This is a free translation into English of Adocia reference document issued in the French language for informational purposes only

ADOCIA
innovative medicine for everyone, everywhere

A French *société anonyme* (corporation) with €684,636.30 in share capital

Registered office: 115 Avenue Lacassagne, 69003 Lyon

Lyon Trade and Companies Registry no. 487 647 737

2015 REFERENCE DOCUMENT

INCLUDING THE COMPANY'S

ANNUAL FINANCIAL REPORT

AND MANAGEMENT REPORT

AMF | AUTORITÉ DES MARCHÉS FINANCIERS

This reference document was filed with the Autorité des marchés financiers (the "AMF") April 8, 2016 in accordance with Article 212-13 of its General Regulation. It may be used to support a financial transaction if supplemented by a transaction note approved by the AMF. This document was prepared by the issuer and engages the responsibility of its signatories.

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

TABLE OF CONTENTS

CROSS-REFERENCE TABLE

The cross-reference table below will facilitate locating in this reference document:

The information contained in the annual financial report (Article L. 451-1-2 of the French Monetary and Financial Code and Article 222-3 of the AMF's General Regulation); and

The information contained in the annual management report (Article L. 225-100 et seq. of the French Commercial Code).

Annual financial report	**Reference document**
1. Responsibility statement	§ 1.2
2. Corporate annual financial statements - French GAAP	§ 20.3
3. Corporate annual financial statements – IFRS	§ 20.1
4. Management report	See Appendix below
5. Chairman's report on internal control	Annexe I
6. Annual information document	§ 5.1.5
7. Information on statutory auditors' fees	§ 2.3
8. Statutory auditors' report on the annual financial statements prepared under French GAAP and IFRS	§ 20.2 et 20.4
9. Statutory auditors' report on the chairman's report	Annexe II

Annual management report	**Reference document**
1. Position and business of the company during the past fiscal year	§ 6 et § 20
2. Review of financial statements and results – Appropriation of income – Information on dividends distributed – Non-tax deductible expenses	§ 9 et § 20
3. Information on supplier payment terms	§ 20.3 note 3.3.3
4. Progress made and difficulties encountered	§ 6
5. Major risks and uncertainties faced by the company / Use of financial instruments by the company	§ 4
6. Research and development activities	§ 6
7. Foreseeable changes and outlook	§ 6
8. Significant events since the fiscal year-end	§ 20.8
9. Equity interests held by employees	§ 17
10. Executive management of the company	§ 16
11. Information on corporate officers	§ 15.1
12. Acquisition of significant equity interests in, or control of, companies headquartered in France; disposals of such equity interests	§ 20.3 note 1.3
13. Activities of subsidiaries and controlled entities	§ 20.3 note 7.2
14. Information on shareholder structure and treasury shares – Share redemption programs	§ 18.1 - 18.2 et 21.1.4
15. Changes during the fiscal year to the company's shareholder structure	§ 21.2.2
16. Changes in the share price – Risk of price changes	§ 21.2.2
17. Summary of transactions in the company's securities during the past fiscal year by persons referred to in Article L. 621-18-2 of the French Monetary and Financial Code	§ 15.4
18. Information required by Article L. 225-100-3 of the French Commercial Code	§ 16.6
19. Employment and environmental information	§ 8.3 – 8.4 et 17.7
20. Table showing the company's results over the last five fiscal years	§ 20.5
21. Authorizations to effect capital increases	§ 21.2

Notice

In this reference document, the terms "Adocia" and 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 11 Briercliff Dove Canyon CA 92679, U.S.A.

The consolidated financial statements prepared under IFRS for the fiscal year ended December 2015 are presented on pages 191 to 222 of this reference document. The statutory auditors' report on the corporate financial statements prepared under IFRS for the fiscal year ended December 31, 2015 is on pages 223 to 226 of this reference document.

The corporate financial statements prepared under French GAAP for the fiscal year ended December 31, 2015 are presented on pages 227 to 243 of this reference document. The statutory auditor's report on the corporate financial statements prepared under French GAAP for the fiscal year ended December 31, 2015 is on pages 244 to 246.

This reference document presents or incorporates by reference the company's audited financial statements for the fiscal years ended December 31, 2013, December 31, 2014 and December 31, 2015.

Pursuant to Article 28 of Commission Regulation (EC) No 809/2004 of April 29, 2004, the annual and consolidated accounts 2014 and 2013, respectively established under French GAAP and IFRS, are incorporated by reference in this reference document

A glossary containing the definitions of certain technical terms used in this reference document, as well as an index of abbreviations used, can be found in Chapter 26. Terms indicated by an asterisk (*) are defined in the glossary.

Disclaimer

Market and competition information

This reference document contains, in particular in Chapter 6 “Overview of Activities”, information about the company’s markets and competitive position. This information is taken inter alia 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 reference 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 is subject to change or amendment due to uncertainties associated with inter alia the economic, financial, competitive and regulatory environment. This information is provided in the various sections of this reference document and includes particulars about the company’s intentions, estimates and objectives with respect to inter alia the market in which it operates and its strategy, growth, results, financial position, cash position and forecasts. The forward-looking information in this reference document is provided only as of the filing date of this reference 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 implied in any forward-looking information. Lastly, it should be kept in mind 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 Chapter 4 “Risk Factors” of this reference 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, income and outlook. Furthermore, other risks of which the company is not aware or that it does not deem significant as of the filing date of this reference document may also have a material adverse impact.

1 PERSONS RESPONSIBLE FOR THE REFERENCE DOCUMENT

1.1 Person responsible for the reference document

Mr. Gérard Soula, Chairman and Chief Executive Officer

1.2 Responsibility statement

"I hereby certify, after having taken all reasonable measures to this effect, that to my knowledge the information contained in this reference document is accurate and contains no omissions likely to affect its import.

I hereby certify that, to my knowledge, the financial statements were prepared in accordance with applicable accounting standards and give a true and fair view of the assets, financial position and results of the Company and its subsidiary and that the information listed under the management report page 5 present a true picture of business developments, results and financial position of the Company and its subsidiary as well as a description of the principal risks and uncertainties they face.

I have obtained a letter from the statutory auditors certifying completion of their work in which they state that they have verified the information in this reference document relating to the company's financial position and financial statements, and that they have read the reference document in its entirety.

The statutory auditors issued reports, without comments, on the annual financial statements for the fiscal year ended December 31, 2015. The reports are provided on pages 223 to 226 (consolidated financial statements prepared in accordance with IFRS) and pages 244 to 246 (corporate financial statements prepared in accordance with French standards) of this reference document.

The statutory auditors issued reports on the financial information for the fiscal year ended December 2014, which is incorporated by reference in this document. The reports are provided on pages 224 to 226 (consolidated financial statements) and pages 243 to 245 (annual financial statements) of the 2014 reference document under n°R.15-032 filed by the AMF on April 30, 2015.

The statutory auditors issued reports on the financial information for the fiscal year ended December 31, 2013, which is incorporated by reference in this document. The reports are provided on pages 197 to 199 (corporate financial statements prepared in accordance with IFRS) and pages 217 to 219 (corporate financial statements prepared in accordance with French standards) of 2013 n°R.14-020 which was filed with the AMF on April 24, 2014.

Executed in Lyon, on April 8 2016

Gérard Soula
Chairman and Chief Executive Officer

1.3 Person responsible for financial information

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

2 STATUTORY AUDITORS

2.1 Principal statutory auditors

ODICEO
represented by Mr. Sylvain Boccon-Gibod, a partner
115 Boulevard Stalingrad, 69100 Villeurbanne
member of the Lyon regional statutory auditors' association

Appointed by a decision adopted by the sole shareholder on July 31, 2006 until the general shareholders' meeting convened to vote on the financial statements for the fiscal year ended December 31, 2011. This term of office was renewed by the general shareholders' meeting held on June 15, 2012 for a period of six fiscal years, which will expire at the conclusion of the ordinary general shareholders' meeting convened to vote on the financial statements for the fiscal year ending December 31, 2017.

Ernst & Young et Autres
represented by Mr. Sylvain Lauria, a partner
1-2 place des saisons, 92 400 Courbevoie La Défense,
member of the Versailles regional statutory auditors' association

Appointed by the combined general shareholders' meeting held on October 24, 2011 for a period of six fiscal years, which will expire at the conclusion of the ordinary general shareholders' meeting convened to vote on the financial statements for the fiscal year ending December 31, 2016.

2.2 Alternate statutory auditors

Monsieur Pierre Grafmeyer
115, boulevard Stalingrad, 69100 Villeurbanne,
member of the Lyon regional statutory auditors' association,

Appointed by a decision adopted by the sole shareholder on July 31, 2006 until the general shareholders' meeting convened to vote on the financial statements for the fiscal year ended December 31, 2011. This term of office was renewed by the general shareholders' meeting held on June 15, 2012 for a period of six fiscal years, which will expire at the conclusion of the ordinary general shareholders' meeting convened to vote on the financial statements for the fiscal year ending December 31, 2017.

AUDITEX
Tour Ernst & Young, Faubourg de l'Arche, 92037 La Défense Cedex,
member of the Versailles regional statutory auditors' association,

Appointed by the combined general shareholders' meeting held on October 24, 2011 for a period of six fiscal years, which will expire at the conclusion of the ordinary general shareholders' meeting convened to vote on the financial statements for the fiscal year ending December 31, 2016.

During the period covered by the historical financial information, no statutory auditor has resigned or been removed from office.

2.3 Certificate of fees paid to statutory auditors

The table below shows the statutory auditors' fees that the company has paid during the last two years:

(€ thousands)	Ernst & Young		Odicéo	
	2015	2014	2015	2014
Audit services				
* statutory audior services, certification, review of individual and consolidated financial statements	33	38	33	38
* other services and due diligence directly related to the statutory audit assignment	4	4		
Subtotal	37	41	33	38
Other services				
* tax				
* others				
Subtotal				
TOTAL	**37**	**41**	**33**	**38**

The amounts above do not include VAT.

3 SELECTED FINANCIAL INFORMATION

The selected financial information presented in this Chapter 3 is taken from the company's financial statements for the fiscal years ended December 31, 2014 and December 31, 2015, which were prepared in accordance with IFRS and are shown in section 20.1 of this reference document.

The consolidated financial statements prepared under IFRS are presenteted in paragraph 20.1 of this reference document. Only corporate financial statements prepared under French Gaap are legitimately legal and are reproduced in annex of this reference document with the statutory auditor's reports.

This financial information should be read in conjunction with (i) the review of the company's income and financial position presented in Chapter 9 of this reference document and (ii) the review of the company's cash position and equity presented in Chapter 10 of this reference document.

Selected financial information for the fiscal years ended December 31, 2014 and December 31, 2015 (IFRS)

Selected financial information taken from the income statement:

(IFRS - € thousands)	**FY 2015 (12 months)**	**FY 2014 (12 months)**
Licencing revenues	19 888 (*)	383 (**)
Research and collaborative agreements	17 048	321
Revenue (a)	**36 936**	**704**
Research tax credit	6 768	3 461
Grants, public financing	1 050	(2)
Other revenue (b)	**7 818**	**3 459**
Operating revenue (a)+(b)	**44 753**	**4 163**
Research and development expenses	(28 625)	(17 006)
General and administrative expenses	(6 025)	(4 319)
Operating expenses	**(34 651)**	**(21 324)**
OPERATING INCOME / (loss)	**10 103**	**(17 161)**
FINANCIAL INCOME	**2 118**	**524**
Tax	333	(4 078)
NET INCOME / (loss)	**12 553**	**(20 715)**

(*) Recognition of the up front payment of $50 million (€41 million) received from Eli Lilly after the license's agreement signed with Eli Lilly on December 18, 2004 on a linear basis over the expected duration of the development plan, for an amount of €10.7 million for the fiscal year 2015. Recognition of the payment of a milestone (milestone payment) of $10 million (€9.1 million) received from Eli Lilly in December 2015.

(**)Recognition of the initial payment (up-front payment) of $50 million (€41 million) received from Eli Lilly after the signing of the license agreement with Eli Lilly December 18, 2014, linearly over the anticipated duration of the contract for an amount of €0.4 million on the year 2014.

Selected financial information taken from the balance sheet:

(IFRS - € thousands)	FY 2015 (12 months)	FY 2014 (12 months)
NON-CURRENT ASSETS	**2 112**	**1 786**
of which: laboratory equipment	812	557
of which: other fixed tangible assets	1 118	418
CURRENT ASSETS	**85 983**	**50 758**
of which: cash and cash equivalents	72 062	49 800
TOTAL ASSETS	**88 095**	**52 544**
EQUITY	**47 052**	**2 505**
NON-CURRENT LIABILITIES	**20 636**	**1 124**
of which: long-term financial debts	702	728
CURRENT LIABILITIES	**20 407**	**48 915**
TOTAL LIABILITIES	**88 095**	**52 544**

Selected financial information taken from the cash flow statement:

(IFRS - € thousands)	FY 2015 (12 months)	FY 2014 (12 months)
Net cash flow generated by the business	(6 216)	30 560
Net cash flow in connection with investment transactions	(1 304)	(174)
Net cash flow in connection with financing transactions	29 782	
CHANGES IN NET CASH	**22 262**	**30 386**
Cash and cash equivalents at the start of the year	49 800	19 415
Cash and cash equivalents at year-end	72 062	49 800

4 RISK FACTORS

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

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

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

4.1 Risks associated with implementation of the Company's strategy

4.1.1 The company is dependent on its BiocChaperone® and DriveIn(r) technological plateforms.

The Company does not plan to develop or market therapeutic products directly. The Company's main strategy is to develop innovative formulations for various therapeutic proteins based on its BioChaperone® and Drive*In*® technologies, and then to license use thereof to major players in the pharmaceutical, biotechnology and medical devices industries, who would then develop and market therapeutic products. For example, in December 2014 the Company signed a license and collaborative agreement with Eli Lilly focused on the development of an ultra-rapid insulin, known as BioChaperone® Lispro.

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

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

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

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

The Company's medium-term strategy depends on its ability to enter into lasting partnership agreements with major players in the pharmaceutical, biotechnology and medical devices industries, on the basis of the results of feasibility studies and clinical trials it conducts. The Company does not plan to produce or market its products and does not have the human, material and financial resources necessary to develop, manufacture and market therapeutic products using its technology. As part of its strategy, when proof of concept has been obtained for humans or animals, the Company intends to license products derived from its BioChaperone® and *DriveIn*® technologies to industrial partners in the pharmaceutical, biotechnology or medical device markets who have the human, material and financial resources necessary to conduct and successfully complete the clinical trials required by law,

apply for market authorization, and produce and market the products. Accordingly, the Company plans to sign license and collaborative agreements, pursuant to which its partners, will be responsible for developing, manufacturing and marketing products incorporating the Company's technology and will agree to pay royalties to the Company on any sales of such products, once commercialized.

However, the research and results of clinical trials that the Company carries out itself may fail to yield product candidates or may fail to yield candidates that are sufficiently safe, efficacious and innovative to attract major players in the pharmaceutical, biotechnology and medical devices industries to sign license and collaborative agreements for the Company's products and technologies.

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

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

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

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

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

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

The Company cannot be certain that it will be able to initiate and maintain partnerships, that any partnerships will be scientifically and/or commercially successful or that the Company will receive revenues from any of these agreements. For example, in 2011, the Company entered into a license and collaborative agreement with Eli Lilly with respect to the development of a formulation of a fast acting insulin analog. In 2013, the Company and Eli Lilly agreed not to continue further joint research under this licensing agreement. Factors that may affect the success of the Company's collaborations include the following:

- partners may not employ all the resources necessary to obtain the results expected from the agreements entered into with the Company. In particular, if these partners experience budgetary restrictions or give priority to other development programs, this could delay or prevent altogether approval of potential products incorporating the Company's technology, which is an indispensable stage for the success of its commercial policy;

- conflicts could arise between the Company and certain of its industrial partners. In particular, the Company cannot guarantee that none of its partners will design or attempt to set up a commercial business that uses a technology that competes with that of the Company, or uses all or part of the Company's technology, or decide to prioritize internal development of products in markets which compete with the Company's product candidates, and which would therefore compete with the Company's business (see the section below on risks associated with competition);
- current or future partners could limit or terminate their relationships with the Company, which could lead to additional costs, delays, and difficulties in the development of, or in obtaining approval by regulatory authorities for, or successfully commercializing, our product candidates which could have a material adverse impact on the Company's business, financial position, income, expansion and outlook. Limitation or termination of an agreement could make it difficult for the Company to attract new partners or adversely affect its reputation in the business and financial communities, cause the Company to lose expertise and could even lead to the disclosure of key confidential information derived from the Company's research and development program, despite the fact that the relevant partners may be contractually bound to the Company by a confidentiality obligation.

Furthermore, the Company's current revenues depend in large part on the license and collaborative agreement signed with Eli Lilly in December 2014 focused on the development of a ultra-rapid insulin, known as BioChaperone Lispro. Under the terms of the agreement, Adocia received a total upfront fee of $50 million and a millestone payment of $10 million in December 2015 with the potential for future payments of up to $270 million if the product reaches certain development and regulatory milestones, and sales milestones up to $240 million, as well as tiered sales royalties. There can be no guarantee that the collaboration will meet the development and regulatory milestones in order to receive the anticipated revenues and any decision by Eli Lilly to discontinue its agreement with the Company could have a material adverse effect on its business, results of operations and prospects.

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

4.2 Risks associated with the Compny's business

4.2.1 Research programs and clinical studies are lenghtly, time consuming, expensive and have uncertain outcomes.

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

If a product candidate passes the preclinical stage, the Company must then develop and design clinical trials to test specific characteristics of the candidate. In order to carry out clinical trials, the Company must first obtain appropriate authorizations to conduct clinical trials in the countries where the Company will seek market authorization. The Company cannot predict the time that will be necessary for regulatory authorities to review the trial protocol and approve the files submitted to them. For example, with respect to the Company's Phase III clinical trials for the treatment of diabetic foot ulcer conducted in India, the Company filed the request for authorization with the Drug Controller General of India in September 2012 but the processing of the application was delayed by the internal reorganization of the Indian regulatory authority, and the Company did not receive final authorization until August 2014.

The completion of clinical trials will depend on various factors, such as the therapeutic indication in question, the size of the population affected, clinical trial design, qualification and initialization of clinical trial sites, availability of the investigational product, , the proximity of patients to clinical test sites, the eligibility criteria for trials, rates of 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 pre-specified 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.

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

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

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

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

manufacturers with which the Company and its partners contract for clinical and manufacturing supplies, and changes in governmental regulations or regulatory delays.

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

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

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

Delays in obtaining regulatory approvals may:

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

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

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

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

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

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

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

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

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

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

The Company's competitors may have:

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

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

4.3 Risks associated with the Company's organization

4.3.1 The Company's success depends on certain key employees.

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

The Company has taken out a "key person" insurance policy covering its chairman and founder Gérard Soula (see section 4.7 of our 2013 Reference Document "Insurance and risk coverage"), his departure or the departure of Olivier Soula and/or Rémi Soula or other key employees of the Company could cause:

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

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

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

4.3.2 Company's inability to manage internal growth

In connection with its development, the Company is in the process of recruiting additional staff and expanding its operating capacity significantly.

In this respect, the Company will *inter alia* have to:

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

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

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

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

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

and qualities of proteins at a competitive price, which could delay the start or completion of clinical trials.

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

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

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

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

The Company relies on specialized healthcare institutions, including clinical research organizations and clinical investigators to conduct clinical trials of its product candidates, which are necessary to obtaining proof of concept in order to license the Company's technologies. Although the Company relies on these parties for high quality execution of the Company's clinical trials, the Company is unable to control all aspects of their activities. If these third parties do not carry out their contractual duties or obligations or meet expected deadlines, if the third parties need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to failure to adhere to the Company's clinical protocols or good clinical practices or for other reasons, the Company's current or planned clinical studies, such as the Phase III study for BioChaperone PDGF in India, 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. For example, the Company's Phase III clinical trials for BioChaperone PDGF are conducted through an Indian contract research organization and the 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.

4.4 Regulatory and legal risks

4.4.1 The Company and its partners may never obtain the regulatory approvals the Company and its partners need to market their products.

The Company has only limited experience in filing and pursuing applications necessary to obtain regulatory approval or licensure. The Company cannot ensure that its product candidates will be approved or licensed for marketing, even in circumstances where the Company is collaborating with a partner who has more experience in seeking market authorization. The process of applying for regulatory approval is expensive, often takes many years and can vary substantially based upon the type, complexity and novelty of the product candidates involved. If any of the Company's product candidates are not approved, this could have a material adverse effect on the Company's business, results of operations and prospects and the value of the Company's Shares.

4.4.2 The Company is subject to extensive and costly governmental regulation.

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

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

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

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

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

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

4.4.3 The Company relies on its intellectual property rights and other rights.

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

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

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

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. The outcome of the patent prosecution for biotechnology and pharmaceutical products is generally highly uncertain, and involves complex legal and scientific questions. The standards which patent offices in different countries use to grant patents, or to define the subject matter or scope of allowable claims, are not always applied predictably or uniformly, and can change without prior notice. Neither the Company nor its partners can be certain that the Company was the first to make the inventions claimed in the Company's pending patent applications, or that the Company or its partners were the first to file for protection of the inventions described in those applications. As a result, the Company could experience difficulties in being granted certain of the patents or trademarks for which it has filed, or may in the future file, applications, including applications that are currently undergoing or may, in the future, undergo the examination or registration process.

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. The patents licensed to the Company could be challenged, discovered to have been issued on the basis of insufficient incorrect documentation or disclosure and/or held to be unenforceable.

Therefore, the Company cannot guarantee with certainty that:

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

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

4.4.4 The exclusive nature of the Company'sintellectual property rights coul be circumvented by third parties or the Company's competitors

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

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

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

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

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

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

4.4.5 The Company may face intellectual property litigation from holders claining patent infringement in connection with any of the Company's product candidates.

The Company may infringe or violate the intellectual property rights of others by 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 Domain Name Dispute Resolution Policy (UDRP) proceedings or an infringement action brought by a third party claiming prior trademark rights. Therefore, the Company cannot guarantee with certainty that its products do not infringe patents or trademarks owned by third parties.

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

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

4.4.6 The Company may face product liability claims related to the use or misuse of its products and products employing its technology, which may have material adverse impact on the Company's reputation, business, results of operations and prospects.

The Company's business exposes the Company 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, despite the fact that 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 health care 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 financial risk as a result thereof (Refer to paragraph 4.7 of the reference document 2014 "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.

4.4.7 The Company may be subject to litigation and claims that could materially adversely affect the Company's business.

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

4.4.8 The Company's and its partners' ability to generate revenue from any products that the Company and its partners may develop will depend on reimbursement and drug pricing policies and regulations.

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

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

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

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

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

4.4.9 The company's operations pose health and safety risks associated with hazardous substance use, technical facilities and the environment.

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

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

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

4.5 Financial risks

4.5.1 The Company has incurred a cumulative loss since its creation. If the Company does not generate significant revenues, it may never be profitable.

Since its creation in 2005, the Company has posted operating losses each year. As of December 31, 2015, its total net losses presented under IFRS rules (including losses carried forward) were €32.3 million, including a net income of €12.6 million for the fiscal year ended December 31, 2015.

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

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

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

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

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

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

4.5.2 The Company will require substantial additional funds to develop its products and technologies which may be difficult to obtain.

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

- The Company's financing needs and the timing thereof depend on factors that are largely beyond the Company's control, such as:
- higher costs and slower progress than anticipated for its research and development programs and clinical trials;
- the costs of preparing, filing, defending and maintaining its patents and other intellectual property rights;
- the scope of preliminary research work and the time periods necessary to conclude license agreements with industrial partners;
- the costs necessary to deal with technological developments and markets;
- higher costs and longer time periods than anticipated to obtain regulatory authorizations, including the time required to prepare applications to be submitted to the authorities with jurisdiction; and
- new development opportunities for new products or the acquisition of technologies, products or companies.

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

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

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

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

4.5.3 The Company could, in the future, issue new shares or other equity linked financial instruments as part of its employee and management incentive based compensation.

Pursuant to its policy to motivate its managers, directors and employees, since its creation, the Company has issued or granted stock warrants and business founders' stock warrants (BSPCE), and has granted bonus shares. The maximum possible dilution from financial instruments in existence as of December 31, 2015 is 4.25% on a fully diluted capital basis.

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

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

4.5.4 Since its creation, the Company has received significant amounts under subsidized research programs.

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

As of December 31, 2015 and since its creation in 2005, the Company has received the following financial assistance:

As of December 31, 2015 (€ thousands)	**Amount granted**	**Amount received**	**Amount refunded**
OSEO refundable advances	3 470	3 470	1 620
OSEO - FEDER grants	605	605	
COFACE refundable advances	91	91	
Total financial assistance	**4 166**	**4 166**	**1 120**

The amounts and payment dates of current and future grants depend on various factors beyond the Company's control, such as a decision not to distribute or to freeze credits. Delays in paying or the non-

payment of these grants, which finance part of the Company's growth, could materially adversely impact its business, financial position, income, expansion and outlook.

4.5.5 The Company receives public subsidies and a research tax credit to help finance its activities.

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

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

Thus, in 2014, the Company received reimbursement of the research tax credit reported for 2013 in the amount of €3.2 million, and it recognized a research tax credit in the amount of €3.5 million for expenses incurred in 2014. The Company has realized a tax benefit in fiscal year 2014, the amount of research tax credit generated on these expenditures in 2014 could thus be immediately charged to the income tax due for the fiscal year 2014, the amount of which thus decreased by €4.1 million to €0.6 million.

Under the year 2015, the Company recorded an amount of €6.8 million under the research tax credit that appears in its receivables , and for which it will seek reimbursement in 2016.

With respect to 2015 and subsequent years, it cannot be ruled out that the tax authorities may dispute the methods that the Company uses to calculate its research and development expenses, or that the research tax credit may be lost due to statutory amendments or a dispute with the tax authorities, despite the fact that the Company feels it is in compliance with the expense documentation and eligibility requirements. Such occurrence could have a material adverse impact on the Company's income, financial position and outlook.

4.6 Market risks

4.6.1 The majority of the Company's operating costs are incurred in euro but its current and future revenues may be invoiced in a different currency.

The majority of the Company's expenses are incurred in euro. However, as a result of the agreement signed with Eli Lilly in December 2014, a major part of the Company's future revenues, in addition to the upfront payment already received in connection with that agreement, will be denominated in US dollars. As a result, the Company is exposed to risk in relation to fluctuations in the euro-US dollar exchange rate. In addition, if the Company signs additional license or cooperation agreements with US pharmaceutical groups, it may be exposed to additional euro-US dollar exchange rate risk.

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.

4.6.2 The Company is exposed to changes in interest rates in the course of managing its cash and cash equivalents.

To date, the Company has no loans, other than non-interest bearing reimbursable advances.

Nevertheless, 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 €49.8 million as of December

31, 2014 and €72 million as of December 31, 2015. This item includes term deposits, accounts that pay fixed interest and investments in money market mutual funds. The Company's policy is to invest exclusively in liquid products with no risk to capital.

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

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

4.6.3 Liquidity risk

Historically, the company has financed its growth primarily by increasing its equity through capital increases. It has never taken out bank loans. Consequently, the company is not exposed to liquidity risks due to the application of early repayment clauses in bank loans.

The company's cash and cash equivalents totaled €49.8 million as of December 31, 2014 and 72 million as of December 31, 2015. The company conducted a specific review of its liquidity risk and considers that it is in a position to meet its financial obligations that will fall due within the next 12 months. Indeed, at the end of December 2015 and after payment of the € 10 million milestones from Lilly, the cash and cash equivalents of the Company amount to €72.1 million. Including debts, which mainly relate to Bpifrance refundable debts for a total €0.9 million, the net cash was €71.2 million. This level of cash enables the company to fund its planed clinical development (see paragraph 6.1.3 of tis reference document) and the development of its technology platform *DriveIn*.

In particular, the company considers that it is in a position to pay the upcoming reimbursements of Bpifrance reimbursable advances, being specified that no reimbursement is planed during the 2016 year (see parapgraph 22.1, 22.2 and 22.3 of this reference document for more dtails on this reimbursable advances).

As described in Note 3.10 to the consolidated financial statements of the Company, prepared under IFRS rules,contained in paragraph 20.1. of this reference document, long-term financial liabilities of the Company include only repayable advances.

