulations

## 6.5 Cross Reference tables

### 6.5.1. Annual financial report cross reference table

<b>Annual financial report</b>	<b>Chapter(s)/Section(s)</b>
1 Responsibility statement	6.1
2 Corporate annual financial statements -French GAAP	4.3
3 Consolidated annual financial statements -IFRS	4.1
4 Management report	see index below
5 Corporate governance report	Chapter 3
6 Information on statutory auditors' fee	4.3.3.8
7 Statutory auditors' report on the annual financial statements prepared under French GAAP and IFRS	4.2 and 4.4

### 6.5.2. Management report cross reference table

<b>Annual management report</b>	<b>Chapter(s)/Section(s)</b>
1 Position and business of the Company during the past fiscal year	1.3
2 Review of financial statements and results	Chapter 4
Appropriation of income -Information on dividends distributed	4.3.3.4
Non -tax deductible expenses	4.3.3.5
3 Information on supplier payment term	4.3.3.3 Note 11
4 Progress made or difficulties encountered	1.3
5 Major risks and uncertainties faced by the Company / Use of financial instruments by the Company	1.4
6 Research and development activities	1.3

<b>Annual management report</b>	<b>Chapter(s)/Section(s)</b>
7 Foreseeable changes and outlook	1.3
8 Significant events since the fiscal year-end	4.3.3.9
9 Equity interests held by employees	2.2.1.2 et 4.3.3.7
10 Acquisition of significant equity interests in, or control of, companies headquartered in France; disposals of such equity interest	Chapters 4 and 1
11 Activities of subsidiaries and controlled entities	Chapters 4 and 1
12 Information on shareholder structure and treasury shares – Share buyback program	5.1.4
13 Changes in the shareholder structure during the fiscal year	5.2.2
14 Changes in the share price – Risk of price change	5.2.2
15 Summary of transactions in the Company's securities during the past fiscal year by executives and persons referred to in Article L.621-18-2 of the French Monetary and Financial Code	3.2.3
16 Employment and environmental information	Chapter 2
17 Table showing results over the last five fiscal years	4.3.3.10
18 Internal control and risk management procedures implemented by the Company	3.3



### 6.5.3. Cross-reference table of the universal registration document

<b>Sections of appendices 1 and 2 of the delegated regulations (UE) 2019/980 from March 14, 2019</b>	<b>Chapter(s) /Section(s)</b>
<b>1. RESPONSIBLE PERSONS, INFORMATION FROM THIRD PARTY, EXPERT REPORTS AND APPROVAL OF THE COMPETENT AUTHORITY</b>	<b>Chapter 6</b>
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1.3 Declaration or expert report, information related to the expert and declaration of consent	6.1.3
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<b>2. LEGAL AUDITORS</b>	<b>6.2.1</b>
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<b>3. RISK FACTORS</b>	<b>1.4</b>
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4.3 Date of incorporation and life of the Company	1.1.1
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<b>5. OVERVIEW OF THE ACTIVITIES</b>	<b>Chapter 1</b>
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Sections of appendices 1 and 2 of the delegated regulations (UE) 2019/980 from March 14, 2019		Chapter(s) /Section(s)
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8.4	Information regarding any restrictions on the use of capital that may affect the operations of the Company	Chapter 5
8.5	Expected sources of funding necessary to honor the commitments referred to in 5.7.2 above	
<b>9</b>	<b>REGULATORY ENVIRONMENT</b>	<b>Chapter 1</b>
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11.1	Profit forecasts or estimates published	
11.2	Statement setting out the main forecast assumptions	
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16.3	Direct or indirect control of the Company	5.4
16.4	Agreement whose implementation could lead to a change of control	None
<b>17</b>	<b>TRANSACTIONS WITH RELATED PARTIES</b>	<b>Chapter 4 and 5.5</b>
<b>18</b>	<b>FINANCIAL INFORMATION RELATED TO THE ASSETS AND LIABILITIES, THE FINANCIAL SITUATION AND THE RESULTS OF THE COMPANY</b>	<b>Chapter 4</b>
18.1	Historical financial information	
18.1.1	audited historical financial information for the last three financial years and the audit report	
18.1.2	Change of accounting reference date	
18.1.3	Accounting standards	
18.1.4	Changes in accounting standards	
18.1.5	Balance sheet, income statement, change in equity, cash flow tables, accounting methods and explanatory notes	
18.1.6	Consolidated financial statements	
18.1.7	Date of the last financial information	
18.2	Interim and other financial information	
18.3	Audit of historical annual financial information	
18.3.1	Independent audit of historical annual financial information	
18.3.2	Other audited information	
18.3.3	Source of unaudited information and reasons for non-audit	
18.4	Pro forma financial information	
18.5	Dividend policy	
18.5.1	Description of the dividend distribution policy and any applicable restrictions	
18.5.2	Amount of dividends per share for the last three financial years	
18.6	Legal and arbitration proceedings	
18.7	Significant change in the financial position of the Company	
<b>19</b>	<b>ADDITIONAL INFORMATION</b>	<b>Chapter 5</b>
19.1	Social capital	5.1
19.1.1	Amount of subscribed capital, number of shares issued and fully paid up and nominal value per share, number of shares authorized	5.1
19.1.2	Information relating to shares not representing capital	5.1.2
19.1.3	Number, book value and nominal value of shares held by the Company	5.1.4
19.1.4	Information relating to convertible, exchangeable securities, or warrants	Chapter 5
19.1.5	Information on the conditions governing any right of acquisition and / or any obligation attached to the authorized capital, not issued, or on any company aiming to increase the capital	
19.1.6	Information on the capital of any member of the Group who is the subject of an option or a conditional or unconditional agreement providing for placing it under option	none
19.1.7	History of share capital	5.1
19.2	Constitution and statutes	5.3
19.2.1	Register and corporate object	5.3.1
19.2.2	Rights, privileges, and restrictions attached to each class of shares	5.3.3

Sections of appendices 1 and 2 of the delegated regulations (UE) 2019/980 from March 14, 2019	Chapter(s) /Section(s)
19.2.3	5.3.5
20	1.2.5.1
21	

## 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>Ankylosis</b>	Immobility of a joint caused by injury or disease.
<b>Anionic group</b>	Negatively charged group of ions (anions)
<b>Anticoagulation</b>	Phenomenon that prevents the transformation of liquid blood into a more or less gelatinous and consistent substance
<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 countries in the world.



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