4.6.4 Equity risk

None.

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

The price of the Company's shares is subject to significant volatility. Over the course of the last 13 months, the Company's share price has increased sharply. For example, on December 31, 2014, the Company's share price was €48.25 while on December 31, 2015, the Company's share price was €73.22. In addition, the average daily trading volume also significantly increased over this period from approximately 90,000 shares in 2014 to approximately 70,580 shares traded daily in 2015. Finally, following the sale by some of the Company's historical shareholders of their stakes, the public float also increased from 48% at the end of January 2015 to 60% at the end of December 2015.

In addition to the occurrence of the risks described herein, the market price of the Company's share 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, includingannouncements 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;
- announcements concerning changes to the Company's management team; and
- announcements concerning the scope of the Company's assets (acquisitions, sales, etc.).

Furthermore, the stock markets experience significant fluctuations that are not always related to the income or outlook of the companies whose shares are traded. Therefore, such market fluctuations, as well as the economic situation, may also significantly impact the market price of the Company's share.

4.7 Moreover, no extraordinary events have occurred during the same period that, to the company's knowledge, impose on it any additional risk or costs for which provisions have not been recognizedInsurance and risk coverage

The company has adopted a policy to cover the main risks to which it is exposed 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 were €110.5 thousands and €99 thousands in the fiscal years ended December 31, 2014 and December 31, 2015, respectively.

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, with coverage limits of €8.7 million;

- a "business liability" policy, which covers risks in connection with business operations, with maximum coverage limits for all damage, including bodily injury, of €3.5 million per year;

- 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, with annual coverage limits of €3 million.

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 *inter alia* 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 in 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.

4.8 Extraordinary events and disputes

During the 12-month period preceding the filing date of this reference 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 filing date of this reference document, the company is not threatened with any such proceedings.

Besides, no exceptional event arose during the same period had an impact, at the knowledge of the Company(Society), generated additional risk or additional costs that would be not accrued.

5 INFORMATIONS ABOUT THE COMPANY

5.1 History and evolution of the company

5.1.1 Legal name and trade name

The company's legal name is Adocia.

5.1.2 Place of registration and registration number

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

5.1.3 Date of incorporation and term

The company 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 a decision adopted by the general shareholders' meeting held on October 24, 2011.

5.1.4 Registered office of the company, legal form, law governing its business

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 company's registered office is located at 115 Avenue Lacassagne, 69003 Lyon.

The company's contact information is shown below:

Telephone: +33 (0) 4 72 61 06 10
Fax: +33 (0) 4 72 36 39 67
Email: contactinvestisseurs@adocia.com
Website: www.adocia.com

5.1.5 Significant events in the development of the company's business

End 2005	• Creation of the company by Gérard, Olivier and Rémi Soula, who invest €1.6 million.
2006	• First employees hired. The company moves into Merck's former site at 115 Avenue Lacassagne in Lyon. • OSEO grants a reimbursable advance in the amount of €2.25 million for the Osteoporosis project.
2007	• In a first round of equity financing, €12 million is raised from AGF Private Equity (now IdInvest) as lead investor, Société Générale Asset Management (now Amundi Private Equity), Viveris Management and Bioam Gestion, as well as two private investors, Alain Tornier and Jean Deléage, and the founders.
2009	• In a second round of equity financing, €14 million is raised from the company's historical investors and two new investors: Innobio (CDC Entreprises) and SHAM. • Signature of first research contract (feasibility study). • OSEO provides assistance for the Insulin project totaling €840,000, of which €420,000 is in the form of a reimbursable advance and €420,000 is in the form of a grant from the ERDF.
2010	• Following conclusive preclinical trials, Phase I/II clinical trial of BioChaperone® PDGF-BB begun on diabetic foot ulcer (DFU) patients in India. • Following conclusive preclinical trials, Phase I clinical trial of HinsBet® fast-acting human insulin begun on healthy volunteers. • Signature of new research contract (feasibility studies).
2011	• Positive results from the Phase I clinical trial of HinsBet® fast-acting human insulin on healthy volunteers. • Phase IIa clinical trial of HinsBet® fast-acting human insulin begun on type 1 diabetes patients. • End of the Phase I/II clinical trial of BioChaperone®/PDGF-BB on diabetic foot ulcer (DFU) patients in India. • Signature of a license and cooperation agreement with the US pharmaceutical group Eli Lilly and Company covering the development and marketing of Humalog fast-acting insulin analog, which uses BioChaperone® technology.
2012	• The company's initial public offering on the Euronext regulated market in Paris raises €25.4 million (net of transaction expenses). • Publication of clinical results (Phase I/II trial on diabetic foot ulcer patients and Phase IIa trial on type 1 diabetes patients to study fast-acting human insulin). • Eli Lilly begins Phase I trial of BioChaperone® Lispro. • US and European agencies grant a patent for the Biochaperone® PDGF-BB formulation for the treatment of chronic wounds. • Application filed with the Indian regulatory authorities for authorization to conduct a Phase III clinical trial in India.
2013	• The European Medicines Agency issues a positive scientific opinion for conducting a single Phase III European study for the treatment of diabetic foot ulcers. • Adocia and Lilly end their collaboration. Adocia recovers its rights to develop ultra-fast-acting insulin analogs. • Clinical trial begun to study the combination of long-acting insulin glargine with a fast-acting insulin analog.

- Acquisition of an exclusive license to DriveIn® nanotechnology, which improves the effectiveness of anticancer agents by targeting their action in tumors.
-

2014

- Adocia strengthens its diabetic foot ulcer patent portfolio (grant of the BioChaperone® PDGF (Platelet Derived Growth Factor) in Japan and grant in the United States of the polymer used in the PDGF composition).
- Launch of a clinical phase IIa study on the ultra fast acting analog insulin.
- Clinical phase 1-2 positive results for its combination of long-acting insulin glargine and fast acting insulin Lispro BioChaperone® Combo).
- Positive results from phase IIa clinical study of ultra-fast acting BioChaperone® Lispro.
- Initiation of a dose-response Phase IIa clinical study of ultra-fast acting BioChaperone® Lispro
- Positive preclinical results for a concentrated ultra-fat insulin, BioChaperone® Lispro U300
- Launch of a Phase IIa clinical study of Hinsbet, its fast-acting human insulin, in Type 1 diabetes
- Launch of Phase III cinical study in India of treatment for diabetic foot ulcer
- Positive preliminary results from dose response clinical study of ultra-fast acting BioChaperone® Lispro U100, in patients with Type 1 diabetesAdocia and Lilly announce alliance to co-develop ultra-rapîd insulin based on BioChaperone® technology
- Initiation of a clinical study on the post-meal effect of ultra-rapid BioChaperone® Lispro insulin formulation
- Posiitve results from Phase IIa clinical study of fast-acting human insulin, Hinsbet
- Adocia Lily and announce their alliance to co-develop an ultra-fast insulin through technology BioChaperone®

2015

- Launch of a Phase 1b clinical study on the effect of ultra-rapid insulin BioChaperone Lispro on post-prandial glycemic control in type 1 diabetic patients (under Lilly-Adocia partnership)
- Positive Phase 2a study results for HinsBet (BioChaperone human insulin)
- Adocia opens a subsidiary in the USA, Delaware state
- Adocia successfully raises approx. €32 million from healthcare specialist investors
- Positive results from a Phase 1b clinical study on the effect of ultra-rapid insulin BioChaperone Lispro on post-prandial glycemic control in type 1 diabetic patients (under Lilly-Adocia partnership)
- Launch of two Phase 1b clinical studies on BioChaperone Combo: one on the effect of BioChaperone Combo on post-prandial glycemic control in type 1 diabetic patients and one on the pharmacocynamic and pharmacokinetic profiles of BioChaperone Combo in type 2 diabetic patients

	• Launch of a pilot bioequivalence study comparing BioChaperone Lispro U200 and BioChaperone Lispro U100 in healthy volunteers • Launch of a Phase 1b clinical study evaluating the effects of repeated administration of BioChaperone Lisproo in type 1 diabetic patients (under Lilly-Adocia partnership) • Launch of a Phase 1b clinical study evaluating the effects of repeated administration of BioChaperone Lirpso in patients with type 2 diabetes (under Lilly-Adocia partnership) • Launch of a Phase 1b clinical study on the effect of ultra-rapid insulin BioChaperone Lispro on post-prandial glycemic control in type 1 diabetic patients using an insulin pump (under Lilly-Adocia partnership) • Positive results of the Phase 1b clinical study evaluating the effect of BioChaperone Combo on post-meal glycemic control in type 1 diabetic patients • Positive top-line results showing BioChaperone Combo's pharmacodynamic profile to be superior to the one of Humalog Mix75/25 and similar to the one of Lantus + Humalog separate injections, in patients with type 2 diabetes • Positive results of the pilot bioequivalence study comparing BioChaperone Lispro U200 and BioChaperone Lispro U100 in healthy volunteers, triggering a $10 M milestone payment from Lilly.
2016	• Launch of a phase 1b clinical study evaluating ultra-rapid insulin BioChaperone Lispro in healthy Japanese subjects (under Lilly Adocia partnership) • Positive topline results of the study evaluating the effects of repeated administration of BioChaperone Lirpso in type 1 diabetic patients • Creation of a Global Diabetes Medical Advisory Board, consisting of world-reknowned experts in diabetes

5.2 Investments

5.2.1 Major investments

The main investment made by the Company during the last two fiscal years consist basically in the purchase of laboratory equipement, computer equipement and car parks (see notes 3.1, 3.2 et 3.3 of the notes to the company's financial statements prepared in accordance with IFRS for the fiscal years ended on December 31, 2014 and December 31, 2015, in Chapter 20.1 of this reference document).

(IFRS - € thousands)	**FY 2015 (12 months)**	**FY 2014 (12 months)**
Intangible assets		1
Property, plant and equipment	1 434	347
Long-term investments	20	
TOTAL	**1 454**	**349**

5.2.2 Major current and future investments

For the year comming and in order to support its growth, the Company has planned to intensify its investment policy, amoung other things, expanding its facilities and providing them new laboratory equipments.“

On January 18, 2016, the Company signed a preliminary sales agreement with the “Metropole of Lyon” for the acquisition of this property where are located its offices 115 Avenue Lacassagne, 69003 Lyon. The promise of sale is the building called "Pépinière Lacassagne" with a total area of 7.120 m², the land on which the building is located and 43 parking spaces. The purchase price of the whole was set at 5 million euros, excluding VAT and registration fees. The Company plans to finance this acquisition by bank loans (suspensive condition of promise).

With the signature of the preliminary sales agreement, the Company has the right to use and enjoy the property.

The signing of the bill sale is expected during the month of April 2016.

6 OVERVIEW OF ACTIVITIES

6.1 Presentation of Adocia

Adocia is a French biotechnology company founded in December 2005 by Gérard, Olivier and Remi Soula. It is specialized in the development of best-in-class medicines from approved therapeutic molecules, in particular proteins using its BioChaperone® technology and anticancer drugs using its Drive*In*® technology.

6.1.1 Rekying on the BioChaperone® technological platform to be a major player in the area of insulin therapy and healing of chronic wounds resulting from its

The authorized proteins used by Adocia treat widespread pathologies. Innovations to the formulation of these proteins have led to their improved efficacy, to a simpler and broader therapeutic use and thereby to improved quality of life of patients. Among the main therapeutic areas, Adocia initially focused on two market segments:

1. treatment of diabetes by insulin therapy
2. regenerative medicine*, in particular the treatment of chronic wounds* by a growth factor*, platelet derived growth factor-BB (PDGF-BB).

These two proteins, insulin and PDGF-BB are authorized in the United States and Europe and have proven their superior efficacy in their respective areas. Even so, their efficacy and usage could be significantly improved by better formulations.

To this end, Adocia has designed and developed a technological platform using a new family of polymers called BioChaperone® that have the property of spontaneously combining with these proteins. After combining, BioChaperones provide the proteins with new properties:

- an increase in their solubility;
- protection from enzymatic breakdown*;
- stabilization of therapeutic proteins during storage; and
- stabilization of the activity of therapeutic proteins in the presence of cells.

These important properties result in increased efficacy of the therapeutic protein, in particular by facilitating its absorption in the body, by a faster of onset of action and by an increased duration of action. These properties lead to envisioning a significant improvement of existing medical treatments by improving the expression of the properties of therapeutic proteins, by modifying dosages (reduction of dose, of the number of applications and the duration of the treatment) and/or by changing routes of administration of treatments. These properties also enable new fields of applications for a given therapeutic protein to be considered.

In addition to increasing the efficacy of these formulations in comparison to those currently on the market, these new properties will also improve safety and compliance* with pharmaceutical industry regulations concerning proteins combined with BioChaperone®. By the use of BioChaperone®, Adocia has obtained products that can be considered as best-in-class, i.e. having the best therapeutic effects in their therapeutic class.

The BioChaperone® technological platform can also be used for other therapeutic classes of proteins such as monoclonal antibodies or growth hormones.

The company has decided to use the properties of its collection of BioChaperone® polymers for very large markets in the following areas:

- healing of chronic wounds with the treatment of diabetic foot ulcers and developments planned for the treatment of venous ulcers, bedsores* (bedsores, pressure sores, decubitus ulcer) and burns by the combination of BioChaperone® and the growth factor called PDGF-BB (platelet derived growth factor-BB);
- insulin therapy with the treatment of type 1 and type 2 diabetes by insulin in the form of novel formulations of insulins, so-called second generation ("BioChaperone® Insulins"):
  - a fast-acting BioChaperone®-human insulin complex* with a more rapid onset of action that that of human insulin and similar to that of an insulin analog
  - an ultra-fast acting BioChaperone®-insulin analog complex that starts acting more rapidly than an insulin analog alone
  - a BioChaperone® complex containing a fast acting insulin and the lmong –acting insulin analog glargine, forming a single Combo Insulin reuniting the rapid action of the former and the basal action of the latter
- chronic diseases with the market for monoclonal antibodies having many oncology applications (treatment of leukemias*, lymphomas*, breast cancers, colorectal cancers, etc.) and for the treatment of autoimmune and inflammatory diseases (rheumatoid polyarthritis*, Crohn's disease*, multiple sclerosis*, etc.) resulting from the development of a second generation of formulation of monoclonal antibodies ("BioChaperone® mAbs") that:
  - improves the physical stability of monoclonal antibodies to prevent the formation of aggregates that could reduce efficacy and increase the immunogenicity of products;
  - improves the solubility of monoclonal antibodies to enable the preparation of formulations at high concentrations so they can be administered subcutaneously rather than intravenously when the former mode of administration is compatible with the pathology in question and the monoclonal antibody used.

6.1.2 Relying on DriveIn® technological platform to become an emerging player in the area of oncology

Starting in December 2013, Adocia began the development of Drive*In*® nanotechnology for the treatment of cancer. Adocia has obtained exclusive rights for the development and marketing of this patented nanotechnology developed by Professor Sebastien Lecommandoux and his team at the Laboratory of Chemistry of Organic Polymers (LCPO, UMR5629 CNRS - University of Bordeaux I - Polytechnic Institute of Bordeaux). This technology has been shown to be very effective in pre-clinical trials for the transport of drug substances and their delivery to solid tumors, thereby increasing the therapeutic index of these drug substances. This work has been described in several publications in benchmark international scientific journals*.

As a result of elevated efficacy, chemotherapies have been one of the cornerstones of oncology treatment for several decades. These substances nevertheless cause major adverse effects related to the damage they cause to healthy tissues at the same time as destroying cancer cells. This explains why treating cancers with chemotherapy has progressed towards targeted approaches, by using molecules with intrinsic targeting such as monoclonal antibodies, or by developing transporters for chemotherapy molecules that target the treatment of only the tumor and leave healthy tissues intact.

* Upadhyay and al (2009), Biomacromolecules 10:2802-2808; Upadhyay and al (2010), Biomaterials 31: 2882-2892; Upadhyay and al. (2010), Macromol. Biosci., 10:503-512; Upadhyay and al (2012) Nanomedicine: Nanotechnology, Biology and Medicine 8:71-80.

Adocia has opted for the second approach with the development of Drive*In®*, an innovative biomimetic nanotechnology for drug delivery in oncology.

thérapeutiques approuvées. Adocia intends using a dual strategy to develop this nanotechnology. Adocia is planning to develop proprietary products containing doxorubicin and docetaxel, two widely used anti-cancer drugs that could substantially benefit from better penetration in the cells of solid tumors. In addition, Adocia will propose its Drive*In®* technology to pharmaceutical companies in order to optimize the efficacy of their proprietary molecules.

Considerable work is under way by players in this sector in order to discover new oncology treatments but also to improve the performance of authorized products at the same time as attenuating their adverse effects. One of today's major goals of this quest for improvement is to ensure better targeting of solid tumors so the anticancer molecule can concentrate in the tumor, thereby limiting damage to surrounding healthy tissues.

The novelty of Drive*In®* resides in the use of nanoparticles whose surface is composed uniquely of hyaluronic acid, a biopolymer naturally present in the human body, known to interact with the CD44 cell receptor. This receptor is over-expressed in many solid tumors, providing Drive*In®* with its properties of targeting and incorporation in cancer cells. The drug delivered in this way would be more effectively incorporated by cancer cells, whereas existing therapies remain limited for this aspect.

With the acquisition of this new technology platform, the Company is preparing a second generation of innovations in its field of expertise: the delivery of approved therapeutic molecules.

6.1.3 Adocia's economic model

The strategy and economic model of the company involves using the BioChaperone® and Drive*In®* technological platforms for the development of innovative formulations for different therapeutic molecules already authorized, with the goal of becoming best-in-class products.

The company will establish proof of concept of medical efficacy of its innovative formulations by phase I-II clinical trials in humans, sometimes remaining limited to preclinical studies with proof of concept in animals. Once the proof of concept is established, Adocia will license products obtained with its technologies to large pharmaceutical or medical device companies. Adocia is also planning on signing joint development contracts, similar to those currently in force for monoclonal antibodies in order to make best use of its technologies for new applications and with the goal of subsequently signing licensing contracts if initial trials are successful.

Adocia does not plan on producing and marketing its products.

The following diagram is a progress report on different Adocia projects under way at the date of registration of this reference document:

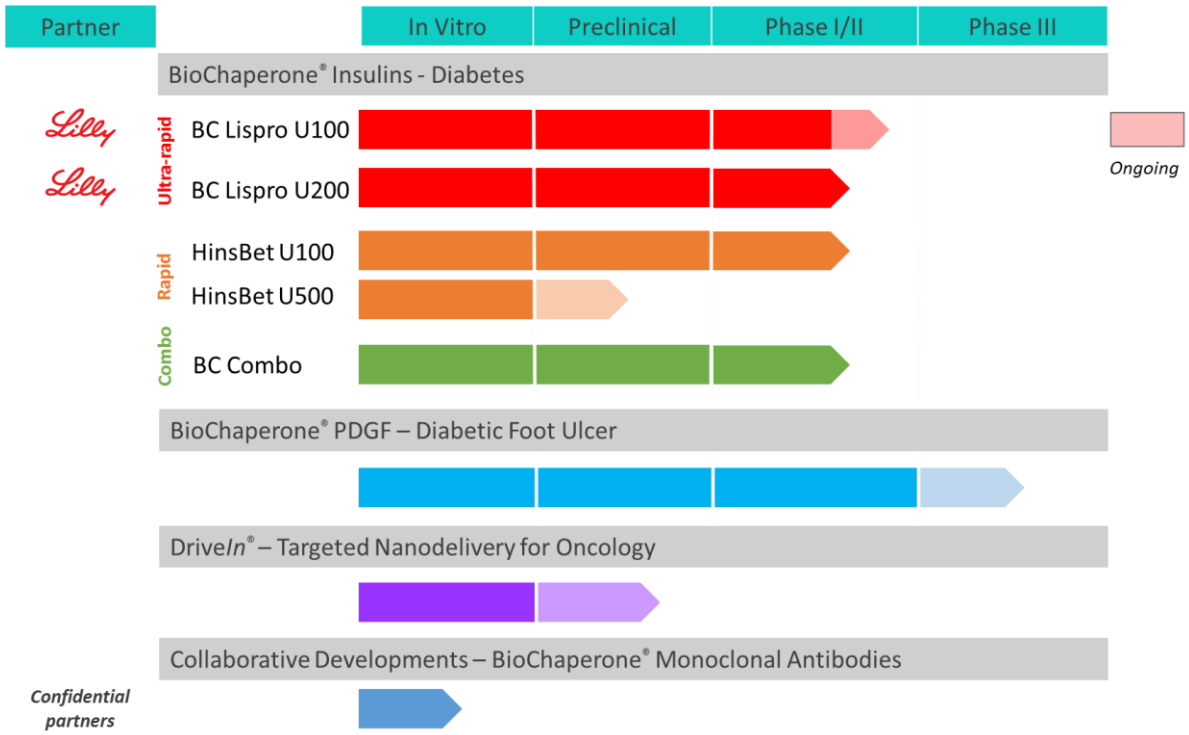


Figure 1 : Adocia Pipeline as of March 24th, 2016. Source: Adocia

During 2015, Adocia pursued the development and the broadening of its insulin franchise :

- **BioChaperone Lispro**, ultra rapid insulin:. Since signing the licensing agreement between Adocia and Eli Lilly in December 2014, both companies have launched 5 clinical studies on BioChaperone Lispro U100. The first showed that BioChaperone Lispro improved post-meal glucose control after a standardized meal in type 1 diabetic patients (compared to Humalog U100). The second confirmed that BioChaperone Lispro improved post-meal glucose control compared to Humalog U100 at the beginning and at the end of a 14 days, outpatient treatment period, during which either treatment was administered three times a day in type 1 diabetes patients. Three other studies are ongoing: one study assesses the effect of BioChaperone Lispro U100 repeated administration in type 2 diabetic patients. A second trial studies the effects of BioChaperone Lispro U100 on post-meal glucose control in type 1 diabetic patients using insulin pumps. A third, launched in January 2016, is evaluating the pharmacokinetic and pharmacodynamics profiles of BioChaperone Lispro U100 in healthy Japanese subjects. Results from all three ongoing studies are expected in H1 2016.

  Adocia also launched a pilot bioequivalence study comparing BioChaperone Lispro U200 to BioChaperone Lispro U100. Positive results from this study were jointly announced by both companies in December 2015. These results triggered a $10 million milestone payment from Lilly.

- **BioChaperone Combo**, a combination of long-acting insulin glargine and fast-acting insulin lispro: Two Phase 1b clinical studies of BioChaperone Combo were launched in 2015. The first demonstrated that the favorable pharmacodynamic and pharmacokinetic profiles observed in a previous study in type 1 diabetic patients translated into an improvement of the post-prandial glycemic control compared to Humalog Mix75/25. The second study on type 2 diabetic patients showed that BioChaperone Combo's pharmacodynamic profile was superior to the one of Humalog Mix75/25 and similar to the one observed with the separate injection of Lantus and Humalog.

- **HinsBet**, fast-acting human insulin: phase II clinical results published in February 2015 demonstrated that Hinsbet is superior to Humulin® (human insulin, Eli Lilly) and has an efficacy identical to Humalog® (insuline lispro, Eli Lilly) in the first hour.

For its project related to the treatment of the diabetic foot ulcer Adocia obtained in August 2014 the Indian Agency's approval to begin a phase III clinical study. The launch of this clinical study, which dossier was filed in September 2012, was delayed due to the reorganization of the indian regulatory authorities (DCGI. The first patients were recruited in December 2014.

In addition, Adocia continued to pursue collaborative agreements with major pharmaceutical companies through feasibilities studies on innovative formulation of monoclonal antibodies

The following table summarized the clinical trials planned for 2016, being clarified that it doesn't include clinical trials provided under the frame of the contract which information shall be confidentialare:

Indication	Product	Event	Expected dates (1)
BioChaperone® Lispro	BC Lispro U100	Further clinical development with Lilly – details remain confidential	2016
BioChaperone® Combo long-acting and fast-acting insulins	BioChaperone® Combo	Project to launch a phase Ib/IIa clinical study in patients with type 2 diabetes using basal insulin, to evaluate the performance of once-a-day BioChaperone Combo as a treatment intensification option	2nd quarter 2016
BioChaperone® Combo long-acting and fast-acting insulins	BioChaperone® Combo	Project to launch a phase Ib/IIa clinical study in patients with type 2 diabetes to observe the progression of BioChaperone Combo towards steady state	2nd quarter 2016
HinsBet® U100 Rapid human insulin	HinsBet® U100	Launch of Phase Ib/IIa study in patients with type 1 diabetes to measure the glycemic control after a standardized meal	2nd quarter 2016
HinsBet® U500 rapid human insulin	HinsBet® U500	Project to launch a phase Ib/IIa clinical study (PK /PD) in patients with type 1 diabetes	4th quarter 2016
BioChaperone PDGF-BB	BC PDGF-BB	Expected launch of a phase III clinical study in the USA (pending positive results from the Indian trial)	H2 2016
BioChaperone PDGF-BB	BC PDGF-BB	Expected launch of a phase III clinical study in Europe (pending positive results from the Indian trial)	H2 2016

Table 1 : Summary of clinical trials planned by Adocia for 2016

As planned at the time of registration of this reference document , provided that the launch of clinical trials is subject to approval from local regulatory authorities

In practice, the above-mentioned clinical trial phases are defined as follows::

The preclinical phase is conducted after laboratory tests *in vitro.* The tests are run on animals with the goal of determining the efficacy and toxicity of the product before its potential administration to

humans. In spite of metabolic differences between animals and humans, preclinical studies are an ethical prerequisite before administration of the product to humans. Animal research is conducted according to very strict rules that precisely describe the conditions of the work and related controls. Animal studies most often involve rats, rabbits or dogs. They provide data on the conditions of absorption, diffusion and elimination of the product, and its metabolism in the species in question.

Phase I is conducted on a small number of healthy volunteers. Its goals are to determine (i) the safety of the molecule in humans, (ii) its optimal route of administration (intravenous, subcutaneous, oral) and (iii) the maximal tolerated dose. Phase I trials usually last between 6 months and one year. In the course of development of some projects, however, phase I trials may not be required. This is because the results of phase I clinical trials on healthy volunteers in a therapeutic area with a specific application may enable a phase II clinical trial to be conducted directly for new applications in the same therapeutic area. In addition, in some cases, such as the treatment of wounds, the products can be tested only on patients and so directly enters phase II.

Phase II is conducted on patients. Its objective is to determine effects (efficacy and safety) of the medicine according to the doses and route(s) of administration determined in phase I. This type of trial generally lasts for 1 to 2 years.

Phase III is conducted on a larger patient population. Its goal it to test the efficacy and safety of the product and to determine the optimal dose (posology). This type of trial generally lasts for 2 to 3 years.

If the results of phase II and III trials demonstrate a genuine advantage in terms of benefits compared to risks, the new drug could be granted a Marketing Authorization/Product license from the competent authority.

6.1.4 Considerable advantages over the competition

Using its BioChaperone® and Drive*In*® technology platforms, Adocia is developing new drugs intended to become best-in-class products in new formulations of therapeutic molecules that have demonstrated their value in treating the same or similar indications to Adocia's targeted indication; most of these products have received international Marketing Authorizations. BioChaperone® polymers have no intrinsic biological activity and are therefore registered with regulatory authorities as new excipients*. As a result, the development of new pharmaceutical products from these therapeutic molecules usually requires less time and less money than the development of a new pharmaceutical molecule. In addition, the risk of failure is lower because the therapeutic molecules in question have already proven their safety and acceptability with no harmful adverse effects for humans.

	Development of a new therapeutic protein	**Development of a new formulation of an authorized therapeutic protein**
Time before Marketing Authorization	**10 to 15 years**	**5 to 8 years**
Development cost	**800 to 1,400 million dollars***	**30 to 50 million dollars**

* Tufts Center for the Study of Drug Development - 2007

Adocia has developed a genuine breakthrough technology with its collection of BioChaperone® polymers having multiple applications in the areas of regenerative medicine, the treatment of chronic pathologies and oncology. The strategy of diversification of indications is a lever against the usual risk of product development. In order to meet public health needs, Adocia is focusing on the development of new innovative formulations that provide a better expression of the intrinsic properties of therapeutic molecules that reinforce their efficacy or provide them with new properties resulting from

the formation of the BioChaperone® polymer/therapeutic molecule complex. The company aims at mass markets, each representing several billion dollars.

Market	Estimated value
BioChaperone®- Growth factor PDGF-BB complex	
Treatment of diabetic foot ulcers	2.2 billion $
BioChaperone® Insulins	
Fast acting BioChaperone®-Human insulin	1 billion $
Ultra fast acting BioChaperone®-insulin analog	4.6 billion $
BioChaperone® combining a fast acting insulin and a slow acting insulin forming Combo Insulin	5 billion $
BioChaperone® mAbs	
Monoclonal antibodies	> 13 billion $
Oncology	
Drive*In*®	48 billion $

Table 2: Estimated values of markets concerned by Adocia innovations (Sources: Adocia, Datamonitor Healthcare, Business Insights).

Beyond innovative responses to public health needs, Adocia's strategy has been designed by management so that the global pharma-economic context is taken into account. The development of treatments can no longer be done without taking costs into account. This is because of increases in the prevalence* and incidence* of the pathologies targeted by Adocia, as well as the expansion of the world's population and its aging, in a policy context of controlling public health expenditures in Western countries and the growing demands of emerging economies. Healthy insurance entities, whether public or private, reimbursing patient costs are increasingly protesting the costs of medicines and medical services. These entities examine not only the safety, compliance and efficacy of products, but also their cost/effectiveness ratio. Political, economic and regulatory pressures, the explosion of generic drugs and general globalization have caused a profound change in the pharmaceutical industry. In this context, Adocia provides credible responses:

- to issues of innovations for large pharmaceutical companies that must face the widespread use of generic drugs and the expiration of many patents in the years to come, by proposing new formulations of their therapeutic proteins with new properties (shorter times of action, sustained action, different routes and/or modes of administration) that can provide heightened efficacy or at least equivalent to current treatments; and
- issues of treatment costs in developed and emerging nations (reduction of dosages, of the number of applications and duration of treatment, new routes and/or modes of administration).

This strategy of taking emerging nations into account is new for a French biotechnology company, but is opportune because of the considerable size of developing markets, and because regulatory requirements for the development of pharmaceutical products remain highly demanding but are not as strict as those of the United States and Europe. Adocia is therefore conducting clinical trials in India for its most advanced product for the treatment of diabetic foot ulcers with the BioChaperone®-Growth factor PDGF-BB complex, before conducting clinical trials in Europe and the United States.

Adocia's economic model is based on signing license contracts for BioChaperone® applications once proof of concept is established in humans, even only in animals. This license model with a system of upfront payments at the moment of signature, of milestones with respect to reaching objectives, and royalties when products are marketed, will enable the company to obtain revenues as projects progress, without having to wait for the products to reach the market. This relatively "low burn-rate" model only requires the company to invest until proof of concept is established, after which the licensee assumes the costs of development and clinical trials.

Adocia has carried out joint development programs with major names in the pharmaceutical industry in the framework of second generation formulations for monoclonal antibodies. These joint work contracts reflect the interest of large pharma companies in BioChaperone® technology and are the first step before signing license contracts if initial studies provide positive results.

In July 2013, Adocia announced that, jointly with Eli Lilly and Company, it was decided not to continue the joint research program in the license contract signed in December 2011 giving access to BioChaperone® technology for the formulation of a fast acting insulin analog.

In December 2014, Adocia and Eli Lilly announced they signed a new exclusive and worlwide licence and collaborative agreement which still relates to the developement of an ultra-rapid insulin based on BioChaperone technology (« **BioChaperone® Lispro**»). This agreement follows the achivement of positive clinical results in the framework of two clinical studies conducted in 2014. The first clinical study provided pharmacokinetic (PK) and pharmacodynamics (PD) of BioChaperone Lispro on patients with type 1 diabetes. These results were communicated at two congresses, through posters: the American Diabetes Association (ADA) in June 2014 and European Association for the Study of Diabetes (EASD) in September 2014. The second clinical trial showed a linear dose-response of BioChaperone Lispro when tested at standard doses of insulin.

Adocia's strategy is to remain focused on innovation, the aspect with the highest added value. The Company has verified that the formulations it develops can be scaled-up to the industrial standards of its partners. The signature of license contracts will enable the company to remain focused on its competitive advantages in the field of polymer chemistry and drug delivery. This is the result of the experience of Adocia and its partners, the latter responsible for clinical development, regulatory questions, production, marketing and sale of products. Similarly, for the treatment of diabetic foot ulcers or BioChaperone® insulins, clinical trials conducted were outsourced to recognized and certified service providers. Almost 80% of Adocia's staff is composed of researchers in varied fields (chemistry, physical chemistry, biology, and veterinary specialists) fully dedicated to the development of innovative products based on BioChaperone® and DriveIn® technologies. The results of Adocia teams have led to a number of patents intended to protect the company's innovations. The company's policy of protection of intellectual property covers BioChaperone® polymers, BioChaperone®/therapeutic molecule complexes and their therapeutic applications.

The company's executive team has solid experience in the management of technological innovation and partnerships with large industrial groups in the fields of both drug delivery technologies for therapeutic proteins and the development of medical devices. Mr. Gérard Soula, founder of Flamel Technologies in 1990 and his sons Olivier and Remi Soula, have actively contributed to the development of the company specialized in drug delivery and that is listed on the NASDAQ in the United States. In particular, they have demonstrated their know-how in terms of managing scientific projects for the development of new formulations of therapeutic molecules and the signature of partnerships and licenses with major players in the pharmaceutical industry such as GlaxoSmithKline, Novo Nordisk, Merck or Bristol-Myers Squibb.

The company also calls on external consultants, in particular Dr. Bernard Cabane, Research Director at the School of Industrial Physics and Chemistry, Paris (ESPCI), Professor Jacques Descotes, Professor at the Poison Control Centre - Centre of Pharmacovigilance, Dr. Jean-Charles Kerihuel, cardiologist and general manager of the company Vertical, Professor Lecommandoux, Research Director, and Professor François Thomas, oncologist at the Jules Bordet Institute and general manager of the company Thomas Conseil.

6.2 Adocia tchnologies

6.2.1 BioChaperone®, a single technological platform with many applications

Adocia has designed and developed a technological platform based on novel polymers, called BioChaperone®. These polymers are devoid of intrinsic biological activity and can spontaneously combine with certain therapeutic proteins. This combining increases the solubility and efficacy of the therapeutic protein and protects it from enzymatic breakdown.

6.2.1.1 History of BioChaperone® technology

The capacity of heparin*, a natural polysaccharide*, to form molecular complexes with growth factors was shown about 15 years ago. This combination with heparin led to the identification of three major properties that increase growth factor efficacy: (i) increase in growth factor solubility, (ii) protection of growth factor from enzymatic breakdown and (iii) prolongation of its time of action.

There are many spontaneous formations of complexes between heparin and growth factors, and the same is true for other therapeutic proteins such as hormones. The following table lists the principal proteins that combine with heparin or heparin sulfate:

Morphogenesis and tissue distribution	
Morphogens	**Coagulation**
Activin	Antithrombin III
Bone morphogenesis proteins (BMP-2,- 4)	Factor Xa
Chordin	Leuserpine
Frizzled peptides	Tissue factor pathway inhibitor
Sonic hedgehog (SHH)	Thrombin
Sprouty peptides	
Wnt (1-13)	**Growth factors**
Constituents of the extracellular matrix	Epidermal growth factors (EGF)
Fibrin	Amphiregulin
Fibronectin	Betacellulin
Interstitial collagen	Heparin-binding GF
Laminins	Neuregulins
Pleiotrophin (HB-GAM)	Fibroblast growth factor (FGF 1-15)
Tenascin	Insulin-like growth factor (IGF-II)
	Platelet derived growth factor (PDGF-AA)
Thrombospondin	Beta transforming growth factor (TGF-β1, 2)
	Vascular endothelial growth factor (VEGF-165,
Vitronectin	189)
Tissue restructuring factors	
Plasminogen tissue activator	**Binding proteins of growth factors (BP)**
Plasminogen activator inhibitor	Follistatin
Vexin protease	Binding proteins (IGFBP-3, -5)
	TGF-β BP
	Proteinases
	Neutrophil elastase
	Cathepsin G

Source: from Bernfield and al. Ann. Rev. Biochem. 1999, 68, 729.

Adocia has developed a first generation of polymers with the goal of mimicking the ability of heparin to interact with growth factors but without the anticoagulation* properties of heparin, while having the possibility of greater versatility in order to act with a larger number of proteins.

These novel polymers, called BioChaperone®, are composed of a sugar backbone, e.g. dextran or pullulan, modified by both anionic groups* (chemical component with a negative electric charge) and hydrophobic amino acids. Adocia alos extended its BioChaperone family to others shorter componants (oligomers or small molecules) presenting the same abilities.

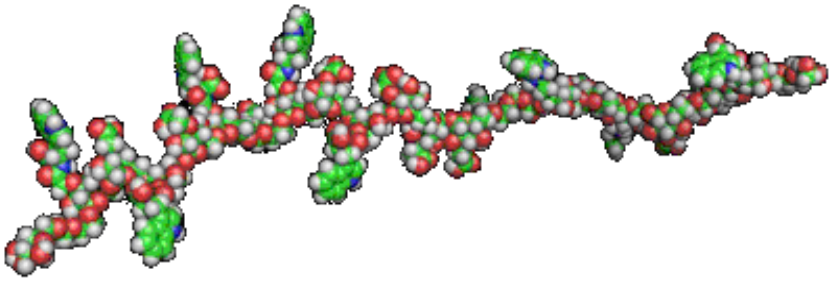
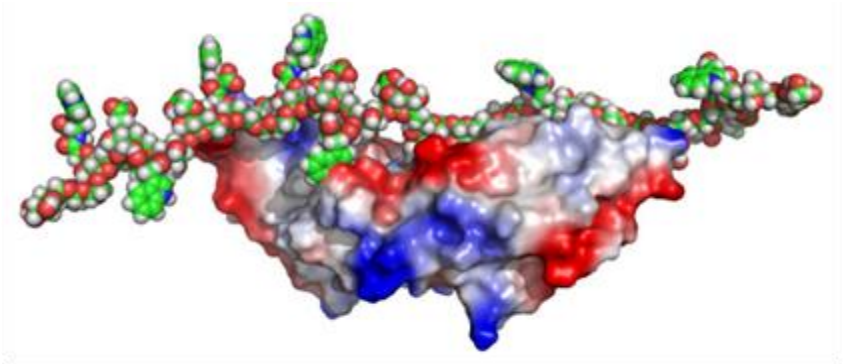


Figure 2 : 3D representation of a BioChaperone® polymer based on a dextran backbone. Source: Adocia

Source : ADOCIA

BioChaperone® polymers form complexes with proteins by binding to their surface (adsorption). The complex forms spontaneously and is based on hydrophobic and electrostatic interactions, and on the formation of hydrogen bonds. These polymers interact reversibly with proteins and without causing any degradation. The complex forms spontaneously when the two constituents are simply mixed in aqueous solution, in other words the process requires no heating or organic solvent and is immediate.



Source : ADOCIA

Figure 3 : 3D representation of the complex between a growth factor and a BioChaperone® polymer based on a dextran backbone.

It has been shown that there are four original key properties of BioChaperone® technology *via* the formation of a complex with the protein:

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

These properties augment the time the protein is present in the body and thereby increase the resulting cellular activity (prolonged time of action of the therapeutic protein and acceleration of its diffusion in the compartment(s) in question).

In addition, BioChaperone® polymers have no intrinsic biological activity and should therefore be registered with regulatory authorities as new excipients.

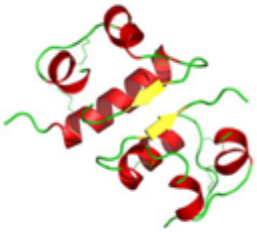
These novel properties will result in higher efficacy of these new formulations with BioChaperone® compared to formulations currently on the therapeutic proteins market, leading to products considered best-in-class, in other words having the best therapeutic effects in their therapeutic class.

Adocia's guiding principle in the development of the BioChaperone® technological platform was to design innovative and easily industrializable formulations of authorized therapeutic proteins with considerable therapeutic value for treating pathologies involving a large number of patients but whose essential properties contain major shortfalls. The intended purposes of pharmaceutical products developed with BioChaperone® technology are to be more efficacious, simpler to use and occasionally even providing new uses consistent with compliance rules of the pharmaceutical industry at competitive costs with respect to existing treatments.

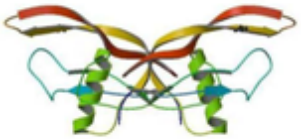
6.2.1.2 BioChaperone®, a unique collection of customized polymers for a large number of therapeutic proteins

At the present time, Adocia research teams have developed more than 350 BioChaperone® polymers, a genuine collection that will grow in size with time. The main distinctions among these polymers are their size, and the type and number of anionic and hydrophobic grafts.

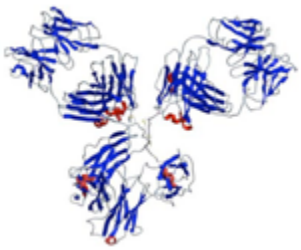
This collection of polymers prepared with the same technological platform and initially developed for growth factors, was rapidly extended to other therapeutic proteins, also authorized, and having considerable therapeutic value, such as insulin, hormones and monoclonal antibodies.



Hormones
Example: Insulin (5.8 kDa)



Growth factors
Example: PDGF-BB (26 kDa)



Monoclonal antibodies
Example: IgG (150 kDa)

BioChaperones are therefore a unique collection of novel customized polymers with a broad range of therapeutic applications.

(refer to section 6.4 "Monoclonal antibodies").

6.2.2 DriveIn®, an innovative approach to targeted delivery in oncology

In December 2013, Adocia began the development of Drive*In*® nanotechnology for the treatment of cancer after acquiring the exclusive rights for development and marketing in the health field of patents covering this nanotechnology. Drive*In*® technology was developed by the group of Professor Sebastien Lecommandoux of the Laboratory of Chemistry of Organic Polymers of the Polytechnic Institute of Bordeaux (University of Bordeaux I).

6.2.2.1 Chemotherapy, a key cancer treatment

Chemotherapy has been one of the cornerstones of the treatment of cancers for decades as a result of high efficacy. Chemotherapy, however, causes considerable adverse effects because it acts on healthy tissues as well as cancerous tissues. In order to reduce these adverse effects, treating cancers with chemotherapy has progressed towards targeted approaches; this has been done by using intrinsically targeted molecules such as monoclonal antibodies, or by the use of transporters of chemotherapy molecules to target the treatment to only the tumor while sparing healthy tissues. Adocia has adopted the latter approach by developing Drive*In®*, a novel biomimetic nanotechnology for drug delivery in oncology.

6.2.2.2 Nanoparticles: an effective delivery method

Nanoparticles are particles smaller than several hundred nanometers and some can be used as drug transporters. A very special value of nanoparticles in oncology is their capacity to accumulate in tumors by what is call the enhanced permeation and retention effect (EPR). The vascularization of tumors is abnormal, in form and structure, with disorganized formation and blood vessels presenting large fenestrations, enabling blood and what it is carrying to emerge towards the tumor. Nanoparticles of a certain size (in contrast to large molecules) tend to diffuse toward the tumor but the abnormal organization of the tumor's blood vessels and the elevated pressure inside the tumor then prevent the nanoparticles from emerging (in contrast to small molecules that escape). This combination of influx and a lack of efflux leads to the passive accumulation of nanoparticles in the tumor. Several technologies use this passive approach to augment accumulation inside tumors:

- Liposomes: they are lipid-based nano-objets. They can be coated with polyethylene glycol (PEG) to render them "stealthy", i.e. prevent their detection by the immune system. Doxil® (Johnson & Johnson) is a pegylated liposomal formulation of doxorubicin (adriamycin), one of the most widely used molecules in oncology. The use of doxorubicin is nevertheless limited by is cumulated cardiac toxicity. The liposomal formulation of Doxil® has significantly reduced the cardiac toxicity of doxorubicin. In 2011, global sales of Doxil® were $402 million. Liposomes are nonetheless relatively unstable and their reproducible production is difficult.
- Albumin nanoparticles: Abraxane is the first product containing in a reversible nanoparticle form paclitaxel, a molecule widely used in oncology, and albumin, one of the most widespread proteins in the human body. The combination of paclitaxel with albumin benefits from the EPR effect and remains "stealthy" in the body. Sales of Abraxane, indicated for breast cancer, pancreatic cancer and stomach cancer, reached $427 million in 2012.
- Nanoparticles based on blocks of copolymers: this more recent approach (also that of Drive*In®*) has not yet reached the market.

Passive targeting by EPR leads to the accumulation of the product in the tumor, but tumors themselves are most often very dense objects in which the circulation of therapeutic products is impeded. In addition, the presence of objects in proximity to the tumor does not automatically result in the uptake of the products by the cells to treat, where the product is to be released.

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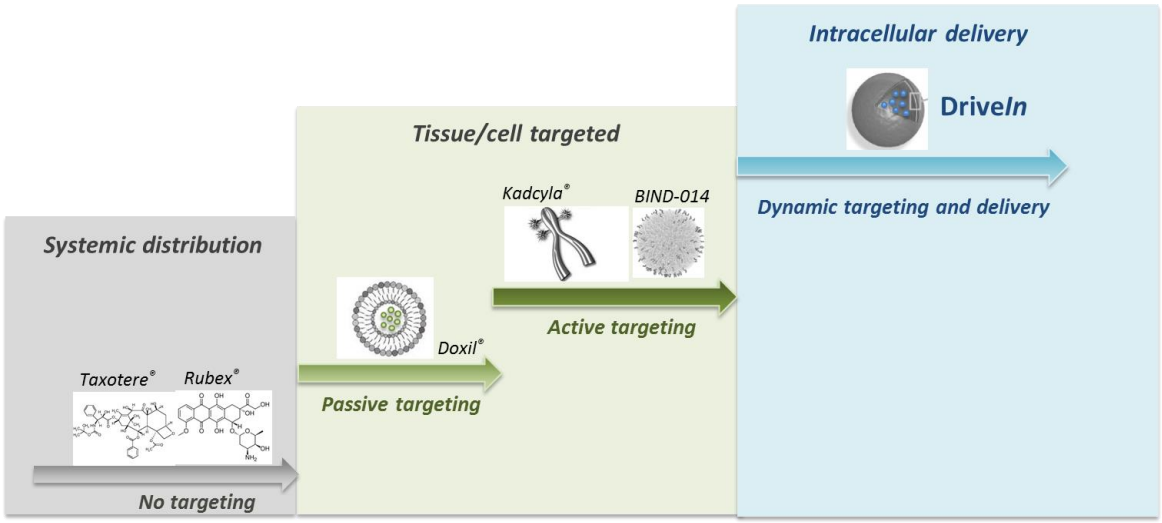


Figure 4 : Progress in therapeutic delivery methods towards active targeting and enabling intracellular delivery of the drug.

Drive*In*®, a biomimetic Trojan Horse invading cancer cells

Drive*In*® is an innovative nanoparticle technology for the active delivery of drugs that enables:

- Better cell uptake and better retention of the active chemical molecule in cancer cells, where it must act.
- Effective targeting (active and passive) towards tumors and cancer cells.

In order to obtain both better targeting and better cell uptake of therapeutic molecules, Adocia uses a breakthrough technological approach: DriveIn® nanoparticles are biomimetic, i.e. they are coated with a substance produced naturally by the human body, hyaluronic acid. **Hyaluronic acid** is responsible for the particular properties of DriveIn:

- Cell uptake: hyaluronic acid is the natural ligand of CD44, a marker of metastatic stem cells (responsible for the spread (metastasis) of cancers). The normal biological role of CD44 is to internalize hyaluronic acid and it is over-expressed in many solid tumors*. DriveIn® nano-particles are therefore naturally internalized in cancer cells once they have interacted with their receptor. Most nanoparticle products on the market or under development are pegylated. The pegylation process results in a repulsive effect on living matter and thereby prevents detection by the immune system and increases its circulation in the bloodstream, but to the detriment of bioefficacy. Pegylated molecules are internalized to a lower extent and are less likely to interact with their ligand. The use of hyaluronic acid enables DriveIn® particles to remain invisible to the immune system, but their affinity for their ligand and their uptake capacity remain intact.

* Elevated expression of CD44 is a marker of metastatic stem cells (Clinical and Developmental Immunology 2012, 12: Article ID 708036) and a marker of poor prognosis for the course of several cancers, for example cancers of the head and neck (PlosOne 2012; 7: e28776), of the gall bladder, the prostate and ovaries (Int. J. Mol. Sci. 2011; 12: 1009) as well as blood tumors.

- Targeting: the hyaluronic acid-coated surface of DriveIn® enables active targeting of cells over-expressing CD44. The nanoparticle design of DriveIn® also benefits from the EPR effect (passive targeting), that concentrates nanoparticles in the environment of the tumor.
- DriveIn® nanoparticles have been designed to act as Trojan Horses that deliver drugs to cancer cells in a targeted and active manner, while preserving healthy tissues.

Drive*In*®, a versatile platform to optimize the delivery of a wide range of molecules

Drive*In*® is a highly effective technological platform that controls all key parameters of nanoparticles (size, shape, encapsulation capacity). In this way, Drive*In*® opens new horizons to a vast array of therapeutic agents, from cytotoxic drugs to targeted inhibitors, and possibly using siRNA*.

6.3 Competing technologies

6.3.1 Cell therapies

Cell therapies are defined as "cell grafts aiming to restore the functions of a tissue or organ when they are damaged by an accident, pathology or by aging"[2].

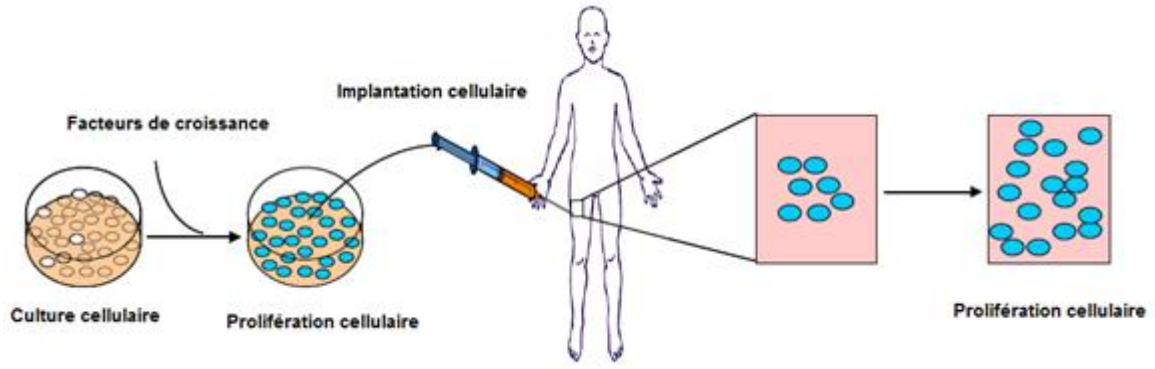
Stem cells, one of the great hopes for regenerative medicine research, are undifferentiated cells with three principal characteristics:

- their self-renewal capacity (capacity to divide and produce new identical stem cells);
- their capacity for differentiation (capacity to give rise to specialized cells forming different tissues and organs provided certain conditions of the environment are present); and
- their capacity to proliferate *in vitro* (in culture).
  - Stem cells are found in the embryo, fetus and umbilical cord blood, as well as after birth in a variety of tissues; the latter type of stem cells, called "adult", have a reduced renewal and differentiation potential.

* Upadhyay and al (2010) Biomaterials 31:2882-2892; Upadhyay and al (2010) Macromol. Biosci, 10: 503-512 ; Upadhyay and al (2012) Nanomedicine: Nanotechnology, Biology, and Medicine 8:71-80; Bui and al (2012) JACS, 134, 20189−20196.

[2] INSERM - Information on Stem Cells and Cell Therapy (in French).

Illustration of the mechanism of cell therapy



Source : ADOCIA

Very broad fields of therapeutic applications are possible with stem cells:

Cell types	Diseases
Nerve cells	Parkinson's disease, Alzheimer's disease, spinal column injury, multiple sclerosis
Heart muscle cells	Myocardial infarct, kidney failure
Insulin cells	Diabetes
Cartilage cells	Arthritis, arthrosis
Blood cells	Cancer, leukemia, immunodeficiencies, blood diseases genetics
Liver cells	Hepatitis, cirrhosis
Skin cells	Burns, wound healing
Bone cells	Osteoporosis
Retinal cells	Macular degeneration
Skeletal muscle cells	Muscular dystrophy

Tableau 3 : Possible fields of applications of cell therapy, depending on the stem cells used. Source: Veterinary Academy of France, Alain Chapel, 21 February 2008.

There are nevertheless a number of limitations to the development of cell therapies related to:

- phenomena observed in very artificial conditions (transgenic animals, "chimeric" animals bearing genetically modified cells, etc.);
- signals responsible for the differentiation of stem cells and their binding to damaged organs not totally identified;
- risks of immunogenicity and infection; and
- elevated mortality rate of implanted cells …
- A far-reaching ethical debate has opened concerning the use of embryonic stem cells and this major aspect must be considered in the future development of cell therapy technologies.

At the present time, about 40 products are marketed globally and the world market for cell and tissue therapies could reach $2.7 billion in 2015[3]. There is also considerable research under way, in particular by American companies such as Advanced Cell Technologies (blindness from degenerative retinopathies, juvenile macular degeneration, age-related macular degeneration), Geron (central

[3] Leem, Cells for Health (in French), 2010. re-edited in Ingenierie cellulaire and tissulaire, Key Technologies 2015, Ministry of Industry, Energy and Digital Economy

nervous system disorders, myocardial infarct, diabetes, arthritis, spinal cord damage) or Stemcells (Alzheimer's disease, arthritis, blindness, burns, multiple sclerosis, heart diseases and more).

In spite of this, clinical results concerning cell therapies are currently limited compared to the number of studies undertaken. The large number of failures can be explained by the elevated immunogenicity and mortality of implanted cells. In the current state of clinical research on markets of interest for Adocia, the BioChaperone® approach involving improved efficacy and safety of formulations of authorized therapeutic proteins is therefore more credible than cell therapy.

6.3.2 Gene therapy

Gene therapy is defined as "the deliberate introduction of genetic material in human somatic cells* in order to correct a genetic defect or compensate for the lack of a protein by providing the gene responsible for its synthesis "4.

Gene therapy involves introducing a treatment gene in a cell so that it produces a defined protein in the case of deficient cells, or else sends a signal causing the self-destruction of the cell in the case of cancer cells.

Every type of gene therapy is based on three basic aspects:

- a therapeutic gene;
- a vector to transport this gene: a "safe" virus, in other words lacking the sequence of its genetic code that causes its pathogenicity, or else a non-viral vector such as a liposome; and
- a target cell where the gene introduced is to be expressed.

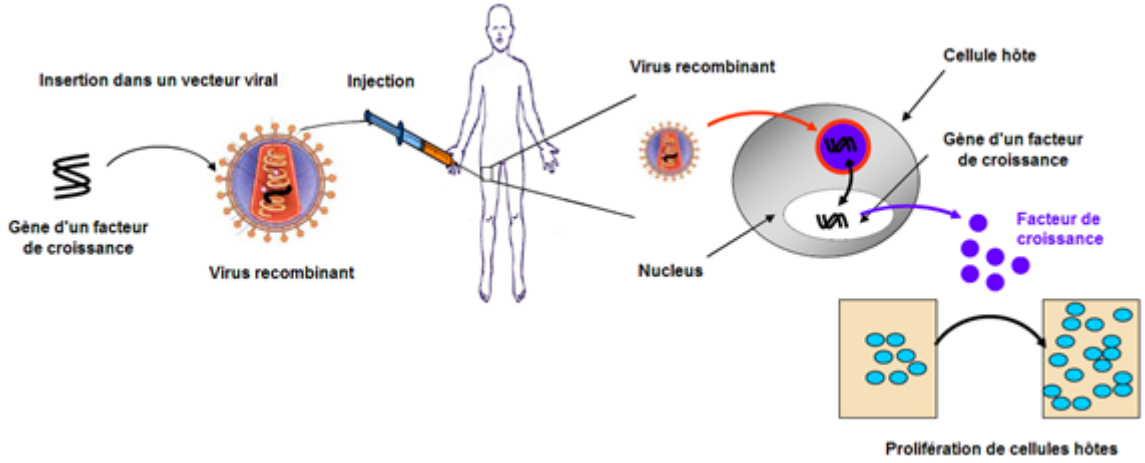


Figure 5 : Diagram of the general gene therapy process. Source: Adocia . Source : ADOCIA

In 2008, according to the INSERM, there were 1,472 gene therapy trials under way throughout the world, of which 39 were in France. More recently, the Ministry of Industry, Energy and Digital Economy[5] stated that there were 1,644 gene therapy trials under way worldwide in June 2010.

Genetic diseases, whether single-gene diseases (cystic fibrosis, myopathies, Huntington's chorea) caused by the abnormal expression of a single gene, or multi-factor diseases resulting from the

[5] Genetic Engineering (in French), Key Technologies 2015, Ministry of Industry, Energy and Digital Economy

combination of several genes or environmental factors, account for only 8.2% of clinical trials started in 2008 and dealing with gene therapy treatments, according to the INSERM. The principal area of gene therapy investigation is the treatment of cancers (melanoma, lung cancer, colon cancer, ovarian cancer, thyroid cancer, liver cancer and more). The vast majority of clinical trials under way in June 2010 were phase I (60.5%) and only 3.5%[6] were phase III trials.

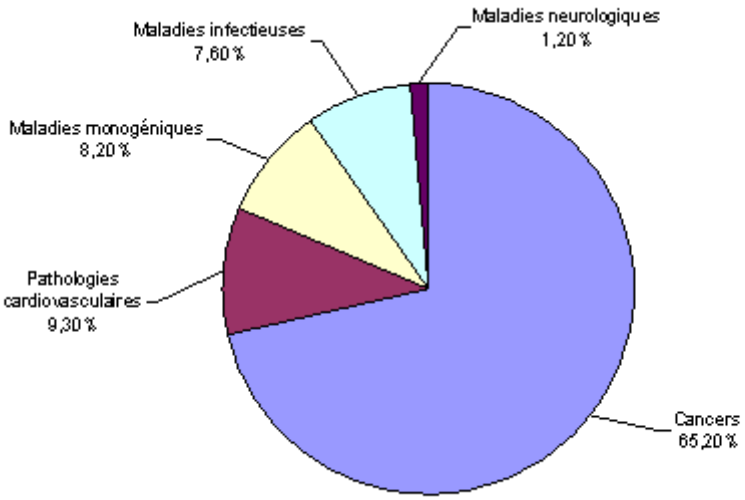


Figure 6 : Distribution of gene therapy clinical trials for the indications targeted in 2008. Source: Inserm

The variety of diseases in question and the reproducibility and simplicity of the concept "one disease - one gene" would seem to make gene therapies a genuine therapeutic revolution. It could therefore be a solution to diseases for which no effective treatment has yet been developed. Major scientific issues nevertheless persist:

- the technique for insertion of a gene in a cell is not yet totally controlled and requires a better understanding of the pathways involved in the insertion of vectors and localization of the gene introduced in the genome;
- gene transfer is not yet a safe and effective procedure;
- the stability and expression of the gene introduced are not yet fully ensured.

In order for gene therapy to be safe and effective, it is imperative to fully control the process of transgenesis*, i.e. all techniques used to introduce a foreign gene in the genome of an organism. At the present time practically all gene therapy clinical trials have failed. There exists no gene therapy treatment that is reliable, internationally recognized and used in practice. These treatments could cause serious adverse effects as was the case for neonates born with severe immunodeficiency ("bubble babies"). Work done by Professor Alain Fischer was initially shown to be a total success revealed by the remission and cure of patients: most of the babies emerged from their bubble to live a normal life. Several years later, however, several of the children treated with gene therapy developed leukemia. The data gathered suggest that the type of vector used could be included in sensitive regions of the genome and that the leukemia may have resulted from the deregulation of certain genes. Furthermore, several cases of mortality were reported after injections of high doses of an adenovirus-derived vector.

[6] John Wiley and Sons, The Journal of Gene Medicine, 2010

These cases showed the necessity for total control of the process, in particular because of vectors affecting other genes or inserting elements that are toxic for the person's genome.

Ethical aspects may also explain the limitations imposed on gene therapies. The French National Ethics Committee* (CNNE) published a recommendation for limiting research to only somatic cells, i.e. cells that will never give rise to gametes (spermatozoa and ovules).

It has been estimated that the world market for gene therapies will be $484 million in 20157 even though no product has yet been granted a Marketing Authorization. The principal parties concerned are American, European (France, Switzerland and the United Kingdom) and Asian (Japan and China) markets.

The elevated risks to patients that currently exist preclude the short- and medium-term development of gene therapy for the treatment of pathologies for which alternative treatments are possible. This technology should therefore not compete with Adocia in its areas of applications.

6.3.3 Monoclonal antibodies

Monoclonal antibodies have become a very effective treatment of cancer, as a complement to chemotherapy. Monoclonal antibodies interfere with a signaling pathway by blocking the targeted receptors or by binding to active molecules. Treatment with a monoclonal antibody is often combined with a companion test to determine beforehand if the patient can or cannot benefit from this treatment. This therapeutic regimen was validated with the development of Herceptin® for patients with HER2-positive breast cancers. The monoclonal antibodies used most often in oncology are listed in Table 4. Monoclonal antibodies are most often administered in a therapeutic regimen including classical chemotherapy..

Name	Target	Name (company)	Global sales (2013)	Indications in oncology
Rituximab	CD20	Rituxan®/Mabthera® (Roche-Genentech)	$6.1 billion	Non-Hodgkin's lymphoma, chronic lymphocytic leukemia
Bevacizumab	VEGF	Avastin® (Roche-Genentech)	$6.3 billion	Metastatic colorectal cancer (mCRC), non-small cell lung cancer (NSCLC), breast cancer, kidney cancer, brain cancer, renal cell carcinoma (RCC), brain tumor
Trastuzumab	HER2	Herceptin® (Roche-Genentech)	$6.45 billion	$HER2^+$ breast cancer, $HER2^+$ stomach cancer
Cetuximab	EGFR	Erbitux® (BMS-Merck-Lilly)	$1.89 billion	$EGFR^+$ mCRC, cancer of the head and neck
Panitunumab	EGFR	Vectibix® (Amgen)	$359 million (2012)	$EGFR^+$ mCRC

Table 4 : Best among monoclonal antibodies (Source: Datamonitor Healthcare, 2013)

6.3.4 Gene therapy and cellular immunotherapy

Beyond aiming to directly interfere with cell division in the treatment of cancer, new approaches have been developed over the last decade with the goals of:

- modifying the genetic code of cancer cells (DNA-based gene therapy) or interfering with its expression (RNA-based gene therapies). These DNA and RNA methods are currently limited by administration difficulties because the vectors are either viruses or nanoparticles. No RNA-based treatment of cancer has yet reached the market;
- activating the patient's immune system so it directly destroys cancer cells (cellular immunotherapy): these methods are still in an early stage of their development. The only immunotherapy on the market is Provenge® (Dendreon): the method involves harvesting the patient's immune cells and modifying them for their activation so they can present an antigen specific to prostate cancer cells. Once re-injected into the patient, they provoke an immune response of the patient against his(her) own cancer. The theoretical advantage of this approach is that the patient is immunized against his(her) own cancer. In spite of this promise, this technique still remains highly limited by issues of stringent production requirements and treatment costs.
  - These approaches are all under development and could be complementary methods to chemotherapy to combat cancer.

6.4 Adocia products developed with BioChaperone® technology

6.4.1 The BioChaperone® PDGF-BB combination for the wound healing market

Adocia has perfected an existing treatment for the wound healing market, in particular diabetic foot ulcers. The treatment involves spraying with a complex composed of BioChaperone® and growth factor PDGF-BB (platelet derived growth factor-BB), authorized for this indication with the marketing of Reframe® gel (Smith & Nephew). The treatment developed by Adocia could also be used to treat venous ulcers, bedsores and burns with PDGF-BB. After the phase I-II clinical trial conducted in India, Adocia received in August 2014, the Indian Drug General Controller (DCGI) authorization to launch a phase III trial in India. Adocia envisages also to conduct phase III clinical trials in Europe and in the United States.

6.4.1.1 The treatment of diabetic foot ulcers

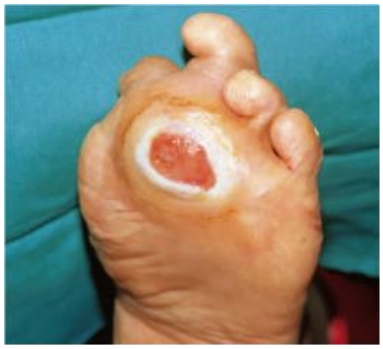
6.4.1.1.1 *The pathology*

The term "diabetic foot" encompasses all pathological manifestations affecting the foot of a patient, directly related to diabetes. About 20% of hospitalizations for diabetes[8] result from complications to the feet and there are two major causes of these pathologies:

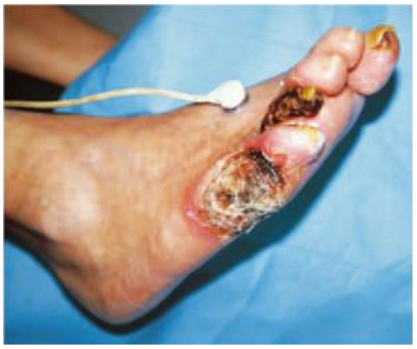
- the involvement of nerves of the foot that can advance all the way to destruction of the nerve fiber*, a condition called neuropathy*; and
- the obstruction of arteries of the leg, called arteriopathy*.

The major risk of this pathology, dominated by the occurrence of an ulceration, is amputation.

[8] CP Fylling (1992) Wound Healing an Update in Comprehensive Wound Management for Prevention of Amputation, Diabetes Spectrum 5: 358-3549 re-edited in Diabetes and Wound healing, Prof. P. Vexiau and Dr. D. Acker (Endocrinology and Diabetes Department, Saint-Louis Hospital, Paris, 2008).



Diabetic foot resulting from neuropathy



Diabetic foot resulting from arteriopathy

Figure 7 : Photographs of neuropathic and neuroischemic diabetic feet. Source: L'Observatoire du mouvement - Le pied diabetique

Neuropathy

Neuropathy is a term that includes all disorders of the peripheral nervous system (motor and sensory nerves and nerves of the extremities) and of the autonomic nervous system that controls organs.

The origin of a neuropathy is primarily metabolic. The accumulation of the sugar sorbitol* in nerves creates an edema, in turn causing destruction of nerve fibers9. These fibers, whether sensory, motor or vegetative, can be damaged by diabetic neuropathy. Sensory nerve involvement predominates and sensitivity to pain gradually disappears. In the most extreme cases, patients continue walking without being aware that the lesion on the bottom of their feet continues to exacerbate.

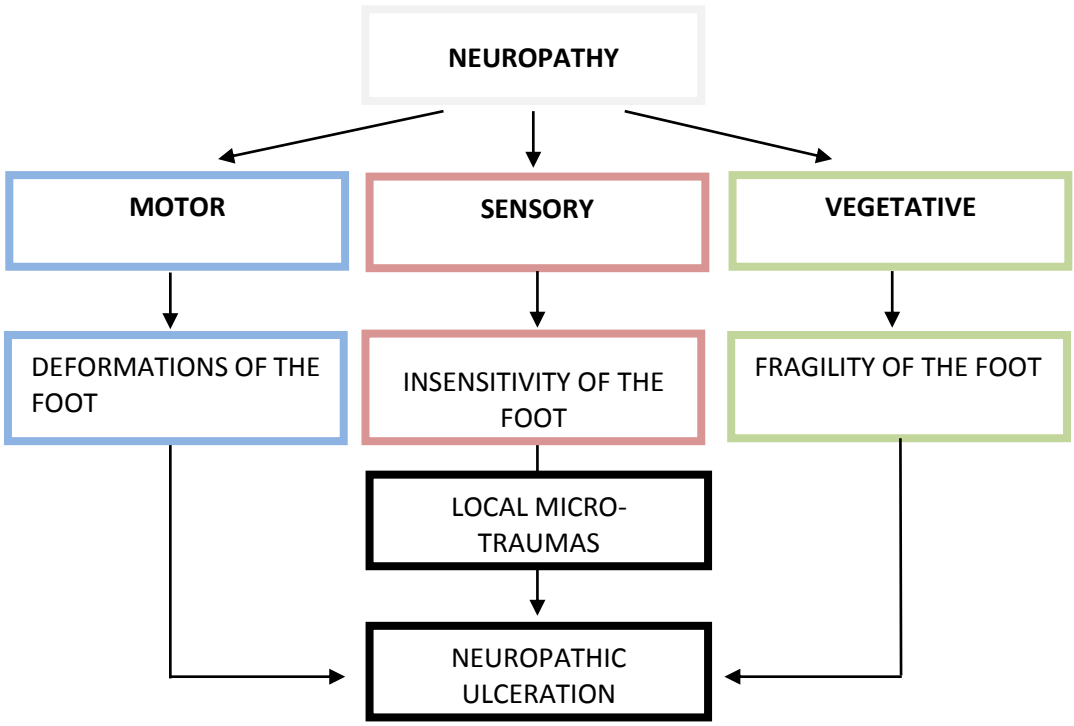


Figure 8 : Role of different involvements of the peripheral nervous system in the appearance of diabetic foot ulcers. Source: The Diabetic Foot (in French) - The situation in 2005, Dr. J-L. Richard (Nutritional Diseases and Diabetes Department, Nîmes University Hospital)

Arteriopathy

There are two possible forms of arteriopathy, an obstruction of blood vessels of the lower extremities:

- microangiopathy, the involvement of capillaries, the tiniest blood vessels, with a functional impact on the feet10 and a negative effect of its wound healing11;
- macroangiopathy, the involvement of arteries causing a narrowing of their diameter (stenosis) resulting from the deposit of cholesterol on their inner wall (atheroma).
  - A reduced blood supply or ischemia* becomes chronic and renders the foot vulnerable to the extent that a slight trauma can lead to the formation of a wound. This ischemic state also limits the capacity of blood to circulate, rapidly becoming insufficient to the point of being unable to cope with an infectious phenomenon or to heal wounds. Ischemia is therefore the cause of diabetic foot ulcers and their exacerbation.

Diabetic foot ulcers appear in only about 15% of cases by arteriopathy, whereas 90% of diabetics with an ulceration are also affected by a neuropathy[12].

Clinical characteristics of diabetic foot ulcers

Neuropathic ulcers	Ischemic ulcers
Foot arm, pulse intact	No pulse/foot not warm
Reduced sensations/calluses	Reduced sensations
Sites of ulcers: top and extremity of toes/ head of metatarsals on plantar surface	Sites of ulcers: foot contour, extremity of toes, heels
Septicemia	Septicemia
Local necrosis	Necrosis and gangrene
Charcot's arthropathy	Critical ischemia: pallor, pain, absence of pulse, foot cold

Table 5 : Clinical characteristics of diabetic foot ulcers. Source: Wesam al Arayedh and Alain Brassard, Mc Gill University Health Center, Montreal - Diabetic foot ulcers

Infection

The development of an infection of diabetic foot ulcers is the aggravating factor of the above-mentioned pathologies and can lead to amputation of the patient's foot and even mortality. The risk of gangrene to a diabetic is 17-fold higher than normal[13].

[12] Boulton AJM, The Diabetic Foot: Neuropathy in Aetiology? Diabet Med 1990; 7:852-858 re-edited in The Diabetic foot - Situation in 2005, Dr. J-L. Richard (Nutritional Diseases and Diabetes Department, Nîmes University Hospital)

[13] R. Most & P. Sinnock (1983) The Epidemiology of lower Extremity Amputations in diabetic Individuals, Diabetes Care 10: 764-776 re-edited in Diabetes and Wound healing, Prof. P. Vexiau and Dr. D. Acker (Endocrinology and Diabetes Department, Saint-Louis Hospital)

Epidemiological data

The worldwide prevalence of diabetics who develop a foot ulcer during their lifetimes has been estimated at 15%[14]; there are 10 million[15] diabetics throughout the world with a foot ulcer. In the United States, the number of diabetics has been estimated at 25.8 million[16] and the prevalence of ulcers among these patients has been estimated at 5% every year[17], i.e. more than 1 million ulcers in the United States. This number should be practically the same in Europe because the number of diabetics and the prevalence of diabetic foot ulcers are comparable. The number of amputations every year resulting from diabetes has been estimated to be more than one million[18] and so diabetes is the leading cause of non-traumatic amputation of feet in developed nations.

In metropolitan France, the number of diabetic patients (type 2 diabetes) with foot ulcers has been estimated at 218,000 for a diabetic population of about 2.2 million according to the ENTRED 2007-2010 study[19], i.e. close to 10% of the total number of diabetics. The same study estimated the number of diabetics undergoing amputation of the foot in 2007 in metropolitan France to be 33,000; this number is 80,000 more in the United States[20]. After an initial ulcer, the 5-year risk of recurrence is estimated at 70%[21].

Furthermore, the fact of being diabetic multiplies the risk of amputation by a factor of 10 to 40[22] and a second amputation is required in almost 50% of cases; in the latter situation, the survival rate is only 58%[23]. The consequences of diabetic foot ulcers multiply the risk of patient death by a factor of 2.4[24].

6.4.1.1.2 *The market*

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[14] Reiber GE. Diabetes foot care: financial implications and practical guidelines. Diabetes Care 1992; 15 (Suppl 1): 29-31

[15] Worldwide Wound Management 2005-2014, MedMarket Diligence Report S225, August 2005, p1-23

[16] American Diabetes Association

[17] Vincent Lopez Row, Diabetic Ulcers, Medscape Reference

[18] Diabetes and Wound healing (in French), Prof. P. Vexiau and Dr. D. Acker (Endocrinology and Diabetes Department, Saint-Louis Hospital, Paris, 2008)

[19] The 2007-2010 Entred study (in French) entitled "National control sample of diabetic individuals" was conducted to better understand the health status of diabetics in France.

[19] The 2007-2010 Entred study (in French) entitled "National control sample of diabetic individuals" was conducted to better understand the health status of diabetics in France. This study was sponsored by the "Institut de veille sanitaire"/Health Watch Institute, that financed the study in partnership with National Health Insurance, the National Institute for Prevention and Health Education, and the National Health Authority.

[20] Evaluation and Treatment of Diabetic Foot Ulcers - Ingrid Kruse and Steven Edelman - Clinical Diabetes • Volume 24, Number 2, 2006

[21] Apelqvist J, Larsson J, Agardh C-D. Long term prognosis of diabetic patients with foot ulcers. J Intern Med 1993; 233: 485-491 re-edited in The Diabetic foot - Situation in 2005, Dr. J-L. Richard (Nutritional Diseases and Diabetes Department, Nîmes University Hospital).

[22] Richard J-L, Parer-Richard C. The Diabetic foot (in French): Epidemiological and economic data, The Diabetic foot. Richard JL, Vannereau D, eds. Paris: Medias Flash. 2002: 23-43.

[23] Apelqvist J, Larsson J, Agardh C-D. Long term prognosis of diabetic patients with foot ulcers. J Intern Med 1993; 233: 485-491

[24] Boyko EJ, Ahroni JH, Smith DG, Davignon D. Increased mortality associated with diabetic foot ulcer. Diabet Med 1996; 13: 967-972

The global diabetic foot ulcers market has recently been evaluated at $3 billion[25]. This figure was released by the British pharmaceutical company Shire, in its May 17, 2011 announcement of the acquisition of Advanced BioHealing for $750 million. This company owns the rights to DERMAGRAFT®, authorized to treat this pathology.

The goal of all concerned in the treatment of diabetic foot ulcers is evidently to maximally limit amputations

The three major types of treatment are:

- removing all load to the foot by orthopedic shoes or a plaster cast;
- local treatments (antiseptics, petroleum jelly gauze, etc.); and
- the use of antibiotics in case of infection.

In this context, manufacturers of orthopedic devices are the first concerned by reducing loads on the foot in order to eliminate all physical stress to the wound.

In parallel to reducing load on the foot, local treatments are possible after debridement (excision) of the wound to dry and limit the spread of the necrosis. This local treatment requires not less than primary dressings* even though they have shown no benefit for wound healing[26]. Another treatment that has been developed involves using negative pressure, called vacuum-assisted closure (VAC), continuous aspiration of the wound to facilitate wound healing[27].

Finally, the wound can be treated with Regranex® (Smith & Nephew), a gel whose drug substance, becaplermin, is a genetic recombination of growth factor PDGF-BB (platelet derived growth factor-BB). This gel stimulates granulation* and wound healing of deep, chronic, pathological diabetic ulcers. Regranex® was granted a Marketing Authorization (refer to section 6.4.2.5 "The Competition") in 1997 in the United States and in 1999 in Europe.

An alternative to these treatments could arise from cell therapy by the use of skin replacements composed of human fibroblasts. Adocia believes that these products, some of which are already on the market, remain expensive to produce and so will be used only in the most severe cases. They will therefore account for only a small market share.

A major socio-economic problem

Diabetic foot ulcers are a major socio-economic problem. According to work by a task force led by diabetic foot ulcer specialists[28], the average cost of primary health care for the treatment of this pathology in the United States is between $7,000 and $10.000; the direct cost of amputation caused by a diabetic foot is estimated at between 30 and 60.000 dollars; the cost of three years of post-operative care has been estimated to be between 43 and 63 thousand dollars. The latter, elevated figure is the result of increased home care and social services needs following the amputation. For diabetic patients presenting this complication, the cost of primary care could be estimated to be between 16 and 27 thousand dollars per patient. It is also relevant to take into account indirect costs,

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[25] Shire to establish new Regenerative Medicine business unit through cash acquisition of Advanced BioHealing, Inc., including US marketed DERMAGRAFT®- Shire - May 17, 2011

[26] Jeffcoate WJ, Price PE, Phillips CJ, Game FL, Mudge E, Davies and al, Randomised controlled trial of the use of three dressing preparations in the management of chronic ulcerations of the foot in diabetes, Health Technol. Assess. 2009;13:1-86 (iii-iv)

[27] Diabetic foot, O. Tazi and C. Debure, Ed. Elsevier Masson

[28] Dr. K. Bakler, Mme A. Foster, Dr. Z.G. Abbas, Dr. A. Bal, Dr. S. Pensey and Dr. V. Vishwanathan – Improving the treatment of diabetic foot ulcers in developing nations

those due to productivity losses by these patients. If we therefore take into account reduced quality of life and lost productivity, it has been estimated that the annual costs of diabetic feet is about $4 billion in the United States.

6.4.1.1.3 *The first phase II clinical trial in India*

Adocia has sponsored a preclinical study using the diabetic rat model with the goal of comparing the effects of Regranex® (1 dose per day for 7 days) and BioChaperone® PDGF-BB complex (1 dose every 2 days for 7 days). The results showed comparable efficacy between the products in terms of wound healing and the quality of granulation tissues.

A phase I/II trial was started in June 2010 in India that included 192 patients in 11 investigation centers. The aim of the trial was to compare the efficacy of the Adocia formulation of PDGF-BB (Platelet Derived Growth factor) combined with BioChaperone® and delivered as a spray, to Regranex® (then commercialized by HealthPoint, later acquired by Smith & Nephew), a gel containing PDGF-BB that is currently the only available treatment for diabetic foot ulcers.

The 192 patients included were divided into four groups: three received PDGF-BB doses of 14.5, 43.75 and 87.5 µg per cm² and per week and the fourth received Regranex® at 43.5 µg par cm² and per week. BioChaperone® PDGF-BB treatments were administered every other day, while Regranex® was applied daily according to treatment protocols authorized by American and European agencies. The study was not blinded because of obvious physical differences between the two preparations, i.e. BioChaperone® PDGF-BB is a spray and Regranex® is a gel. The planned treatment period was 20 weeks or until total wound healing. The aim of the trial was to establish the non-inferiority of BioChaperone® PDGF-BB compared to Regranex® for each dose of the former.

The principal criterion of the trial was the percentage of total wound healing (closure of the lesion) after 20 weeks. The rates of total wound healing were all equal to or greater than that of Regranex®, i.e. 66% after 20 weeks. Criteria of non-inferiority were therefore fulfilled for the three doses of PDGF-BB tested.

One of the outstanding results of this trial is the 80°% rate of wound healing after 20 weeks obtained with the formulation containing only one third of the Regranex® dose, even though the product was applied only once every other day.

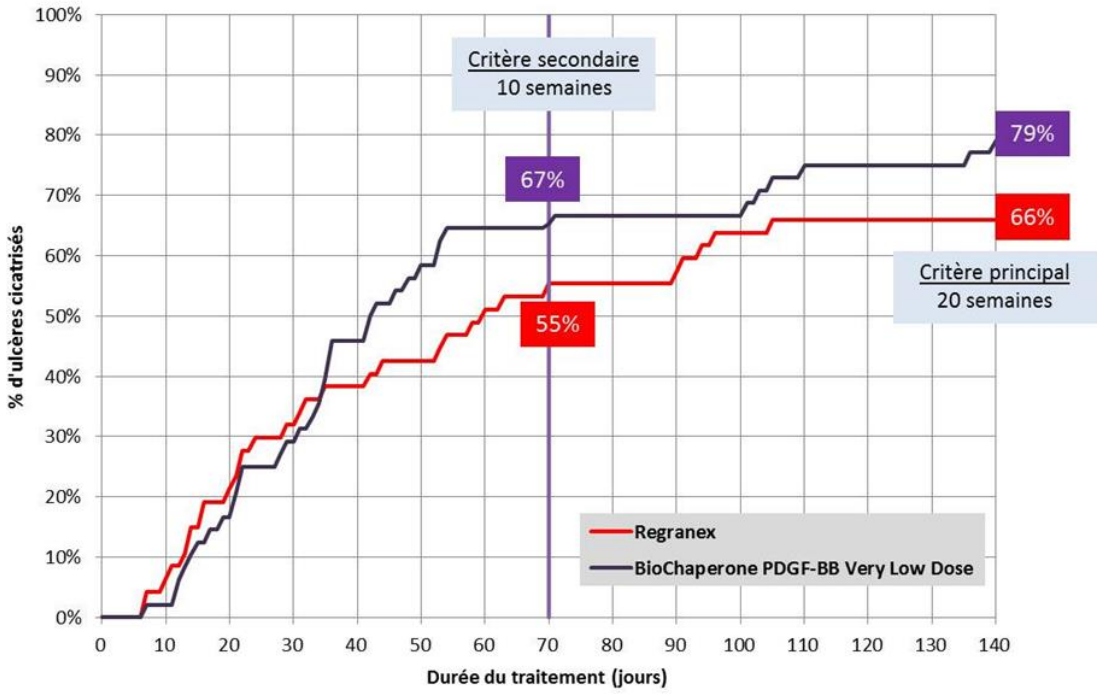


Figure 9 : Incidence of total wound healing of diabetic foot ulcers (final results) in the phase II clinical trial of the treatment of diabetic foot ulcers by BioChaperone® PDGF-BB. Source: Adocia

	Principal criterion Incidence of total closure at 20 weeks	Secondary criterion Incidence of total closure at 10 weeks
Very low dose of BioChaperone® PDGF-BB	79% (38/48)	67% (32/48)
Regranex®	66% (31/47)	55% (26/47)

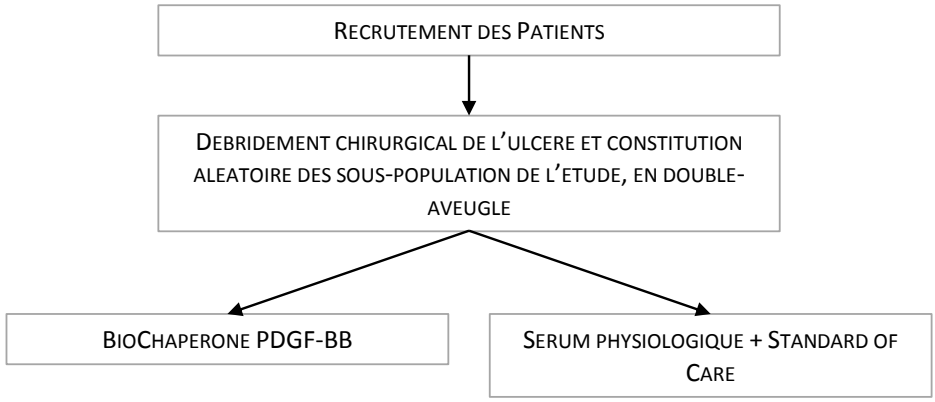
Table 6 : Results of the phase II clinical trial of treatment of diabetic foot ulcers by BioChaperone® PDGF-BB. Source: Adocia

These positive clinical results incited the company to continue development of its project and to prepare a phase II clinical trial in India, using the lowest dose of the BioChaperone® PDGF-BB complex, equivalent to one application of 4.2 µg/cm^2 every other day for 20 weeks.

6.4.1.1.4 *Current and future clinical trials*

In September 2012, Adocia deposited an authorization application with Indian regulatory authorities in order to continue the clinical development of its product and start a phase III clinical trial. The regulatory authority in question underwent a reorganization and the examination of clinical trial applications was suspended for more than 6 months in 2013.

In August 2014, DCGI (Drug Controller General of India) finally gave the approval for Adocia to start a phase III clinical study in India. The first patients were recruited in December 2014. The results of this study are expected for the first semester 2016. The goal of this study is to demonstrate the superiority of the BioChaperone® PDGF-BB complex *vs.* Placebo in 252 patients .



Fréquence des applications : 1 fois tous les 2 jours
Durée du traitement : Max. 20 semaines
Quantité de produit par application : 4,2µg/cm² sous un volume de 17µl/cm²
(c.à.d. 14,6µg/cm²/semaine)

Fréquence des applications : 1 fois tous les 2 jours
Durée du traitement : Max. 20 semaines
Quantité de produit par application : 17µl/cm²

Figure 10 : Design of the phase III clinical trial of BioChaperone® PDGF-BB vs. standard of care

The key elements examined involved two levels:

- Primary efficacy of the treatment measured as the percentage of patients for whom total wound healing of the ulcer was obtained after 20 weeks.
- Secondary efficacy of the treatment measured by:
  - the percentage of patients for whom total wound healing of the ulcer was obtained after 10 weeks,
  - the time required for total wound healing of the ulcer,
  - the extent of reduction of the surface of the ulcer during treatment and
  - the rate of recurrence of the ulcer after surveillance of 3 months post-wound healing.

Results from this study will support the submission of the dossier for market approval to local regulatory authorities, which could be filed by the end of 2016. The study is performed by Makrocare, a global contract research organization with offices in the USA, Europe, India, Singapour and Japan. This company follows the Good clinical practices (GCP).

ADOCIA then plans to launch two phase III clinical trials, one in Europe and the other in the USA during the second semester 2016. These studies would target mainly diabetic foot ulcers with a neuro-vascular origin (neuroischemic DFU), which generally display lower rates of healing. As announced in a press release on March 18th 2013 (cf. Chapter 12), EMA confirmed that only one European Phase III study would be required for market approval, as data from the Indian Phase III, if positive, would be considered as supportive to the market approval authorization dossier.

At the date this reference document was registered, Regranex® had not yet been granted an MA for neuroischemic diabetic foot ulcer.

6.4.1.1.5 *Progress provided by BioChaperone® technology*

Adocia has developed a new pharmaceutical product by combining a growth factor, PDGF-BB, authorized since 1997 by the FDA and 1999 by the EMA with one of its BioChaperone® polymers. This new formulation resulted in an increased solubility of PDGF-BB, its protection against enzymatic breakdown and a prolongation of its duration of action.

As a result, for an efficacy at least equivalent, the new product is applied every other day while Regranex® is applied daily; in addition, the dose of PDGF-BB required for wound healing was divided by 3 in comparison to Regranex®. BioChaperone® also led to a change in the method of administration of the growth factor: it is not a non-sterile gel, but a multi-use sterile spray to monitor the dose administered and easier application on the zone to treat.

Finally, the considerable economic advantage of the BioChaperone® PDGF-BB complex involves reduced production costs and the final cost of the product because of the reduced quantity of drug substance used. This assumes more importance since the cost of Regranex® treatment is relatively high, limiting its prescription frequency. Lower cost could lead to widespread use of the treatment and prescription earlier in the course of patient management, which would reduce treatment duration, increase the rate of total wound healing and therefore lower the risk of.

6.4.1.2 Future treatments

6.4.1.2.1 *Treatment of venous ulcers*

An ulcer of the leg is characterized by a chronic skin lesion that does not heal unassisted. This type of lesion can have several causes, including vascular disorders (venous, arterial or both), infections, blood diseases, cancers or inflammatory diseases. In 80%[30] of cases ulcers of the leg result from vascular disorders (venous blood reflux, obstruction creating a venous stasis*); in these cases we speak of venous ulcers.

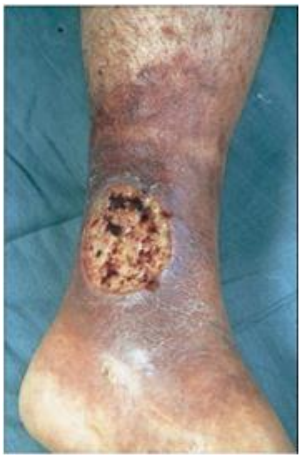


Figure 11 : Internal, sub-malleolar venous ulcers on a fibrous substratum. Source: National College of Dermatology Professors

[30] Venous leg ulcer Society of Vascular Medicine Scholars and Society of Vascular Surgery Professors, June 2010

Venous ulcers are generally characterized by their isolated presence on the patient's leg at the level of the internal malleolus, in other words the inner side of the ankle at the lower extremity of the tibia, or above it. Venous ulcers are usually very large but with little or no pain, and their shape may be round, oval of polylobate.

The appearance of the bottom of the ulcer is also variable:

- a bedsore or an adhering fibrinous layer, with a sanious* and purulent bottom if the ulcer is infected;
- red, clean and smooth granulation tissue for ulcers in the course of healing.

The zones around the ulcer are characterized by inflammation of the dermis, the epidermis and/or the hypoderm.

Depending on the study, the prevalence of venous ulcers varies from 0,1% to 0,2%[31]. The percentage of the population having had at least one venous ulcer in a lifetime has been estimated at 1%[32] [33]. Venous ulcers are a pathology that primarily affects the elderly: in a study on this pathology[34], prevalence reached 1.69% in a British sample of 50,000 subjects.

Venous ulcers are predominantly a feminine pathology, with a 1/3 ratio between men and women[35,36].

The rate of relapse is high, sometimes reaching 69%[37] after 12 mois.

Before treating the causes of venous leg ulcer, which generally involves serious surgery, and to potentially avoid surgical treatment such as skin graft, standard of care in venous ulcer includes local treatment aiming to dry up and circumscribe the wound to facilitate healing. These may involve different dressings such as polyurethane films, hydrocolloids, absorbing polymers, hydrogels and collagen dressings.

Similarities between the mechanisms of healing observed in diabetic foot ulcer and in venous leg ulcer have led ADOCIA to envision testing the BioChaperone PDGF-BB complex in a Phase III clinical trial in India for the treatment of venous leg ulcer.

6.4.1.2.2 *Bedsores*

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[31] Plébologie, 3ème édition, A.-A Ramelet, M. Perrin, P. Kern et H. Bounameaux, Ed. Masson
[32] Plébologie, 3ème édition, A.-A. Ramelet, M. Perrin, P. Kern et H. Bounameaux, Ed. Masson
[33] Dale JJ, Callam MJ, Ruckley CV, Herper DR, Berry PN. Chronic ulcers of the leg : a study of prevalence in a Scottish community. Health Bul, 1983; 41 : 310-314
[34] Margolis et al.2002 repris dans Plébologie, 3ème édition, A.-A. Ramelet, M. Perrin, P. Kern et H. Bounameaux, Ed. Masson
[35] Evans CJ, Fowkes FGR, Ruckley CV, Lee AJ, Prevalence of varicose veins and chronic venous insufficiency in men and women in the general population, Edinburgh Vein Study. J Epidemiol Community Health, 1999; 53 : 149-153
[36] Kurz X; Kahn SR, Abenhaim L, et al. Chronic venous disorders of the leg : epidemiology, outcomes, diagnosis and management : summary of an evidence-based report of the VEINES task force, Int Angiol, 1999 ; 18 : 83-102
[37] Nelson EA, Cullum N, Jones J. Venous leg ulcers, Clin Evid, 2004 : 2774-2792
[38] Labalette C. & al. Epidémiologie des escarres : résultats de l'enquête nationale de prévalence des escarres chez les patients hospitalisés « Perse 2004 » L'escarre 2007 ; 34 : 15-17

Similarities also exist between bedsores (eschars), diabetic foot ulcers and venous ulcers (localization in the lower part of the body, ulceration from a vascular cause, role of diabetes as aggravating factor, a lack of novel treatment with growth factors, serious consequences that could lead to amputation, etc). This explains why Adocia considers that wound healing of bedsores with the BioChaperone® PDGF-BB complex could be an interesting axis of development.

A bedsore is the more or less restricted destruction of a tissue resulting from its reduced vascularization. Bedsores are most often seen in bedridden and hospitalized patients, facilitated by the overall lower health status of these subjects (malnutrition, dehydration, etc.) or in a situation of prolonged compression on a limited skin surface, in particular on protrusions, i.e. the heel, sacrum, elbow, shoulder blade, etc.

The prevalence of bedsores in a French population of hospitalized patients has been estimated at 8.9%[38].

The severity of lesions involves simple skin redness, edema of varying hardness, all the way to necrosis of the skin, followed by that of underlying fat (adipose tissue) and muscles. Lesions may progress to the point of bone involvement, sometimes causing osteitis (bone inflammation). In the absence of treatment, the main risk aside from spread of the edema is superinfection that in the most extreme cases could require amputation. Treatment varies with the stage of bedsores, primarily involving local treatment and the use of dressings such as hydrocolloids to facilitate skin regeneration. In the most extreme cases a skin graft may be necessary. The parallel use of pain killers, even morphine-based products, is generally indispensable.

6.4.1.2.3 *Burns*

A burn is defined as the partial or total destruction of the skin, of tissues and even of bone. Severity depends on several parameters, in particular localization, depth, extent of the body surface, as well as the cause (heat, caustic substance or product, combustion, radiation, electrocution, extreme cold, etc.). Burns are categorized in four degrees:

- first degree burn: only the epidermis is affected;
- second degree burn: the dermis is affected and in the case of deep burns, regeneration of the dermis may not be possible because of vascular damage or the destruction of stem cells;
- third degree burn: if the burned surface is too large to heal, a skin graft becomes indispensable in light of the destruction of all skin cells; and
- fourth degree burn: muscles and/or bones are also damaged. The treatment of the most severe burns is obligatorily surgical (excision, skin graft).
    - Superficial (first degree) burns can be treated locally with ointments. In this context of local treatment, many growth factors are used in order to promote all aspects of wound healing.

In 2007 in France, 400.000 burns were reported, of which 10,000 required hospitalization. The number of third and fourth degree victims was estimated at 3,700 among whom about a thousand succumbed to their injuries[39].

[39] DHOS/O4 circular No. 2007-391 of October 29, 2007 concerning the treatment of major burn victims. Ministry of Heath

6.4.1.3 The competition

6.4.1.3.1 *Regranex®*

Regranex is a non-sterile aqueous gel supplied in multidoses tubes containing 100 µg of rhPDGF-BB per gram (0.01%), marketed (only in the USA, at the present date of this document) by SMITH & NEPHEW following the buyout of HEALTHPOINT THERAPEUTICS in November 2012. SMITH & NEPHEW launched a program, named Regranex 360, to help and assist both primary care providers and patients to use Regranex more easily. Moreover, the last publications about the safety of Regranex again that there is neither an increase in cancer risk nor any mortality increase due to cancer associated with the treatment[40].

Regranex's Marketing Authorization indication in Europe (1999) and in the United States (1997) is limited to the treatment, combined with suitable care of the lesion, of deep, chronic diabetic ulcers of exclusively neuropathic origin, non-ischemic, and whose surface is smaller than or equal to 5 cm^2. Regranex® is formulated at an acid pH and contains methyl paraben, propyl paraben and m-cresol; the presence of non-resorbable materials such as carboxymethyl cellulose may cause inflammations.

Dosage is one application per day for local treatment of the ulcer. Application and dressing are conducted by a healthcare professional. The maximum treatment period is 20 weeks and requires 3 tubes of Regranex® whose unit cost is about €350 in France. The total cost of treatment is very high in light of the cost of Regranex® and nursing costs.

On June 9, 2008, the FDA required a black box warning concerning the elevated risk of mortality from cancer if more than 3 tubes of Regranex® are used. The FDA nevertheless indicated that Regranex® did not increase the risk of cancer. The European Medicines Agency (EMA) concluded that the data did not demonstrate an effect (positive or negative) of Regranex® on the incidence of cancer or mortality from cancer. Johnson & Johnson, the proprietor of Regranex® at the time, withdrew the product from the European market in 2010. Regranex® then underwent several transfers and acquisitions and has not re-entered the European market since. As mentioned previously, the last toxicological studies show that there is no increased cancer-associated mortality risk with Regranex, even when using more than three tubes.

6.4.1.3.2 *Skin replacements*

Skin replacements are competitors of the BioChaperone® complex, even if Adocia believes that they should account for only a limited market share as a result of their high costs.

The Dermagraft® technology, already approved by the FDA, seemed to be the most advanced treatment. The product was marketed by ADVANCED BIOHEALING, bought out by SHIRE in May 2011 ($750 million), which evaluated the market share at 5%, which amounted to $ 146 million turnover.[29] in USA for 2010. However, SHIRE sold Dermagraft® to ORGANOGENESIS (the company that marketed the competitor product Apligraf®) in January 2014 for only $300 million. Consequently to this transaction, SHIRE recorded a loss of $950 million , by comparison to the purchase price three years before. Dermagraft® is still marketed by ORGANOGENESIS.

[29] Shire Press release of May 17, 2011.
[40] Miller DR et al. Pharmacoepidemiology and Drug Safety 2014

Similar products were approved by the FDA like Apligraf® (ORGANOGENESIS), GraftJacket® (WRIGHT) or Oasis Wound Matrix® (COOK BIOTECH).

The sales of skin substitutes remain lower than the initially expected, due in part to their high price and to quality assessment processes that turned out to be more complex than initially planned (which for instance lead to a product recall issue in 1999 for Dermagraft).

Product (company):	**Dermagraft® (Shire)**	**Apligraf® (Organogenesis)**	**GraftJacket@ (Wright)**	**Oasis Wound Matrix (Smith&Nephew)**
Authorized indications:	Diabetic foot ulcer (>6 weeks)	Diabetic foot ulcer and venous ulcers (>3 weeks)	Diabetic foot ulcer (>3 weeks)	Diabetic foot ulcer and venous ulcers (>4 weeks)
Types of cells:	Dermis	Epidermis and dermis	Dermis	Dermis
Origin of cells:	Human cells	Human cells	Cadaver cell s	Porcine cells
Shelf life:	6 months	2 weeks	2 years	2 years

Table 7 : Skin replacements on the market. Source: Annual reports of named companies

6.4.1.3.3 *Other cell therapies*

NUOTHERAPEUTICS (ex-CYTOMEDICS) launched Aurix® in 2013. Aurix® is an autolog graft of the own platelets of the patient to the wound. The principle is based on the secretion of growth factor by these cells, for example PDGF. In 2014, this company recast its marketing approach by recruiting a specialized team in this field.

MACROCURE launched CureXcell® on the israelian market in 2014. CureXcell is a autologous graft of activated lymphocutes aiming to decrease inflammation and promote wound healing. Macorcure forecasted a launch in USA in 2017, followed by Europe in 2018. However, the company announced in October 2015 that the US Phase 3 clinical study in patients with a diabetic foot ulcer failed to meet both its primary endpoint (complete wound closure at 16 weeks) and secondary endpoints. The company announced that it would further analyses to better understand the reasons of this failure.

Let us note that these new approaches may only be applicable to the hospital setting and are recommended for the most difficult cases already resistant to other therapies. Moreover, the route of administration is based on multiple injections.

6.4.1.3.4 *Other products under development*

In 2014, two companies announced negative results in phase III of competitive products for the treatment of diabetic foot ulcer:

- OLYMPUS was involved in wound healing with the development of Fiblast® (FGF-2 fibroblast growth factor 2; a spray of the growth factor extracted from fibroblasts) marketed in Japan by KAKEN for the following indications bed sore, burns andleg ulcer. The fibroblasts produce collagen and elastin that are localized between the cells and that are major constituents of the conjunctive tissue. However, the negative results obtained with this product in a phase III clinical study in Europe have been published in August 2014.

- SMITH & NEPHEW announced in October 2014 negative results of their product HP802-247 (acquired through the buyout of HEALTHPOINT) in a Phase III clinical study. HP802-47 is a spray of live cells to treat venous leg ulcer.

In 2015 three additional companies announced negative Phase III results of competitive products for the treatment of diabetic foot ulcer

- DERMASCIENCES, developed an angiotensin analog peptide (DSC127), involved in the arterial pressure regulation. A Phase II clinical study including 75 patients had shown equilvalent results to Regranex® to promote wound healing. The treatment protocol was to apply the product once daimy for 4 weeks. DERMASCIENCE had launched two phase III clinical studies in the USA for the treatment of diabetic foot ulcer. In November 2015, the company announced it would terminate Phase III development of DSC127 in diabetic foot ulcer following the results of an interim analysis suggesting lack of efficacy of the product.
- CYTOTOOLS developed DermaPro, a product derived from chloridric acid. Following positive Phase III results, the product was approved in India late in 2015 for use in patients with diabetic foot ulcer. The product is distributed in India by Centaur, Cytotools' partner. However, Cytotools announced in December 2015 the failure of a seoncd, larger phase III clinical study including more than 300 patients with diabetic foot ulcer in 7 countries. In those patients, DermaPro failed to demonstrate any difference with placebo (saline solution) after 12 weeks of treatment.
- MACROCURE also announced negative Phase III results of CureXCell (cf. previous paragraph 6.4.1.3.3 "Other cellular therapies").

HEALOR developed a treatment based on a peptide that modulates protein kinase C activity. A clinical study with 22 patients is completed. The treatment should be applied daily for 4 weeks.

Finally, FIRSTSTRING develops Granexin®, an analog peptide to channel connexin 43 for the treatment of venous leg ulcer, diabetic foot ulcer, and scars. This product entered a phase III clinical study in India in 2014 and showed better wound closure than compression bandages at 12 weeks to treat venous leg ulcer. In 2015, positive results from a Phase II study in 60 Indian patients with diabetic foot ulcer were also published. In 2015, the FDA approved a submission for the product to enter Phase II trial in the US. A pivotal Phase III study in patients with acute surgical wounds is planned for 2016.

6.4.2 BioChaperone® insulins for the treatment of diabetes

Adocia decided to profit from its BioChaperone® technological platform to enter the insulin therapy diabetes treatment market with new innovative insulin formulations. This market accounted for $23 billion in 2013[40].

6.4.2.1 The pathology

Diabetes is defined as an increase in the levels of blood glucose. The two major causes of diabetes are the absence of insulin secretion by pancreatic cells (type 1 diabetes) or reduced secretion of insulin in the pancreas and/or poor use of insulin by the body (type 2 diabetes). In addition, type 2 diabetes is often associated with other pathologies such as obesity, cardiovascular diseases and hypertension.

Worldwide, more than 415 million people currently suffer from diabetes. It has been forecasted that this prevalence will grow to 642 million people in 2040, an average growth of 55% globally, which reaches 65% in emerging countries [41].

[41] Diabetes International Foundation – Diabets Atlas Seventh Edition, 2015

The types of diabetes

Type 1 diabetes appears in young subjects and among all diabetics, type 1 has been estimated to affect 10% of this population[42]. The symptoms of this disease are excessive urination (polyuria) occasionally with acetone in the urine, intense thirst (polydipsia), excessive appetite (polyphagia), although the subjects lose weight, their blood glucose levels are high, greater than 1.4 g/L fasting (hyperglycemia) and excessive levels of sugar in the urine (glycosuria). Type 1 diabetes is an autoimmune disease: type 1 diabetics manufacture antibodies that attack the person's own pancreatic cells, in particular those synthesizing insulin in the islets of Langerhans*. Type 1 diabetes becomes unavoidable after the vast majority of these islets are destroyed (about 90%). The link between this autoimmune disease and a hereditary predisposition is not sufficient to explain the occurrence of type 1 diabetes: in 90% of new cases, there was no family history of type 1 diabetes and the risk of developing type 1 diabetes when one of the two parents is afflicted is less than 2 or 3%[43].

Type 2 diabetes is characterized primarily by the resistance of cells to insulin, called insulin resistance, even if the synthesis of this hormone tends to decrease in the elderly. Type 2 diabetes has been estimated to affect 90% of the diabetic population[44]. This metabolic disease prevents what is called glycoregulation (control of blood sugar levels), thereby causing diabetes. The abnormally high production of insulin by the pancreas ultimately damages the islets of Langerhans, leading to an insulin deficiency. Type 2 diabetes is considered to be asymptomatic and is often discovered after blood tests that reveal elevated blood glucose levels, i.e. hyperglycemia. Genetic predisposition is a predominant factor and overweight is an aggravating cause of type 2 diabetes.

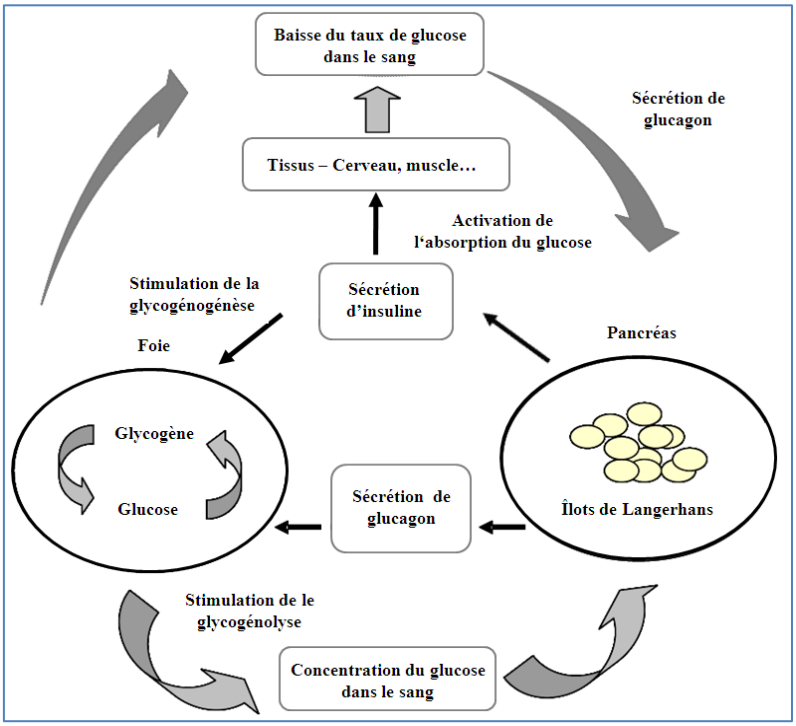

Figure 12 : Production and action of insulin. Source: Business Insights/International Diabetes Federation

[42] Business Insights - The Diabetes Market Outlook to 2016 - May 2011
[43] Diabetology Department, Prof. Altman, Georges Pompidou European Hospital (http://www.hegp.fr/diabeto/causetype1.html)
[44] Business Insights - The Diabetes Market Outlook to 2016 - May 2011

Other forms of diabetes, called secondary because they are the result of other dysfunctions or pathologies, exist but their prevalence is marginal: genetic defects involving insulin secretion, genetic defects involving insulin sensitivity, diabetes from pancreatitis or pancreatic cancer, diabetes caused by a drug or toxic substance, etc. Pregnancy may also cause diabetes, which could be a type 2 diabetes precursor if is disappears after birth.

Complications of diabetes

Cardiovascular complications are the principal cause of death of type 2 diabetes patients: cardiovascular morbidity and mortality are increased by a factor of 2 to 3 in men and by 4 to 5 in women. About 20% of cerebrovascular accidents (stroke) occur in diabetics. In the long term, diabetes can cause lesions to the heart, blood vessels, eyes, kidneys and nerves, such as [45]:

- diabetic retinopathy, an important cause of blindness resulting from the accumulation of damage to the small vessels of the retina; after 15 years, about 2% of diabetic lose their sight and about 10 % have a severe visual handicap;
- diabetic neuropathies, damage to nerves caused by diabetes; up to 50% of diabetics are afflicted. Diabetic neuropathies can cause a wide variety of problems but usual symptoms are tingling, pain, numbness or weakness of the feet and hands;
- the neuropathy, combined with poor blood flow, can increase the risk of foot ulcer that could require amputation;
- diabetes is among the principal causes of kidney failure and between 10 and 20% of diabetics die from this cause;
- diabetes increases the risk of cardiopathy and cerebrovascular accident and 50% of diabetics die from a cardiovascular disease; and
- the overall risk of death is at least twice as high in diabetics.

Treatment of diabetes with insulin

The treatment of diabetes by insulin therapy is broken down into two parts. Initially, prandial treatment (at mealtimes) of diabetes is implemented to control blood glucose after a meal, and secondly the basal treatment of diabetes in order to control continuous blood glucose due to hepatic glucogenesis. Prandial treatment involves so-called fast insulins and basal treatment is with so-called slow insulins.

Prandial treatment

In healthy subjects, a sudden increase in blood glucose is compensated by an equally abrupt increase in the endogenous insulin concentration in the blood. This maintains the blood glucose concentration between 4.4 mmol/L (0.80 g/L) and 7 mmol/L (1.4 g/L). Blood glucose control is considered ideal when the blood glucose concentration remains between these two limits.

[45] Diabetology Department, Prof. Altman, Georges Pompidou European Hospital http://www.hegp.fr/diabeto/causetype2.html)

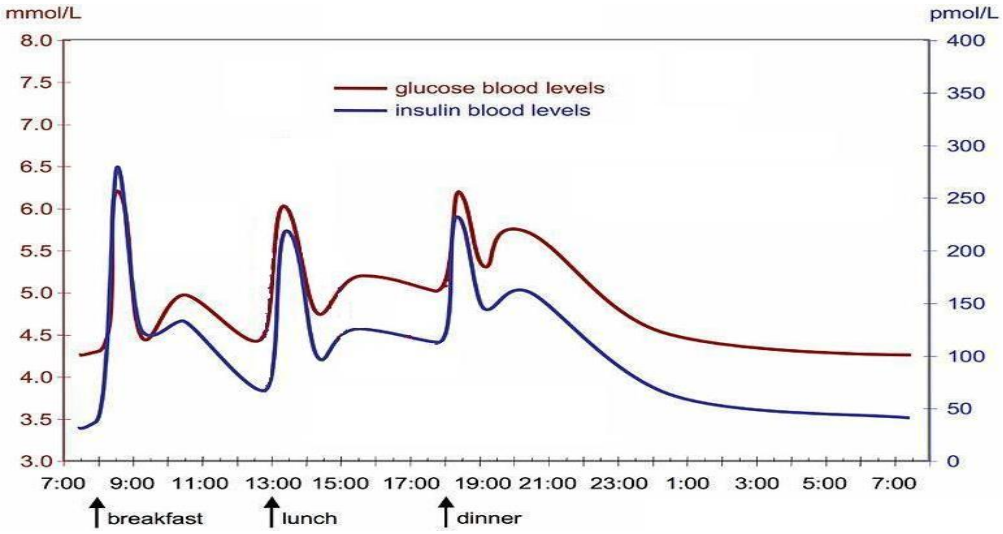

Figure 13 : Blood glucose and insulin in healthy subjects. Source: Adocia

If the glucose concentration decreases below 0.80 g/L, the subject is hypoglycemic (exposing the patient to a risk of mortality) and when it rises above 1.4 g/L, the subject is hyperglycemic.

Glucose regulation is defective in diabetic patients, so that the patient is hyperglycemic, in particular after meals. It is therefore of utmost importance to start insulin treatment in order to control blood glucose at levels as close as possible to those of healthy subjects. There are two major types of treatment available that have resulted from recombinant insulin production technology: those using human insulin and those using an analog of human insulin.

Three human insulin products are on the market: Actrapid® (Novo Nordisk), Insuman® (Sanofi-Aventis) and Humulin® (Eli Lilly). The disadvantage of human insulin treatments is that they are relatively slow acting. After the subcutaneous injection of these products, the profile of insulinmia (insulin levels in the blood) is delayed by about 30 minutes compared to healthy subjects. Diabetics therefore have to plan meals and take their injection about 30 minutes before starting the meal. In addition, human insulin treatments do not prevent hyperglycemia and hypoglycemia. These products also tend to make patients overweight and augment cardiovascular risks.

The primary sequence of insulin analogs is modified in comparison to that of human insulin. There are three fast acting insulin analogs currently on the market: NovoLog® (Novo Nordisk), Humalog® (Eli Lilly), and Apidra® (Sanofi-Aventis). Fast acting insulin analogs have the following advantages: improved post-prandial blood glucose regulation, with a reduced risk of hypoglycemia and hyperglycemia, less weight gain and enhanced patient comfort because insulin injection times and dosages are more flexible. Research on new treatments with an even shorter response time is continuing with the goal of reaching normal post-prandial blood glucose control in healthy volunteers. These new insulin treatments are called "ultra fast". The objective in terms of the pharmacokinetic profiles of insulins is shown in the following diagram.

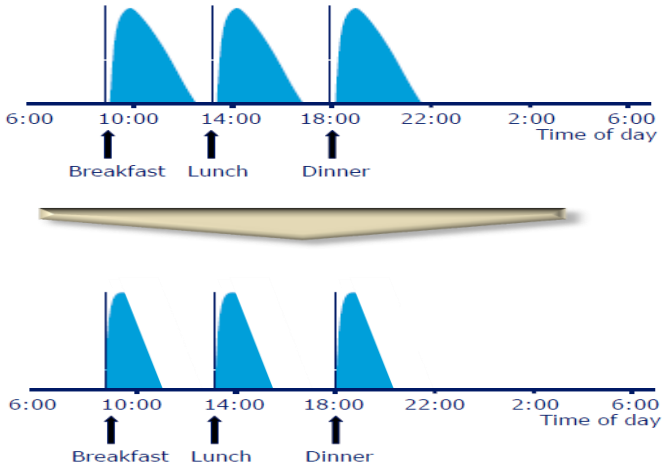

Figure 14 : Objectives in terms of pharmacokinetic profile of ultra fast insulin analogs, for better post-prandial blood glucose control. Source: Adocia

The advantage of an ultra fast insulin for patients is that is can be administered at mealtimes, rather than before. In addition, the medical advantages of analogs compared to human insulin could be increased, for example by reducing the number of hypoglycemic episodes and weight gain.

Basal treatment

In addition to prandial treatment, it is also necessary to use slow acting insulin (called basal insulin). The goal of basal insulin is to closely reproduce the cycle of endogenous insulin secretion between meals or overnight in patients who no longer produce the hormone or in whom production is abnormal. This insulin class enables sustained release of insulin between meals and therefore maintains an insulin level in the blood sufficient to control blood glucose[46].

Four long acting insulins are currently on the market to meet the need for 24-hours sustained release: Lantus® (SANOFI), Toujeo® (SANOFI), Levemir® (NOVO NORDISK) and Tresiba® (NOVO NORDISK). These four products stand out for theirability to cover the needs of patients over 24 hours. In the case of Levemir, two injections per day are most often required to cover 24 hours. In the case of Lantus®, one injection per day is sufficient in the majority of cases, which explains the success of this product with a turnover of $7.4 billion in 2014 (from SANOFI press release last 5 february 2015). Tresiba® demonstrated a longer action duration than Lantus®, which can reach 36 hours , which guarantees only one injection per day.After having been approved in Europe, Tresiba was approved in the United States in September 2015 (FDA having previously asked for resubmission with additional data showing the absence of cardio-vascular risks for insulin degludec).Toujeo, a new concentrated formulation of insulin glargine (the insulin analog used for Lantus), was approved by the FDA in February 2015. This product is concentrated at 300IU/mL,which thrice the concentration of Lantus (100 IU/mL). This increase in insulin concentration leads to a longer action profile which guarantees a 24 hours duration of action, like Tresiba®. Toujeo® was approved in Europe in april 2015.

A first biosimilar of insulin glargine (Basaglar, Lilly), was launched in 2015. It is marketed worldwide except for the US, where the commercialization was delayed by a legal action from Sanofi. In September 2015, Sanofi and Lilly settled this lawsuit, allowing the launch of Basaglar in the US in December 2016. Under this agreement, Lilly will pay royalties to Sanofi on Basaglar's US sales.

[46] Another approach consists in insulin infusion using a pump.

More recently, some companies have started developing “ultra-long-acting” insulins (once-a-week administration). Although such a presentation would significantly limit the number of basal insulin injections, the challenge lies in the ability of the companies to develop a product displaying a truly “flat” pharmacokinetic and pharmacodynamic profile, to limit the risk of acute insulin overdose and consequently of severe hypoglycemia due to the administration of a weekly dose in one setting.

- By the end of 2014, Novo announced that LAI287, a once-weekly insulin, had entered Phase I development
- In November 2015, Sanofi announced having acquired the rights for development and commercialization of a portfolio of antidiabetic treatment developed by Korean company Hanmi. This portfolio includes 1/epfeglenatide, an agonist to GLP1 receptors (GLP1-RA) in late stage development, with a long duration of action 2/a once weekly insulin (LAPS-insulin) and 3/a fixed dose combination of GLP1-RA and insulin to be administered once weekly. Hanmi received an upfront payment of €400 million. Hanmi is also eligible to up to €3.5 bn in development and commercialization milestones, as well as double-digit royalties on net sales of the products covered by the agreement.

Premixed insulins and Combos

In the aim to simplify the treatment, some products have been developed to cover the need of prandial and basal insulin simultaneously with one product. This is the case of premixed insulin products (“Premix”) that contain a soluble fraction of insulin, the rapid-acting fraction, and a cristallized fraction, the long-acting fraction. These products have the advantage to decrease the number of products to use, one instead of two, and to reduce the number of injections, two instead of three or four for a basal/bolus therapy.

The commercialized premixed insulins (NOVO NORDISK and ELI LILLY) incorporate a mix of rapid-acting insulin, human or analog, with protamine (a higly cationic protein) in different proportions. Protamine induces the coarcevation of some insulin molecules, which leads to formation of microcrystals that remain injectable. After the injection, the free fraction of insulin (non crystalized) has a fast profile of action whereas the precipitated fraction of microcrystals dissolves slowly in the subcutaneous medium, which accounts forthe slow action profile. Moreover, the two differents action profiles are modulated among the proportion of protamine. However, the cristalized fraction of currently marketed premixed insulins does not allow to answer the need for basal treatment up to 24 hours. Consequently, patients need to inject twice daily to cover their insulin needs until the next morning. Finally, it should be noted that this partial coacervation approach of insulin, be it human or analog, has a major drawback in terms of patient safety. Indeed, the formation of microcrystals can lead to partial sedimentation or needle clotting (needle used for insulinotherapy are very fine) and consequently to the delivery of an inappropriate dose (risk of hyper/hypoglycemia).

Furthermore, the pharmacokinetic profile of premixed insulin (cf. upper panel, below) is not optimal as it remains too far from the physiological profile. This makes premixed insulin a lees favorable solution in terms of medical benefits. The two main drawbacks are a slower prandial action and a relatively short basal action. Consequently, a patient treated with premix is innapropriately exposed to high quantities of insulin which leads to more frequent hypoglycemia events and a higher weight gain. .

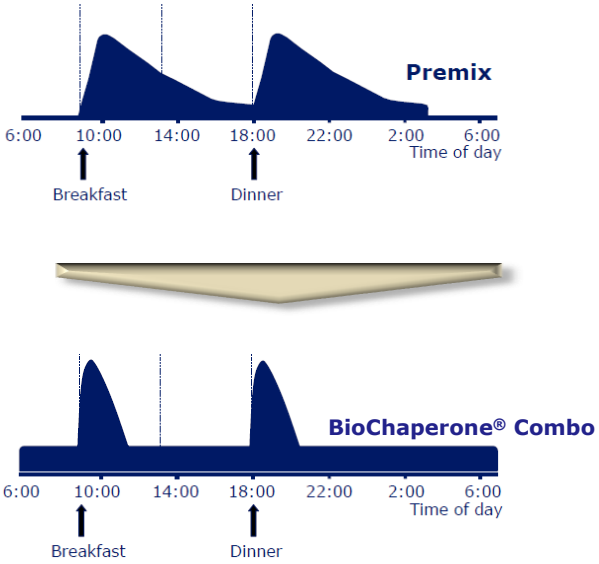

Figure 15 : Pharmacokinetic Goals for insulin combo about

There is a real need for a treatment that combines a prandial and a basal insulin in the same solution wih a pharmacokinetic profile closer to the one shown in the lower panel of the figure above. This combination of insulins, called a “combo”, could allow to limit the number of injections to one or two daily whileoffering an optimal insulinotherapy treatment, since its effect would be closer to the endogenous physiologic profile.

This approach has been validated by NOVO NORDISK, which developed a combination of the basal insulin degludec (Tresiba®) with prandial insulin aspart (NovoRapid®). This product, named Ryzodeg®, as Tresiba®, was approved in a large number of countries before getting approved in the USA in 2015 following positive results of an additional cardiovascular safety study asked by the FDA. This combo of basal and prandial insulins offers better control of blood glucose and reduces the hypoglycemia events by comparison to the premix, as shown in clinical studies.

There would be a substantial benfit in providing a combinaition of insulins based on insulin glargine as basal insulin as it has been used for 15 years and has a proven safety track-record. However, the chemical properties of insulin glargine forbids it to be mixed with prandial analogs. Indeed, as soon as insulin glagine is mixed with other insulins, it precipitates. For this reason, it is clearly specified on the posology data sheet that Lantus® must not be mixed with other insulins.

Thanks to BioChaperone®, the solubility profile of insulin glargine can be modified, which permits to mix glargine with all other prandial insulin analogs at a neutral pH. ADOCIA develops BioChaperone® Combo, a combination of insulin glargine and insulin lispro, one of the gold-standard prandial analog insulin. This combination has been tested in clinical studies by comparison to others premixed insulin analogs and have shown a faster and a longer action profile.

On the long term, combos of prandial and basal insulin analogs should replace premixed insulins like NovoMix® and Humalog Mix® as treatment options.

Epidemiology

Diabetes is a chronic disease affecting millions of people all over the world that will increase in emerging nations in the years to come. The International Diabetes Federation[48] has estimated that between 2015 and 2040, the number of diabetic patients in the world will increase by almost 55% (in the 20 to 79 year-old population), from 415 million people today to 642 million. The increases in Europe (+19%) and North America (+37%) are predicted to be lower than the global average, but emerging nations will without doubt have to face an explosion in the prevalence of diabetes (141% in Africa, 79% in Southeast Asia and +104% in the Eastern Mediterranean and Middle East…).

Geographic zones	Prevalence in 2013	Prevalence in 2035	Rate of increase
Africa	14.2 million	34.2 million	+141%
Eastern Mediterranean and Middle East	35 million	72.1 million	+ 104%
Europe	59.8 million	71.1 million	+19%
North America	44.37 million	60.5 million	+37%
Central and South America	29.6 million	48.8 million	+65%
Southeast Asia	78 million	140 million	+79%
Asia-Pacific	153 million	215 million	+41%

Table 8 : Estimations of increases in the number of diabetics in the 20 to 79 year-old population in the world. Source: International Diabetes Federation, 2013

This phenomenon will increase the number of diabetics in the same population. By 2035, the percentage of the diabetic population in all regions except Europe and Africa is expected to exceed 8% (Source: International Diabetes Federation, 2013).

[48] Diabetes Atlas 7th edition (2015), International Diabetes Federation

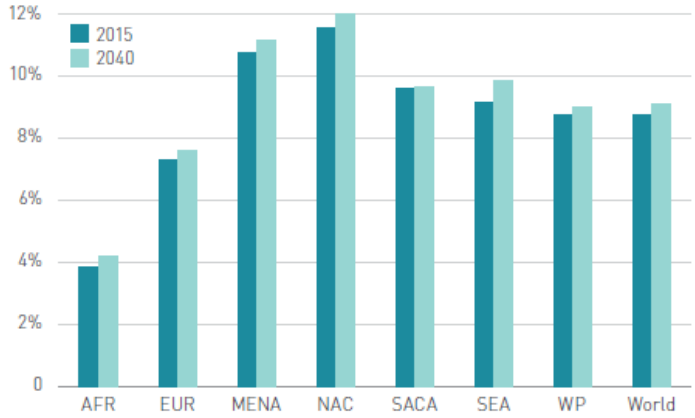

Figure 16 : Prevalence of diabetes (in percentage) per region, in the 20 to 79 year-old population in 2015 and predictions for 2040. Source: International Diabetes Federation. AFR: Africa, EUR: Europe, MENA: Middle East and North Africa; NAC: North America and the Caribbean; SACA: South America/Central America; SEA: Southeast Asia, AP: Asia-Pacific; WP: West Pacific

The 2007-2010 ENTRED study[49] provided a qualitative picture of the diabetic population in metropolitan France. The most common form of diabetes is type 2 and concerns 2.2 million patients, i.e. 92% of the total number of diabetics estimated at 2.4 million. The treatment of type 2 diabetes is of long duration because the average time a patient has had the pathology is 11 years. This duration of treatment is even longer, 17 years, for type 1 diabetes patients. Type 2 diabetes is a pathology of the elderly with a mean age of 66 years and one quarter of the diabetic population (type 2) is older than 75. Type 1 diabetes affects a younger population whose men age is 42 years. The sex distribution of diabetes is practically equal for men (54%) and women (46%).

6.4.2.2 The market

According to Novo Nordisk*, the world market for the insulin treatment of diabetes increased by 13.9% between 2003 and 2013, accounting for more than $23.5 billion, i.e. close to 50% of the total market for antidiabetic drugs. The domination of insulin over other drug classes is explained simply by the fact that insulin is the only way to control blood glucose in type 1 diabetic patients and that the use of insulin will ultimately become as unavoidable as for type 2 diabetic patients.

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[49] The goal of the 2007-2010 ENTRED study (French acronym of "National representative control study of diabetics") was to extend knowledge on the heath status of diabetics in France. This study was sponsored by the "Institut de veille sanitaire"/Health Watch Institute, that financed the study in partnership with National Health Insurance, the National Institute for Prevention and Health Education, and the National Health Authority.

* Novo Nordisk, presentation at the Handelsbanken Large Cap Seminar Stockholm, September 2013

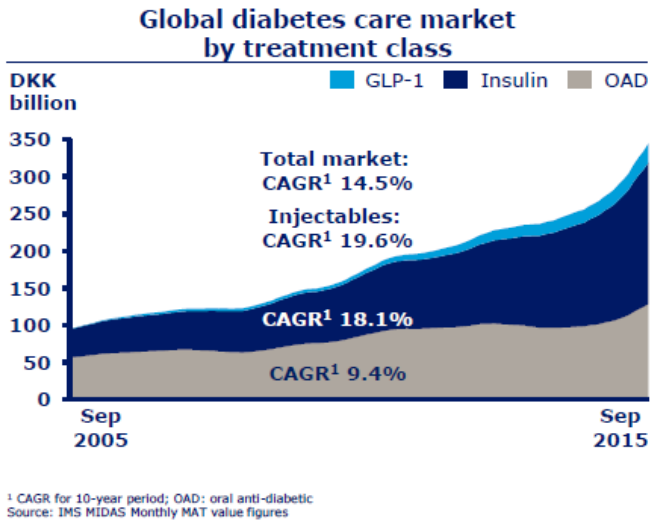


Figure 17 : Global diabetes market per therapeutic class and changes between 2004 and 2015 (Source: Novo Nordisk, Capital Markets Day 2015)

Segmentation of the insulin market is conditioned by the time before onset, and duration of action of insulin. In this context, the appearance of human insulin analogs for basal treatment of the disease has transformed the insulin market that is now dominated by Lantus® (Sanofi Aventis), on the market since the early 2000s. This product alone accounts for 30% of the market with sales of more than $7.2 billion in 2014. The sales of its competitor Levemir® (Novo Nordisk) were more than $2.3 billion in 2014.

The segment of fast acting insulins (prandial treatment) is dominated by human insulin analogs, in spite of the higher cost compared to human insulin, whose post-injection time of action is between 20 and 30 minutes. The two flagship products are NovoLog® (Novo Nordisk) with sales of $3.2 billion in 2014) and Humalog® (Eli Lilly) with sales of $1.9 billion. Eli Lilly with Humulin® dominates the medium term action insulins segment with sales of more than 1 billion of dollars 2014. Finally, sales in the premix segment were more than $5 billion in 2014 and close to $1.8 billion for NovoMix® from Nordisk.

	Prandial Treatment (Fast Acting) Maintain post-meal blood glucose control	**Basal treatment (Long Acting)** Maintain blood-glucose control throughout the day	**Basal-Prandial treatment (intermediate-acting and/or premixed insulin)** Injection unique pour une action prandiale et basale
Novo Nordisk	NovoLog® (3,2 Mds USD)/ (out of patent 2014) Novolin® N& R ($1.8 B USD)	Levemir® ($2,3 B) Tresiba® (Approved in Europe/Japan in 2012 ; in the US in 2015)out of patent 2024	Novomix® ($1,8 B) Novolin Mix
Eli Lilly	Humalog® ($1,9 B / out of patent 2013) Humulin ($1 B)	/	Humalogmix ($0.9 B) Humulin NPH
Sanofi	Apidra ($0.4 B out of patent 2017) Insuman ($0.2 B)	Lantus ($7.2 B out of patent 2015)	Insuman NPH

Table 9 : Overoew of the 2014 insulin market. Source : Companies annual reports, ADOCIA's estimates.

As the first insulin analogs patent fall into the public domain, the insulin market should be impacted on the long term; on the one hand by the entry of biosimilars (such as Lilly's insulin glargine,

Abasaglar®/Basaglar®, which should enter the insulin market in December 2016) and on the other hand by the entry of new products showing better performance. Furthermore, the growing diabetes epidemics may compel healthcare systems, including in the US, to put higher pressure on prices. For instance, Sanofi announced a decrease of Lantus sales of 19.5% for the third quarter 2015, which was mainly attributed to higher rebate deals made with public health management companies, which are responsible for buying medicines in the US.

This $22 billion market nonetheless continues to grow.

6.4.2.3 Adocia's strategy, which consists in developing innovative products at a competitive cost seems to fit market evolution. Clinical trials conducted by Adocia

6.4.2.3.1 *Hinsbet® human insulin (acronym for Human insulin is Better)*

A pre-clinical study on pigs (the most widely used animal model for studies of insulin pharmacokinetics and pharmacodynamics*) sponsored by Adocia showed that HinsBet® reduces the time to onset of action of human insulin.

A phase I trial also sponsored by Adocia was carried out by the German contract research organization (CRO) I.K.F.E (refer to section 6.6.3.2 Controlling subcontracted clinical trials) in November and December 2010; the final trial report was published in April 2011. The double-blind randomized crossover study included 12 healthy male volunteers and its general objectives were to establish treatment safety because this was the first exposure of humans to this formulation, and to determine the pharmacodynamic and pharmacokinetic profiles of HinsBet® in comparison to NovoLog® (fast insulin analog produced by Novo Nordisk) and to Actrapid® (human fast insulin produced by Novo Nordisk).

Three consecutive glucose clamp technique cycles* were run: this method involves the injection of glucose via infusion to maintain the patient's blood glucose constant to compensate the hypoglycemia caused by an insulin injection. Each subject received the equivalent of 12 IU* of insulin and was monitored for 6 hours during which the glucose level was held constant by the infusion of glucose to compensate for the drop in levels of insulin injected.

The principal objective of the trial was determining the time required to reach the maximum of infused glucose, called glucose infusion rate (GIR-Tmax). The secondary objectives of the trial were to determine the maximum infused glucose (GIRmax), the time to reach half-GIRmax (GIR-T50), the maximum blood insulin concentration (INSmax), the time required to reach the maximum and half-maximum of the plasma insulin concentration (INS-Tmax and INS-T50) and finally the number and type of adverse effects.

The results were very promising. First, all HinsBet® injections were well accepted and no adverse effect was reported. In addition, changes in the GIR showed that the response time of HinsBet® was similar to that of NovoLog® (insulin analog) and that HinsBet® produced its effect (decreased blood glucose) 20 minutes earlier than Actrapid® (human insulin).

Results of the phase IIa trial on 20 type 1 diabetics (Germany): HinsBet® (BioChaperone® human insulin) compared to a fast acting analog, NovoLog®

After the phase I results were obtained, Adocia decided to continue the clinical development of HinsBet® by conducting a phase II clinical trial in type 1 diabetics.

The double blind, randomized, cross-over trial was conducted in one center on 20 type 1 diabetics using the glucose clamp technique. The aim of the trial was to compare the pharmacokinetic profiles,

pharmacodynamic profiles and safety of HinsBet® compared to NovoRapid®, a fast insulin analog, after three consecutive injections of each product to each patient.

The results showed the hypoglycemiant effect of the optimized HinsBet® formulation is just as rapid as that of NovoRapid® (insulin aspart, one of the modern fast insulins). In addition, in the course of the trial no adverse effect and no modification of clinical parameters were found. The local safety of HinsBet® was judged to be very good and comparable to that of NovoRapid®. Finally, repeated administration as three consecutive injections of HinsBet® revealed intra- and inter-individual variabilities of pharmacological parameters similar to those of NovoRapid®.

New optimized formulation of HinsBet®: results of the phase IIa clinical trial

Based on the phase I clinical results from the first formulation and on the promising preclinical results of the new formulation, ADOCIA launched in july 2014 a phase IIa clinical study based on the "second generation" formulation of HinsBet®.

The phase IIa clinical study compared the pharmacokineticand pharmacodynamics profiles of HinsBet®, Humalog® (insulin analog lispro) and Humulin® (Human insulin) with 36 type I diabetic patients. The first results of this study were published last February 2015.

In this double-blind, cross-over study, the pharmacokinetic and pharmacodynamic profiles of Hinsbet® were compared with Humulin® and Humalog®. 36 type I diabetic patients received a single dose of 0.2 U/ kg of HinsBet®, Humulin® or Humalog® under euglycemic clamp (ClampArt®, blood glucose target of 100 mg/dL, clamp duration of 10h after infusion). The three formulations were well tolerated and did not induce any local reaction. The results showed that HinsBet® was significantly faster than human insulin in type I diabetic patients: Onset of action 70% earlier and a doubled metabolic effect. This formulation of human insulin, HinsBet® was similar to Humalog® during the first hour, which is the critical part for post-meal glycemic control.

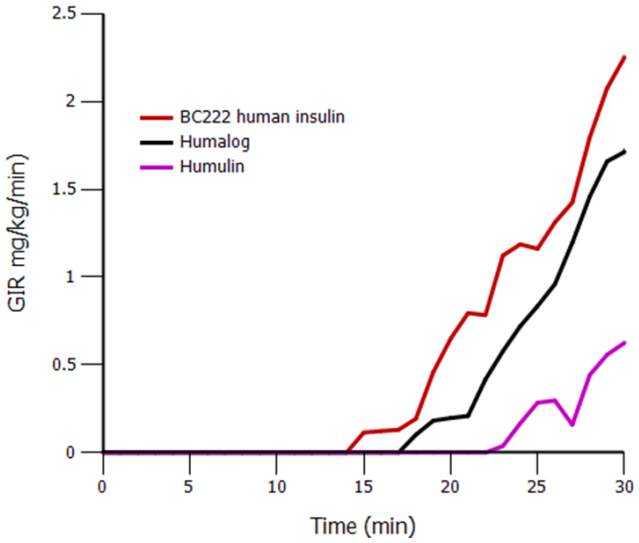


Figure 18 : Profils pharmacodynamiques de la nouvelle formulation d'HinsBet (courbe rouge), d'Humalog (courbe noire) et d'Humulin (courbe violette) obtenus chez 36 patients diabétiques de type 1.

Based on these results, ADOCIA will pursue the development of HinsBet® U100. ADOCIA has also decided to develop a concentrated formulation of HinsBet® at 500 UI/ml. Such a concentrated formulation could allow to answer to the needs of a growing population of highly insulinoresistant patients who need daily insulin doses more than two to three times higher than the standard doses.

Today, the main treatment option for these patients is Humulin® U500 (ELI LILLY), a human insulin formulation at 500 UI/ml, 5 times more concentrated than the standard products. This product generates growing income in USA that are estimated to be over $300 million (from *Symphony Health*).

Although Humulin® 500 helps reducing the injection volume of total daily insulin, its action is slower than the formulation concentrated at U100 and consequently induces an unmet need of a concentrated human insulin with a faster action profile, at least similar to the U100 UI/ml formulation.

ADOCIA pursues a double strategy consisting in developing:

- HinsBet® U100 for emerging countries where the cost of treatment is ta major preoccupation, and consequently take advantafe of thecheaper cost of human insulin manufacturing compared to insulin analogs. ADOCIA plans to launch a phase II clinical study in Europe in Q1 2016 in order to demonstrate the medical benefit of this insulin.
- HinsBet® U500 in the USA and in Europe, where the share of severely insulinoresistant patients is growing. ADOCIA plans to launch a phase II clinical study in Europe in Q4 2016 for this product.

6.4.2.3.2 *BioChaperone Lispro U100, ultra fact insulin*

The signing of a first partnership with ELI LILLY and the launch of a phase I clinical study

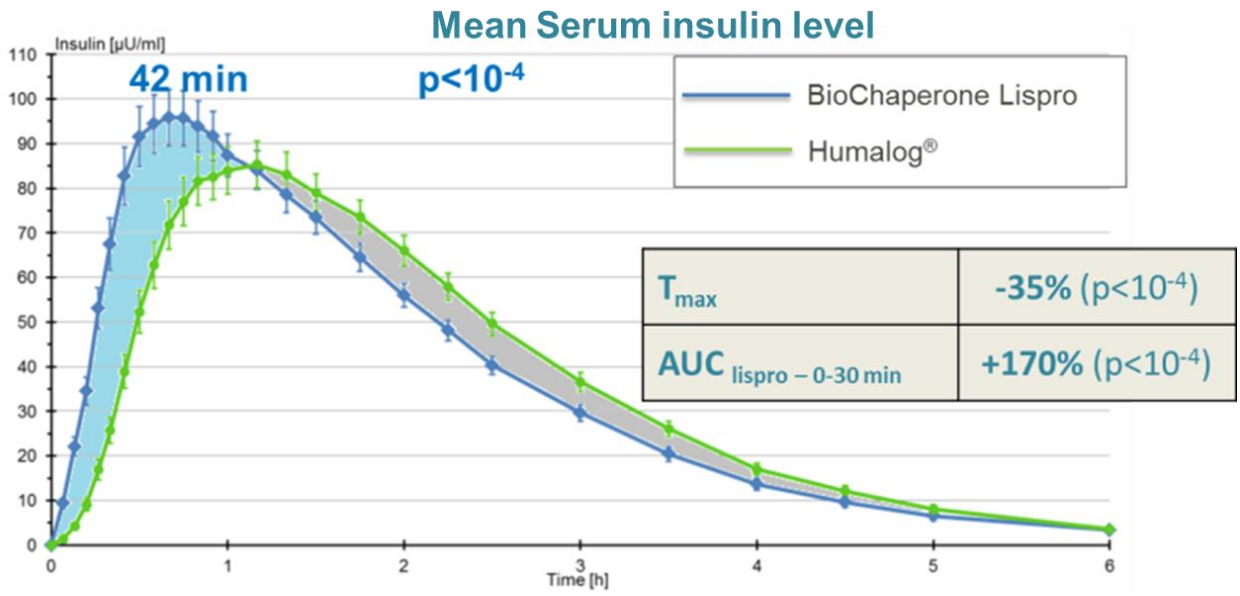
In December 2011, based on the positive preclinical results, ADOCIA signed a licence and collaboration agreement with the pharmaceutical group ELI LILLY. Under the terms of this agreement, ADOCIA agreed to grant ELI LILLY the exclusive worldwide rights of BioChaperone® polymers for the development, the manufacturing and the marketing of BioChaperone® Humalog®. This agreement covered all the potential indications of BioChaperone® Humalog®. ELI LILLY paid for the development, including clinical studies, of BioChaperone® Humalog®. ADOCIA and ELI LILLY managed the collaboration through a conjoint steering committee.

In July 2013, the company ELI LILLY announced in a press release the end of the partnership by mutual agreement.

Clinical results obtained by ADOCIA after the termination of the first partnership with ELI LILLY

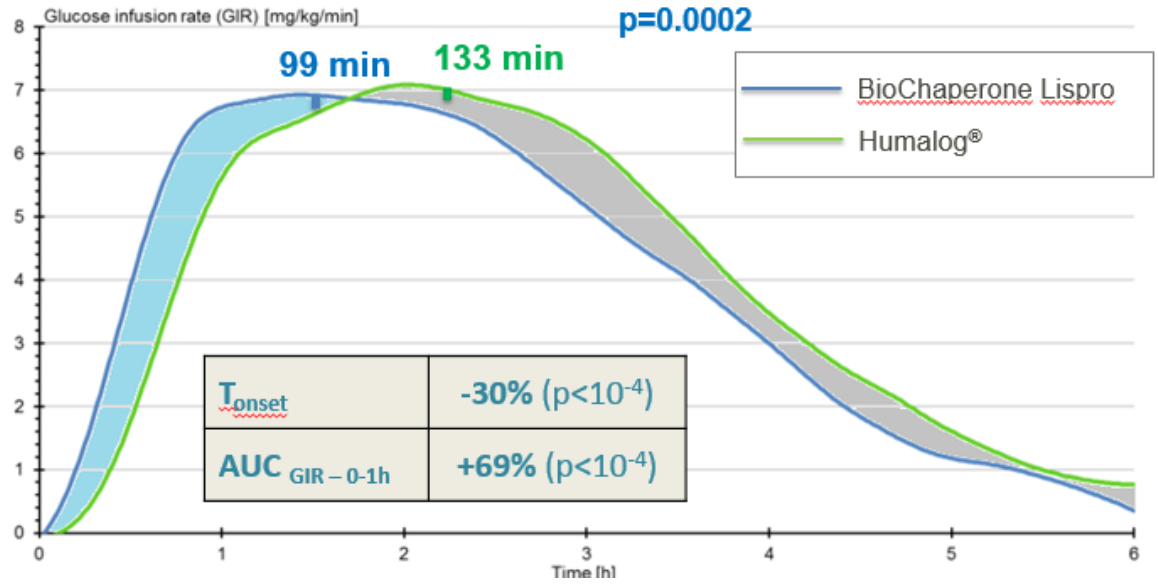
Phase IIa clinical results – First pharmacokinetic and pharmacodynamic study with type I diabetic patients.

Conforted by the promising phase I results, previously obtained during the partnership with ELI LILLY, ADOCIA launched in January 2014 a phase IIa clinical study with 36 type I diabetic patients. The goal of this study was to compare the pharmacokinetic and pharmcodynamic profile of BioChaperone® Lispro to Humalog®. On April 9th 2014, ADOCIA announced the results of this study: BioChaperone® Lispro acted significatively faster than Humalog® in type I diabetic patients (Onset of action 30% faster and early metabolic effect increased by 69%).



Graph 18 :Pharmacokinetic profile of BioChaperone® Lispro U100 (blue) and Humalog® (Green) obtained with 36 type diabetic patients.

Insulin lispro reached its peak concentration 35% faster with BioChaperone®, and the insulin quantity in the blood during the first 30 minutes is 170% greater when formulated with Biohaperone® compared to Humalog formulation.

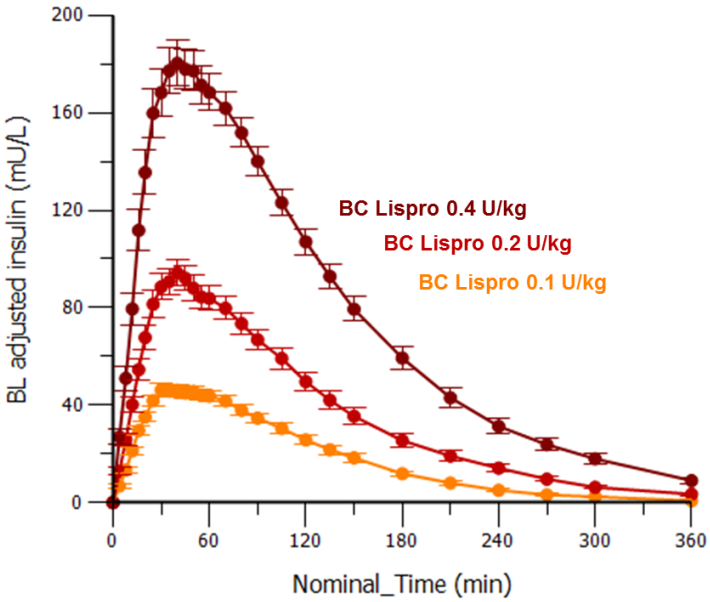


Graph 19 :Pharmacodynamic profile of BioChaperone® Lispro U100 (Blue) and Humalog (Green) obtained with 36 type diabetic patients.

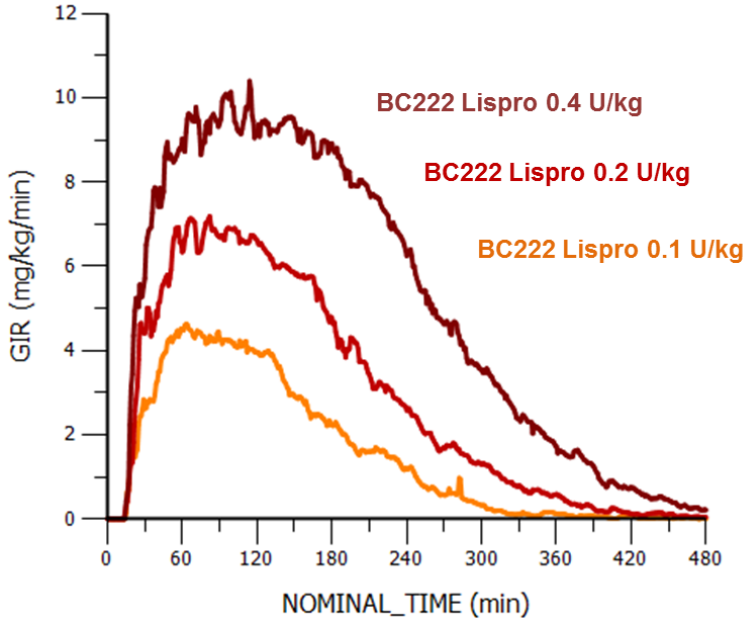
Insulin lispro onset of action is 30% earlier and activity during the first hour post-injection is 69% greater when insulin lispro is formulated withBioChaperone® compared to Humalog formulation. .

Phase IIa clinical results – Second pharmacokinetic and pharmacodynamic study, dose-response, in type I diabetic patients.

Following the positive results obtained in Phase IIa, ADOCIA actively pursued the product development and initiated, as soon as May 2014 a second Phase IIa clinical study in type 1 diabetes patients. This study aimed to evaluate the linearity of the effect of BioChaperone Lispro U100 at different doses in a range that would cover most patients' needs. Positive results from this study were announced in September 2014.



Graph 20 :Pharmacokinetic profiles of BioChaperone® Lispro U100 at 3 differents doses (0.1 ; 0.2 ; 0.4 IU/kg) obtained in 37 type I diabetic patients.



Graph 21 : Pharmacodynamic profiles of BioChaperone® Lispro U100 at 3 differents doses (01.; 0.2; 0.4 IU/kg) obtained in 37 type I diabetic patients.

Across an usual dose range of prandial insulin, BioChaperone® Lispro retains an ultra-fast absorbtion profile, as it was demonstrated at the pharmacokinetic and pharmacodynamic level. Moreover, the pharmacokinetic effect is linear on the all doses tested (normalization test).

Second partnership agreement with Eli Lilly

These results convinced ELI LILLY to start a new collaboration with AOCIA. On December 19th 2014, ADOCIA and ELI LILLY announced a global licence agreement on the development of an ultra-fast insulin , BioChaperone® Lispro. The agreement covers the development of a formulation of BioChaperone® Lispro at the standard concentration U100 and a more concentrated formulation, most probably at 200 IU, BioChaperone® U200.

Launch of 5 Phase 1b clinical trials with Eli Lilly in 2015 – 3 completed studies

Phase 1b clinical results – Study on the post-prandial effect of BioChaperone Lispro U100 in type 1 diabetic patients after a standardized meal.

ADOCIA and LILLY jointly announced in January 2015 that ADOCIA would initate a first clinical study under the partnership. This Phase Ib/IIa trial aimed to evaluate the improvement in post-prandial glycemic control obtained with BioChaperone Lispro compared to Humalog in type 1 diabetic patients, after a standardized meal. Results from this study were jointly announced in June 2015. They showed a 61% reduction of post-prandial 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 and early exposure increased by 168% at the same dose for BioChaperone Lispro compared to Humalog.

Phase 1b clinical results – Pilot study evaluating the potential for bioequivalence of BioChaperone Lispro U200 formulation compared to BioChaperone Lispro U100, based on their pharmacokinetic and pharmacodynamics profiles in healthy volunteers.

Cf. following section – BioChaperone Lispro U200, ultra-rapid concentrated insulin

Initiation and positive topline results from a Phase 1b clinical study: Repeated administration of BioChaperone Lispro U100 in type 1 diabetes patients.

In August 2015, ADOCIA and LILLY jointly announced the initiation of a Phase Ib clinical trial comparing the effects of daily administration of BioChaperone Lispro and Humalog at every meal, either before the meal or 15 minutes after the meal, over a period of two weeks, on post-prandial glycemic control in type 1 diabetes patients. Results are expected in 2016.Results from this study, announced on March 14th 2016, showed (i) At the beginning of each 14-day treatment period, BioChaperone Lispro U100 demonstrated a statistically significant 31 percent reduction in blood glucose excursion over the first two hours compared to Humalog injected at the time of a solid meal and (ii) After 14 days of treatment, a statistically significant 42 percent reduction in blood glucose excursion over the first two hours was observed with BioChaperone Lispro U100 over Humalog, when the treatments were injected at mealtime.

Initiation of a Phase 1b clinical study: Repeated administration of BioChaperone Lispro U100 in type 2 diabetes patients.

In September 2015, ADOCIA and LILLY jointly announced the initiation of a Phase Ib clinical trial comparing the effects of daily administration of BioChaperone Lispro and Humalog at every meal, immediately before the meal, over a period of two weeks, on post-prandial glycemic control in type 2 diabetes patients. Results are expected in 2016.

Initiation of a Phase 1b clinical study: Evaluation of BioChaperone Lispro U100 in type 1 diabetes patients using an insulin pump.

In October 2015, ADOCIA and LILLY jointly announced the initiation of a Phase Ib clinical study comparing the effects of BioChaperone Lispro and Humalog on post-prandial glycemic control in type 1 diabetes patients using insulin pumps, over a period of two weeks. Results are expected in 2016.

6.4.2.3.3 *BioChaperone® Lispro U200, ultra fast concentrated insulin*

In June 2014, ADOCIA announced the development of BioChaperone 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® at 100 UI / ml. This ultra-fast action is similar to the profile obtained with BioChaperone® Lispro U100 in the same model.

Such a concentrated formulation of BioChaperone® Lispro is covered in the agreement signed with Eli Lilly on December 19th 2014. The development planned in this partnership includes a concentrated formulation BioChaperone® Lispro U200, concentrated at 200 UI/ml. The first preclinical results demonstrated that the formulation BioChaperone® Lispro U200 could be bioequivalent to BioChaperone Lispro U100 (Figure 23).

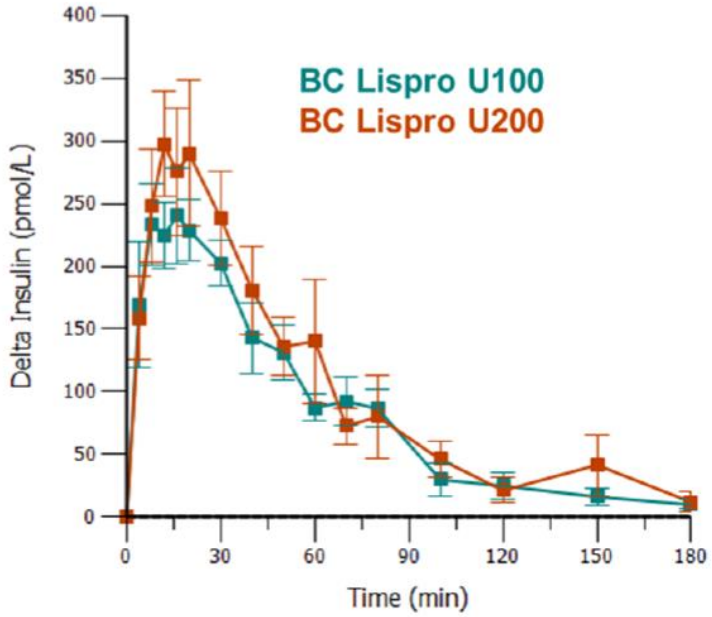


Figure 22 :Pharmacokinetic profiles of BioChaperone® Lsipro U200 (red) and BioChaperone® Lispro U100 (green) at 0.125 IU/kg obtained in a pig model.

Following the agreement with Eli Lilly, Adocia and Eli Lilly decided to develop a foamulation at 200 IU/mL, since Eli Lilly commercializes a 200 IU formulation of Humaloh, Humalog U200. In a first preclinical study, AODCIA showed that the BioChaperone technology could improve the performance of prandial insulin analogs at high concentration. To our knowledge, BioChaperone Lispro U200 is the first concentrated prandial insulin to display an ultra-rapid profile.

Phase 1 b clinical results: Study evaluating the potential for bioequivalence of BioChaperone Lispro U200 formulation compared to BioChaperone Lispro U100, based on their pharmacokinetic and pharmacodynamics profiles in healthy volunteers.

ADOCIA announced in August 2015 the initiation of a Phase IB clinical trial comparing the pharmacokinetic and pharmacodynamics profiles of BioChaperone Lispro U200, a formulation twice as concentrated of BioChaperone Lispro, to those of BioChaperone Lispro U100. This pilot study aimed to demonstrate the potential for bioequivalence between the products. In December 2015, Lilly and Adocia jointly announced that BioChaperone Lispro U200 had met all the study's predefined criteria (two standard bioequivalence parameters C_{max} and $AUC_{lispro(0\text{-}infini)}$,; and two parameters supporting ultra-rapid properties $AUC_{lispro\ (0\text{-}1h)}$ and early $t_{50\%\ Cmax\ lispro}$). These positive feasibility result support the development of BioChaperone Lispro U200 based on demonstration of bioequivalence.

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

6.4.2.3.4 *Combination of prandial insulin and basal insulin*

BioChaperone® technology allows to solubilise insulin glargine at neutral pH, which makes it compatible with any prandial insulin, includingrapid-acting analogs (Apidra®, Humalog® and NovoLog®). Based on these *in vitro* results, ADOCIA decided to develop the combination of insulin glargine insulin and insulin lispro, two gold standard products in diabetes treatment. A first precilinical proof of concept was done by showing the complete solubility of both insulin at the same pH with good stability. The pharmacokinetic and pharmacodynamic profiles did not show any substantial modification of the rapidity of the rapid-acting analog (lispro) by the addition of insulin glargine and BioChaperone, and the duration of action of insulin glargine was alsopreserved. The onset of action of prandial insulin and the duration of action of basal insulin are the main targeted criteria to improve theperformance of a combo product, compared to premixed insulin.

Phase I/IIa clinical results – First pharmacokinetic and pharmacodynamics clinical study in patients with type I diabetes

Based on positive preclinical results, ADOCIA initiated a phase I/II clinical in twenty patients with type I diabetes in November 2013. This study aimed to show that this combination may offer diabetic patients a better blood glucose control than the premixed insulins like Humalog Mix® based on insulin lispro (Eli Lilly) or Novomix® based on insulin aspart (Novo Nordisk). With this objective, the pharmacodynamics and pharmacokinetics profiles of the combination BioChaperone glargine lispro were compared to thos ofHumalogMix, in a cross-over study in 20 type I diabetic patients under euglycemic clamp.

The preliminary results of this study were announced in February 2014 and the complete results were announced in March 2014:

- The onset of action of BioChaperone Combo is at least 30% faster than that of Humalog Mix.
- The duration of action observed for BioChaperone Combo is superior to 30 hours in the majority of patients whereas it was 18 hours with Humalog Mix.
- BioChaperone Combo formulation is well tolelrated, similar to Humalog Mix®.

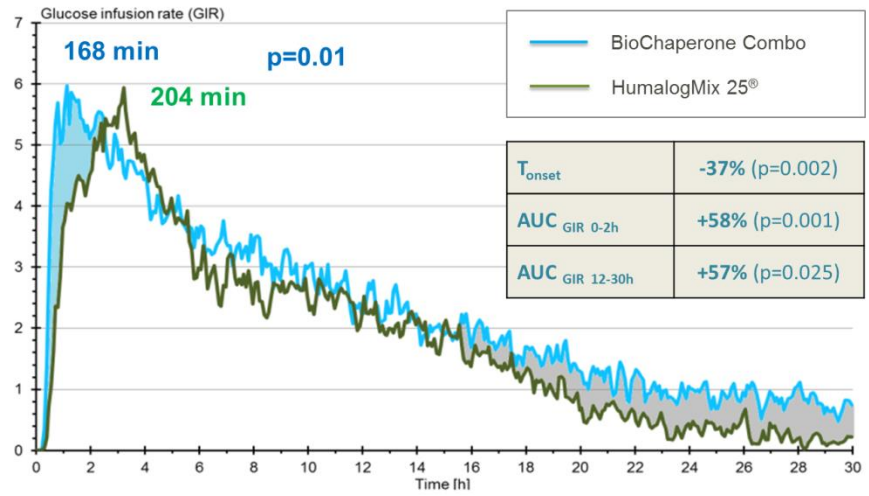


Figure 24 : Pharmacodynamic profile of BioChaperone Combo (blue) and HumalogMix (green) in 20 type I diabetic patients.

The insulin effect is 37% faster and 58% higher during the first two hours for BioChaperone Combo compared to Humalog Mix. It also lasts for 12h additional hours compared to HumalogMix, and prolonged until 30h (which is comparable to what is observer with insulin gGlargine alone).

Glycemic control up to 30 hours was confirmed by glycemic measurements. In a euglycemic clamp protocol in type diabetic I patient, the glycemia is maintained around 100 mg/dL as long as some insulin remains active in the blood. In the premixed insulin case, glycemia was no longer controlled after 18 hours.

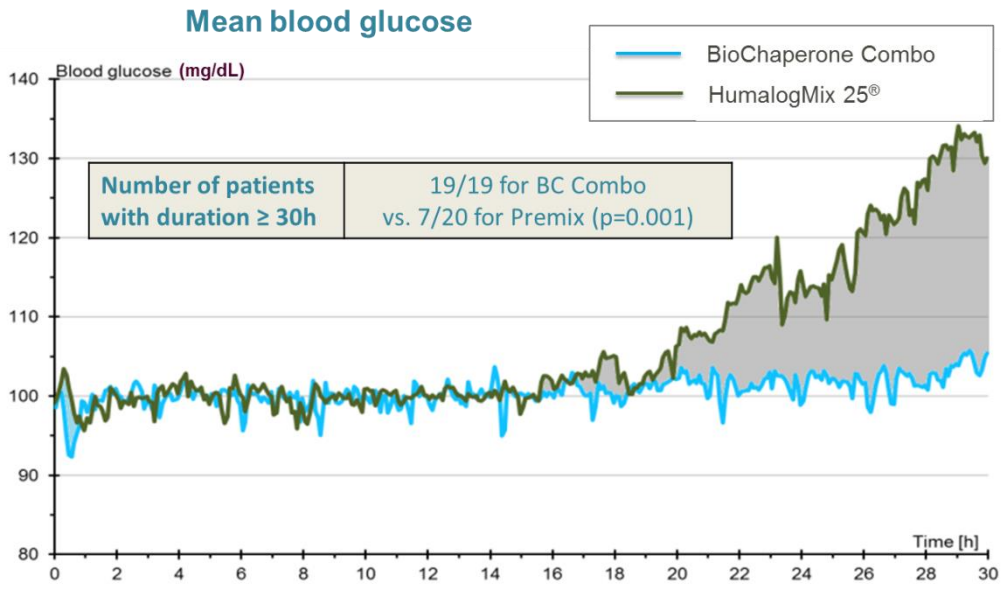


Figure 25: Glycemic profiles of BioChaperone Combo (blue line) and Humalog Mix (green line) observed in 20 type 1 diabetic patients.

In July 2015, Adocia announced the initiation of two Phase Ib clinical trials evaluating BioChaperone Combo:

- The first Phase Ib clinical trial aimed to evaluate the improvement of postprandial glycemic control in type 1 diabetes patients after one injection of BioChaperone Combo at meal time, compared to one injection of Hulmalog® Mix75/25 at mealtime

- The second Phase Ib clinical trial in type 2 diabetes patients aimed to compare the pharmacokinetic and pharmacodynamics profiles of BioChaperone Combo to those of Humalog® Mix75/25 and to the separate injection of Lantus® and Humalog®.

Phase Ib clinical results – Evaluation of the effect of BioChaperone Combo on post-prandial glycemic control in type 1 diabetes patients

In early November 2015, ADOCIA announced positive topline results from the clinical Phase Ib trial evaluating the postprandial effect of BioChaperone Combo in 28 patients with type 1 diabetes. The randomized, crossover, double-blind study, compared the effect on post-prandial glucose of individualized doses of BioChaperone Combo and Humalog® Mix™75/25 (Eli Lilly) injected at the time of a standardized meal . The study met its primary endpoint, demonstrating that BioChaperone Combo decreased postprandial blood glucose significantly more than Humalog® Mix™75/25 during the first two hours ($\Delta AUC_{BG(0\text{-}2h)}$). The minimal blood glucose observed during the period was also significantly better controlled with BioChaperone Combo vs. Humalog® Mix75/25™. Although this study was not powered to measure differences in hypoglycemia incidence between both treatment arms, a lower number of hypoglycemia events was observed with BioChaperone Combo vs. Humalog® Mix75/25™.

Phase Ib clinical results – Pharmacokinetic and pharmacodynamics study in patients with type 2 diabetes, comparing BioChaperone Combo to HumalogMix® 75/25™ and to the separate injection of Lantus® and Humalog®.

In late November 2015, ADOCIA announced positive topline results for the Phase Ib clnical trial comparing the pharmacokinetic and pharmacodynamics profiles of BioChaperone Combo to those of Humalog® Mix75/25 and to the separate injection of Lantus® and Humalog® in patients with type 2 diabetes.

The randomized, crossover, double-blind, Phase Ib clinlical trial evaluated BioChaperone Combo in 24 patients with type 2 diabetes under euglycemic clamp. The topline results compared the pharmacodynamics profile of BioChaperone Combo (single dose of 0.8 U/kg) to those of Humalog Mix75/25™ (Eli Lilly, single dose of 0.8 U/kg) and to the separate and simultaneous injections of Lantus (insuline glargine, Sanofi, single dose of 0.6 U/kg) and Humalog (insuline lispro, Eli Lilly, single dose of 0.2 U/kg).Key parameters in this comparison were the early prandial effect ($AUC_{GIR(0\text{-}2h)}$) and the late basal effect for all three treatments.

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

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

6.4.2.4 Future clinical trials

6.4.2.4.1 *HinsBet®*

The results announced in February 2015 on an optimized formulation of HinsBet® strengthened the potential of the product, on the one hand for the U100 formulation dedicated to emerging countries and on the other hand for the U500 formulation dedicated to insulinoresistant patients.

The company is preparing two Phase II clinical trials in type I diabetic patients in Europe: one Phase II clinical study evaluating HinsBet® U100, expected to start in Q1 2016 in Europe, and one of Phase I/II clinical study evaluating HinsBet® U500, expected to start in Q4 2016 in Europe.

6.4.2.4.2 *BioChaperone Lispro U100 and U200*

As both products are developed under the Lilly-ADOCIA partnership, the clinical development plan is confidential.

6.4.2.4.3 *BioChaperone Combo*

Based on the very positive PK/PD clinical results obtained in patients with type 1 and patients with type 2 diabetes, as well as the good results obtained on post-prandial glucose control with BioChaperone Combo in patients with type 1 diabetes, ADOCIA is actively pursuing the development of BioChaperone Combo in order to macimise the project's value. Two phase II clinical trials aiming to further document the medical benefit of BioChaperone Combo in type 2 diabetes patients should be initiated during the second quarter 2016.

6.4.2.4.4 *The competition for the prandial treatment of diabetes*

Novo Nordisk

Novo Nordisk is developing a new formulation of its fast insulin analog (FiAsp, ultra fast acting insulin aspart) whose action is believed to be more rapid than NovoLog®'s(insulin aspart) . Novo Nordisk launched a phase III program at the end of 2013. The first press releases about the pharmacokinetics and pharmacodynamics profiles of FiAsp (Phase I/II with 52 type I diabetic patients) showed that the product started acting significatively faster than insulin aspart. However, these data did not show a fast-out effect (faster insulin exit from the blood stream/shorter period of action), as was shown for BioChaperone® Lispro U100 in a phase IIa clinical trial. This latter effect is desired, as it could potentially reduce hypoglycemia risk.

In December 2015, Novo Nordisk announced they had submitted FiAsp for market approval both to the European Medicine Agency (EMA, Europe) and to the FDA (USA).

Furthermore, in September 2015, Novo Nordisk obtained US market approval for Tresiba (insulin degludec) and for its combination with prandial insulin aspart (Ryzodeg). Ryzodeg was launched for the first time in Mexico in 2014 and then in India in 2015.

Finally, in January 2015, Novo Nordisk launched Xultophy® a combination of insulin degludec with GLP-1 analog liraglutide, in Switzerland. This launch was fllowed by multiple other European launches. Novo Nordisk filed Xultophy for FDA approval in September 2015.

Biodel

The American company Biodel, as Adocia, has recognized the value of a human insulin product with an action as rapid as that of analogs. Biodel has developed a formulation of fast acting human insulin called VIAject™ (BIOD-090) whose performance seems to be comparable to that of analogs.

VIAject™ is a formulation of human insulin with ethylenediaminetetraacetic acid (EDTA) and citric acid whose pH is around 4.5. The insulin concentration of VIAject™ is 4 times lower than that of products on the market. VIAject™ has been tested in many phase I, II, and III trials. Phase I results had shown that the BIODEL technology enabled the absorption of human insulin (insulinmia) and regulation of glycemia (blood glucose) that was as rapid as the insulin analog lispro and more rapid than Humulin® human insulin at the same doses54.. In phase III, VIAject™ had shown its non-inferiority to a commercial human insulin, Humulin® (Eli Lilly)55. The administration of VIAject™, however, caused pain at the injection site. Biodel applied for a Marketing Authorization of this formulation (VIAject™) in the United States in October 2010, but the FDA rejected the application. The FDA requested Biodel

to conduct a new phase II clinical trial on type 1 and 2 diabetics, based on the judgment that the initial data were insufficient and did not clearly demonstrate superiority of this product.

Biodel conducted new preclinical studies of performance and prepared a new formulation of human insulin, **BIOD-123** whose pharmacokinetic and pharmacodynamic profiles were equivalent to VIAject™ but with attenuated reactions at the injection site. BIOD-123 has been tested in phase I and II trials. In September 2013, Biodel announced positive phase II results showing the non-inferiority of BIOD-123 compared to Humalog® in terms of control of prandial blood glucose (level of HbA1C).

Using the same kind of formulation (citrate EDTA), BIODEL also initiated the development of ultra-rapid formulations of insulin lispro (prandial insulin analog, Humalog®, Eli Lilly), BIOD-250 and BIOD-238. BIOD-250 was tested in a Phase II clinical trial and demonstrated a faster prandial action compared to Humalog, as well as a good tolerability. However, this formulation did not meet the required stability criteria to warrant commercial development. Early in 2014, BIODEL announced they would continue developing a novel formulation meeting those stability criteria. The selection of a candidate formulation was expected to be made mid-2014.

In December 2015; Biodel announced that it would stop its ongoing clinical trials to spare cash and cash equivalent, amounting to approximately $40 million at the time of the press release. .

Halozyme Therapeutics

Halozyme Therapeutics had conducted a clinical trial to demonstrate the increased rate of absorption of human insulin or insulin analogs. Halozyme Therapeutics is developing a recombinant human enzyme, hyaluronidase PH20 that depolymerizes hyaluronic acid in physiological conditions. This polysaccharide is a constituent of the extracellular matrix and is found in a large number of tissues: connective, epithelial and nerve. It is also present in the subcutaneous compartment where the injection of hyaluronidase degrades the matrix. The diffusion of proteins injected with this enzyme is improved, leading to more rapid diffusion of the drug substance from the injection site to the capillary network57. This technology is used for monoclonal antibodies to enable their subcutaneous rather than intravenous administration (products authorized in Europe in 2013 and 2014, in partnership with Roche: Herceptin SC® and MabThera SC®).

In a phase I clinical trial58, the effect of hyaluronidase on the rate of absorption by the blood compartment was demonstrated: there was an increased rate of absorption of human insulin by the combined administration of PH20 with Humulin® and the accelerated absorption of an insulin analog by the combined administration of PH20 with Humalog®.

A phase II clinical trial involving type 1 diabetics also showed the positive effect of PH20 on the pharmacokinetics of human insulin by the combined administration of Humulin® with hyaluronidase. The results also showed a reduction of post-prandial blood glucose and attenuated hypoglycemia in comparison to Humulin® alone.

A phase II clinical trial conducted in 2012 on type 1 diabetics showed the effect of PH20 on the increased absorption rates of two insulin analogs: insulin lispro and insulin aspart. For both insulins, there was improved control of post-prandial blood glucose for analogs formulated with PH20 compared to insulin lispro.

However, today, this enzyme can not ne formulated with insulin and the treatment is based on a co-administration of an ex temporane mix of insulin and hyaluronidase. Halozyme had considered to administrate their ultra-fast analogs in pumps, which would allow to circumvent this difficulty and to access the potential market of the future artificial pancreas.

However, in November 2014, Halozyme Therapeutics announced that the insulin program was not a priority and that the company was focusing on their oncology projects (November 10th 2014 Halozyme press release).

In 2015, there is no more communication from Halozyme on insulin projects, which have been officially dropped from the company's pipeline. Thus, Halozyme is no longer considered as a serious competitor to Adocia's insulin projects.

Mannkind

The company Mannkind was created in 1991 by Alfred Mann. Mannkind acquired Technosphere technology and the Medtone inhaler by purchasing Pharmaceutical Discovery. The acquisition of these technologies resulted in the product Afrezza, a human insulin administered by inhalation. It is an ultra fast human insulin whose concentration peak occurs 12 to 15 minutes after inhalation. Insulin delivered via this route has a shorter time of onset of action and the curve lacks a tail, or trailing edge, in contrast to human insulin administered subcutaneously. Its pharmacokinetic profile is very close to that of insulin secreted by the pancreas in healthy subjects. This results in better control of blood glucose after meals and a reduced proportion of glycated hemoglobin, HbA1c.

Based on these results, Mannkind submitted an initial Marketing Authorization application in 2009. The FDA issued an initial response in March 2010, requiring additional information. Following a meeting with the FDA, Mannkind re-submitted its application that the FDA again rejected in January 2011. In a second response, the FDA did not accept the use of Afrezza in type 1 and type 2 diabetic adults, requiring two additional phase III clinical trials with the new inhaler, called Dreamboat.

In August 2013, the company announced the results of these two phase III clinical trials. They established the product's non-inferiority compared to NovoLog® (insulin aspart, Novo Nordisk) in type 1 diabetics and a superiority over oral antidiabetics in type 2 diabetics; there was no negative change in the results concerning safety, the reduction of the number of hypoglycemia episodes and reduction of weight gain. The company resubmitted its MA application based on these results.

On June 27th 2014, the FDA approved the use of Afrezza (recombinant human insulin as an inhalable powder) to improve glycemic control in adults with diabetes.

This approval was limited by restrictions on patient populations that could be prescribed the drugs (Afrezza was not recommended to smokers and patients with ketoacidosis). The drug also received a "black box warning" (warning on the potential risks associated with a treatment, that must be explicitly displayed on the packaging), relative to the risk of bronchiospasm associated with treatment: this risk prevents patients with asthma or COPD (Chronic pulmonaru obstruction disease) to use Afrezza. Consequently, doctors must realize a pulmonary checkup before prescribing the drug to their patients.

Moreover, the FDA required that Mannkind perform four complementary post-marketing clinical studies :

- A clinical trial to evaluate the pharmacokinetic profile, the safety and the efficacy of Afrezza in pediatric patients.
- A clinial trial to evaluate the potential risk for lung cancer of Afrezza.
- Two pharmacokinetic/pharmacodynamic studies under euglycemic clamp to evaluate the dose-response profile and the variability of the responses between patients.

In August 2014, Mannkind announced a marketing deal with Sanofi that could reach $925 Million dollars. The deal included an upfront payment of $150 million, and $775 millions in potential development and marketing milestone payments. Sanofi also did a $175 million advance to Mannkind to finance R&D expenses. Under the agreement, both companies would share marketing loss and profits at a ratio of 35% for Mannkind and 65% for Sanofi. In 2005, Pfizer had launched an inhalable insulin, Exubera®. This product was a commercial failure quickly removed from the market.

Afrezza was launched in the Unites States in February 2015. As of June 30th 2015, Sanofi reported sales close to $5.5 million, which were significantly lower compared to the forecasts Mannkind had produced in 2014. This led Mannkind to three successive lay-offs plans in 2015. In December 2015, Mannkind announced that the company was in debt to Sanofi for more than $40M.

On January 5th, 2016, Sanofi and Mannkind announced the termination of theoir partnership starting April 4th 2016. Mannkind announced it would endeavor to pursue Afrezza's commercialization on its own.

6.4.2.4.5 *The competition for treating diabetes with insulin Combos*

Novo Nordisk

NOVO NORIDSK developed Ryzodeg, a combo of a fast-acting insulin analog (insulin aspart) and a long-acting insulin analog (insulin degludec). Insulin degludec is the latest basal insulin developed by Novo Nordisk, under the brand name Tresiba. Insulin degludec has a longer duration of action compared to insulin detemir (Levemir, Novo Nordisk, which does not cover 24 hours). Tresiba, like Lantus, the current reference basal insulin, is a product that can be injected daily. Current global sales for Lantus are over $7 billion.

Ryzodeg was tested in multiple clinical trials, both against aspart-based premixed insulin (NovoMix, Novo Nordisk), against Lantus and against Levemir and NovoLog separate injections. These results showed that Ryzodeg is well tolerated both in patients with type 1 and type 2 diabetes, and the product improves glycemic control against Lantus, as well as reducing the number of hypoglycemic events against NovoMix.

In 2013, Ryzodeg and Tresiba received marketing approval in Europe and Japan. Ryzodeg is the first combination of two insulins to be approved. These products were only approved in the IS in September 2015, after Novo Nordisk published interim positive results from complementary cardio-vascular safety studies that had been required by the FDA when the regulatory dossier had been first submitted.

By contrast, Adocia's BioChaperone Combo may benefit from the large amount of positive safety data on insulin glargine (Lantus) and insulin Lispro (Humalog).

BIODEL

BIODEL currently develops an ultra-concentrated formulation of human insulin (U400), BIOD-531, that the company wishes to position both as a competitor to Premix products and as a treatment for severely insulin-resistant patients. BIODEL announced in February 2014 topline results in obese but non diabetic patients, comparing BIOD-531 to Humulin R U500 (500 IU concentrated recombinant human insulin, Eli Lilly) and to Humalog Mix25 (premix product of insulin lispro and insulin lispro protamine, Eli Lilly). BIOD-531 showed a comparable safety and tolerability profile to the one of Humalog Mix25. Compared yo both Humalog Mix25 and Humulin R U-500, results showed an acceleration of the onset of the prandial action. However, BIOD-531 also displayed a shorter basal action (significant compared to Humulin R U-500 and significant on some parameters only when compared to Humalog Mix25).

In August 2014, BIODEL announced results from a Phase II study comparing the effects of BIOD-531, Humalog Mix 25 and Humulin R U-500 on glycemic control throughout the day (one insulin injection, two standardized meals) in patients with type 2 diabetes with a moderate resistance to insulin. Compared to Humalog Mix 25 and Humulin R U-500, BIOD-531 again showed an accelerated prandial action, but a shorter basal action.

However, this study shows that BIOD-531, administered once in the morning (before or after the meal) may allow to maintain a lower glycemic rate during the day compared to both Humalog Mix 25 and Humulin R U-500, injected before breakfast.

In January 2015, Biodel announced results for a phase II study in highly insulin-resistant type 2 diabetes patients. These results suggest that BIODEL may improve glycemic control after a standardized meal compared to both Humalog Mix 25 and Humulin R U-500.

However, in December 2015, Biodel announced that the company had halted recruitment for two ongoing studies on BIOD-531 (studies 3-250 and 3-157) to allow the company to spare their cash position, which at the time of the announcement was around $40M. Biodel has also announced to have taken a council to evaluate strategic options.

6.4.2.5 Progress provided by BioChaperone® technology

The developments under way by Adocia involve all segments of insulin treatment of diabetes (human insulin, insulin analog, Combo). The total value of these markets is more than $7-8 billion and the company could enter them *via* the signature of partnerships (refer to section 6.4.1.2. The market). The company has shown (refer to section 6.4.2.3. Clinical trials conducted by Adocia), using insulins marketed by large pharmaceutical companies, that it is possible to use the BioChaperone® technological platform to eventually produce and market:

- a BioChaperone®-human insulin complex, HinsBet®, with a time to onset of action more rapid than that of a human insulin and similar to that of an insulin analog in a phase I trial and a phase IIa trial;
- A complex BioChaperone® - rapid-acting insulin analog complex (using insulin lispro, Humalog®) with a shorter action duration profile than the insulin analog alone, currently licenced to ELI LILLY and being tested in phase Ib/IIa.
- A complex at neutral pH BioChaperone® / insulin glargine (Lantus®) that allows to combine in a same solution insulin glargine with any rapid-acting insulin analog, (including insulin aspart, insulin lispro or insulin glulisine). This combination also maintains both insulins profiles as observed in a phase II clinical study.

Adocia has also received financial support from the BpiFrance and the Regional European Development Fund (FEDER) in the form of subsidies and upfront loans for a total of €1,640,000 euros (refer to section 22.2 of this reference document Contracts signed with OSEO).

6.4.3 Innovative formulation of monoclonal antibodies

In order to obtain maximal benefit from its BioChaperone® technological platform and ultimately sign license contracts, Adocia is currently working on two joint development programs with major pharma companies to design new formulations of their therapeutic proteins. The goal of these new formulations is to improve efficacy, safety and compliance of the therapeutic proteins of its partners by providing new properties to become best-in-class products. In the framework of these development contracts, Adocia's partners furnish the quantities of therapeutic proteins required for the work and Adocia is reimbursed for costs incurred for research and making BioChaperone® technology available, which have thus far reached €1.18 million.

Monoclonal antibodies were developed in 1975 by Georges Köhler and Cesar Milstein, who received the Nobel Prize in Medicine in 1984 for their work.

Monoclonal antibodies are the products with the highest growth of the pharmaceutical industry. This progress has been rapid because of the number of severe oncology pathologies involved (treatments of leukemias, lymphomas, breast cancers, colorectal cancers, etc.) and their value for the treatment of autoimmune and inflammatory diseases (rheumatoid polyarthritis, Crohn's disease, multiple sclerosis, etc.). An additional reason for rapid growth has been the development of large scale production techniques.

Several monoclonal antibodies have become blockbusters, i.e. with sales over one billion dollars, in particular Remicade® (Johnson & Johnson: $7.7 billion in 2012), Avastin® (Roche: $6.3 billion in 2013), Enbrel® (Amgen & Pfizer: $8.3 billion in 2013), Humira® (Abbott Laboratories: $9.3 billion in 2012), Rituxan®/Mabthera® (Roche, Biogen & Genentech: $6.1 billion in 2013) and Herceptin® (Roche: $6.45 billion in 2013).

These molecules operate primarily as inhibitors, by trapping active proteins or by binding to cell receptors to prevent the binding of ligands. This strategy requires a systemic concentration high enough to block targets and therefore the administration of high doses. In these conditions, stability and formulation issues may predominate and result in therapeutic consequences in terms of efficacy and immunogenicity. In most cases the method of administration involves intravenous infusion after diluting the antibodies in isotonic saline. Some antibodies administered intravenously aggregate during storage and this can cause immune reactions, even reduced antibody activity. The number of subcutaneously administered monoclonal antibodies is increasing. In September 2009, GENMAB and its partner GSK stated that they were re-directing work towards the production of a version for subcutaneous injection of their product Arzerra. This route of administration should be the preferred solution for the pharmaceutical industry but to reach this end, formulations of totally soluble antibodies at high concentrations must be developed.

Adocia is carrying out joint work with two large pharmaceutical companies in order to develop a second generation formulation with the goal of becoming best-in-class products that would improve:

- the physical stability of antibodies to prevent the formation of aggregates that could reduce efficacy and increase immunogenicity of the products;
- the solubility of antibodies to prepare formulations at high concentrations and low viscosity for subcutaneous injection when this route is compatible with the pathology and the antibody used.

The company has also received a subsidy of €63,367 from the OSEO for its research on monoclonal antibodies.

6.5 Adocia oncology products developed with DriveIn® technology

6.5.1 Pathology

Cancers are a pathological cell proliferation in a healthy tissue that threaten the survival of the tissue in question, even the organism itself. This abnormal proliferation results from mutations of cell cycle genes in cancer cells that may arise from hereditary anomalies and/or environmental factors (life style, exposure to carcinogens, infections, etc.)..

Cancers are currently one of the leading causes of death in developed nations. The most frequent cancers in the global population are lung cancer, breast cancer and colorectal cancer (see Table 10).

Cancer	Worldwide incidence	Worldwide mortality (yearly, in millions)

	(number of new cases yearly, in millions)	
Non-small cell lung cancer	1.6	1.4
Breast cancer	1.4	0.4
Colorectal cancer	1.2	0.6
Stomach cancer	0.99	0.7
Prostate cancer	0.9	0.3
Liver cancer	0.75	0.69
Cancer of the head and neck	0.74	0.4
Pancreatic cancer	0.28	0.25
Kidney cancer	0.27	0.1
Melanoma	0.2	0.05
Ovarian cancer	0.2	0.14
Multiple myeloma	0.1	0.05

Table 10: Worldwide incidence and mortality from the most frequent cancers (Source: Cancer Research UK)

Mortality rates depend on the type of cancer, its stage of advancement at the time of diagnosis and on available treatments. For example, while the 5 year survival of patients with a stage I ovarian epithelial cancer is 89%, the rate of the same cancer diagnosed at stage IV (metastatic) is only 18% (Source: National Cancer Institute). Similarly, patients with HER2-positive breast cancers (cancer resulting from the mutation of the HER2 gene) can be effectively treated, for example with Herceptin® (Roche, monoclonal antibody), while patients with so-called triple negative breast cancers (resulting from different genetic mutations) have very few therapeutic options available..

Medical needs vary considerably from one cancer to another and the disease therefore remains difficult to eradicate, explaining why oncology research is very active, with the hope of prolonging the lives of patients and improving their therapeutic management.

6.5.2 DriveIn® oncology products

6.5.2.1 Types of treatment

The therapeutic oncology arsenal has become greatly diversified over the past several years. The first line of treatment for most solid tumors is surgery that excises accessible and delimited tumors. Surgery may be concomitant with, or followed by chemotherapy at a later time, whose purpose is to make cancer cells enter apoptosis (pre-programmed cell death). In a substantial number of cases, surgery and chemotherapy may, however, be unusable, insufficient or ineffective. Recourse to drug therapy is therefore very important and several types of treatments are available.

6.5.2.1.1 *Chemotherapy*

Chemotherapy is the treatment of cancer with chemical molecules and remains the lynchpin of therapeutic management in oncology; the first chemotherapy treatments were developed in the 1940s. The principal treatments currently on the market belong to several large families of molecules discovered between the 1950s and 1990s: taxans, platinum derivatives, anthracyclins, alkaloids, and nitrogen mustards in particular (see Table 11). In most cases, the drugs containing these molecules are administered intravenously. Many of them are now in the public domain (patents expired) and are still extensively used as first line treatment (in particular taxans, platinates and anthracyclins).

Molecule (public domain)	Name (company)	Market (year)	Peak of sales (year)
Docetaxel (2010)	Taxotere® (Sanofi)	$742 million (2012)	$3.1 billion (2010)
Pemetrexed (2015-2022)	Alimta® (Eli Lilly)	$2.594 billion (2013)	$2.594 billion (2013)
Temozolomide (2013)	Temodar® (Merck) (Dacarbazine pro-drug)	$2.213 billion (2013)°	2.323 billion (2011)
Oxaliplatin (2013-2016)	Eloxatine® (Sanofi)	$1.229 billion (2013)	$2.17 billion (2006)
Gemcitabin (2010)	Gemzar® (Eli Lilly)	$347 million (2013)	$1.7 billion (2008)
Paclitaxel (2000-2003)	Taxol® (BMS)	$148 million (2011)	$1.6 billion (2000)
Capecitabin (2013)	Xeloda® (Roche Genentech)	$1.435 billion (2013)	$1.624 billion (2012)
Doxorubicin (n.a.) **Liposomal doxorubicin (2009)**	Rubex®, Adriamycin®; Doxil® (J&J)	n.a. $402 million (2011)(*)	n.a. n.a.
Irinotecan	Camptosar® (Pfizer)	$130 million (2013)	$970 million (2007)

Table 11: Chemotherapy best sellers in oncology. Most of these molecules are indicated for the treatment of several types of different cancers. (Source: Datamonitor Healthcare). Sales of Doxil® reported for 2011, before the supply issues encountered by Johnson & Johnson (2012).

These treatments act on cell division, most often with the goal of stopping cell proliferation (treatments called cytostatic) or even killing cells (treatments called cytotoxic). Cancer cells divide to a greater extent and more rapidly than healthy cells and so these treatments preferentially attack rapidly dividing cancer cells. The vast majority of non-cancer cells in the body also divide regularly, however, so chemotherapies also damage healthy tissues. The elevated efficacy of chemotherapies is therefore limited by toxicity to healthy cells that is often extensive. This explains why oncology treatments have progressed to approaches called targeted.

6.5.2.1.2 *Targeted therapy*

In order to increase the therapeutic index (the efficacy/adverse effects ratio) of oncology treatments, research is being oriented toward development of "targeted" treatments, i.e. preferentially aimed at cancer cells and avoiding possible attack on healthy tissues as much as possible. Targeted therapies block the growth of cancer cells by acting specifically on proteins involved in carcinogenesis and tumor growth, rather than targeting all dividing cells. These therapies may be targeted inhibitors (small molecules), monoclonal antibodies or antibody-drug conjugates (ADC).

Targeted inhibitors:

Most marketed targeted inhibitors interfere (by competition or inhibition) with the activity of members of the family of kinases, but their targets may differ. The first targeted inhibitors (Gleevec®, Sutent®) were marketed in the 1990s and had a significant impact on their indications, in particular for leukemia. Most of these products are administered orally. The principal targeted inhibitors on the market are listed in Table 12.

Compound	Target	Name (company)	Worldwide sales (2013)	Indications
Imatinib	Tyr-kinase	Gleevec® (Novartis)	$4.81 billion	Ph+ chronic myeloid leukemia (CML), gastrointestinal stromal tumor (GIST), acute lymphoblastic leukemia (ALL), other rare cancers
Lanalidomide	Immuno-modulator	Revlimid® (Celgene)	$3.77 billion	Myelodysplasic syndrome
Bortezomib	Proteasome	Velcade® (Millenium Pharma-Takeda)	$2.41 billion	Recurrent multiple myeloma, mantle cell lymphoma
Erlotinib	Tyr-kinase	Tarceva® (Roche)	$1.97 million	Non-small cell lung cancer (NSCLC); pancreatic cancer
Dasatinib	Tyr-kinase	Sprycel® (BMS)	$1.37 billion	CML; Ph^+ ALL
Sunitinib	Tyr-kinase	Sutent® (Pfizer)	$1.30 billion	Kidney cancer; GIST; pancreatic cancer
Nilotinib	Tyr-kinase	Tasigna® (Amgen)	$1.12 billion	Ph^+ CML (imatinib-resistant)
Gefitinib	EGFR	Iressa® (AstraZeneca)	$624 million	Breast cancer, NSCLC
Lapatinib	Tyr-kinase	Tykerb® (GSK)	$400 million	$HER2^+$ breast cancer

Table 12: Best sellers of targeted inhibitors. (Source: Datamonitor Healthcare, 2013)

6.5.2.2 Market size and pipeline

The segment of oncology is currently the largest of the pharmaceutical industry market. In 2013, it was estimated at $66 billion (Source: Datamonitor Healthcare). It is also the most active therapeutic area in terms of products under development: in December 2013, Datamonitor inventoried 543 products tested in phase I, 894 products in phase II and 209 in phase III. The vast majority (883) of these molecules under development involves small molecules (chemotherapy and targeted inhibitors).

6.5.3 DriveIn®, an innovative approach to targeted delivery in oncology

Chemotherapies remain one of the cornerstones of treatment in oncology because of their elevated efficacy. These molecules have harmful effects on healthy cells, however, causing toxicities that may

limit the use of these treatments. In order to improve this situation, the active targeting approach is a viable option. DriveIn® technology is promising for active targeting and cell uptake of drugs thet it transports. These properties are due to the ability of its hyaluronic acid surface to interact with the CD44 receptor, a marker of tumor stem cells.

Adocia has developed two products in-house that use DriveIn® technology: DriveIn®-doxorubicin and DriveIn®-docetaxel. Doxorubicin (Adriamycin®, Doxil®, Myocet®, Lipodox®) and docetaxel (Taxotere®) are two of the most widely used drug substances for the treatment of solid tumors. They are now in the public domain but still generate global sales of several hundred million dollars.

Preclinical results

Initial work of DriveIn® was conducted with the goal of showing:

- *In vitro, the principle of cell targeting and increased cell uptake resulting from hyaluronic acid*
- *In vivo* :
  - non-toxicity of nanoparticles
  - improved treatment safety resulting from enhanced selectivity (preferential accumulation in the tumor compared to healthy tissues) and efficacy of the treatment

Increased intracellular presence of DriveIn®-doxorubicin compared to the active molecule alone

Upadhyay and al (2010) worked in vitro on the MCF-7 line of cancer cells (that overexpress CD44, the hyaluronic acid ligand). They compared the cell uptake of doxorubicin and DriveIn®-doxorubicin when the products were added to the culture medium. The authors showed that the uptake of DriveIn®-doxorubicin was at least equivalent to that of doxorubicin alone. After 24 hours, doxorubicin levels started to decrease in cells treated with doxorubicin alone, while drug levels were maintained with DriveIn®-doxorubicin, suggesting better retention of doxorubicin transported and/or better cell uptake of the product (see figure below).

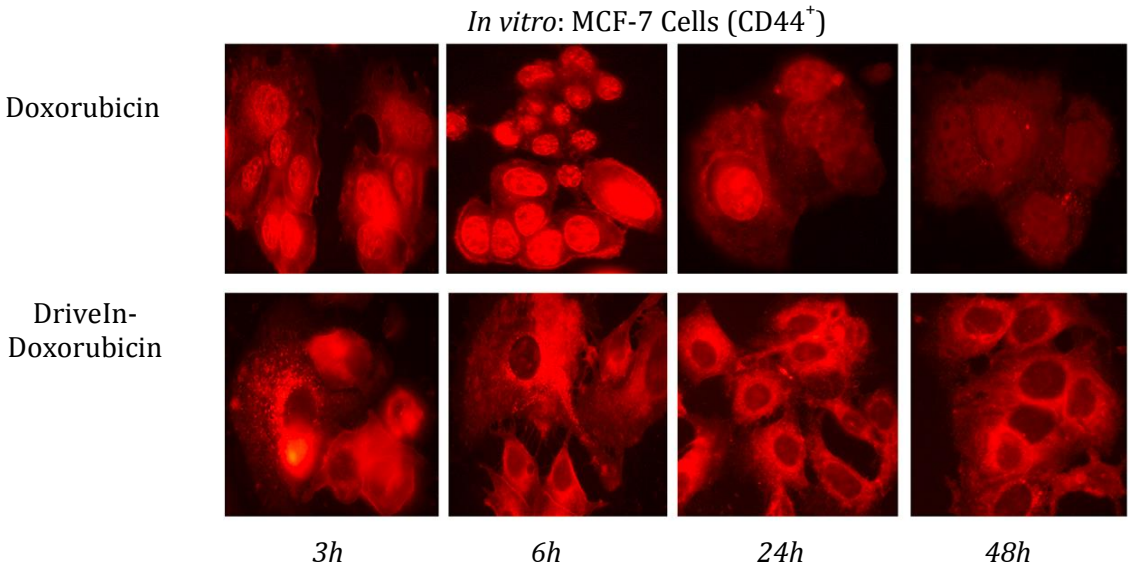


Figure 23 Fluorescence microscopy images of uptake of 10 µM doxorubicin alone by MCF-7 cells (top) and DriveIn®-doxorubicin (bottom) at 3h, 6h, 24h and 48h.

Encapsulation of doxorubicin and mediation of uptake by a hyaluronic acid receptor

Additional experiments showed that adding free hyaluronic acid to the culture medium interferes with the uptake of DriveIn®-doxorubicin with no effect on that of free doxorubicin. This confirms:

- that doxorubicin is well encapsulated in DriveIn® molecules,
- that delivery of doxorubicin inside the cell is mediated by an active mechanism involving hyaluronic acid receptor.

Lack of intrinsic toxicity of nanoparticles, even at high doses.

Based on these very promising results in vitro, experiments in vivo were carried out in mice, using the model of tumors induced by a carcinogen.

The first result was that nanoparticles without doxorubicin show no intrinsic toxicity in this experiment. The comparison of body weight changes of animals between 5 and 25 days, between the placebo (solid circles, black curve) and nanoparticles without doxorubicin (triangles, light blue curve) demonstrate that these changes were the same between 5 and 25 days.

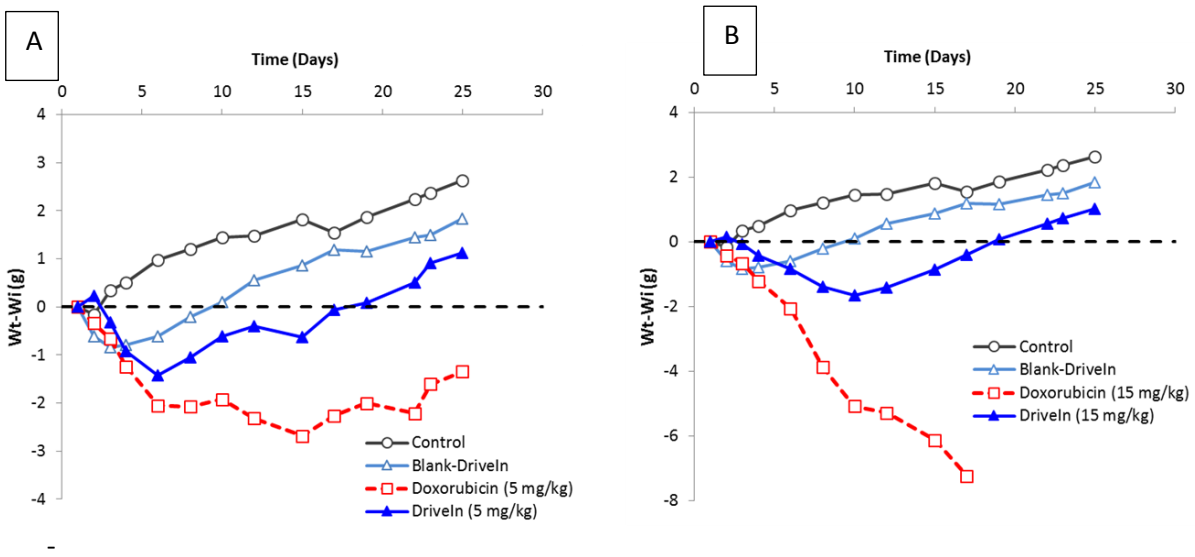


Figure 24 : Body weight curves of EAT-Balb-C mice (6 animals/group) injected with saline solution (control, black curve), DriveIn® nanoparticles alone at 20 mg/kg (Blank-DriveIn®, light blue curve), doxorubicin at 5 mg/kg (red curve panel A) or 15 mg/kg (red curve panel B) and DriveIn® particles containing doxorubicin at 5 mg/kg (dark blue curve panel A) or 15 mg/kg (dark blue curve panel B)

Accumulation of DriveIn®-doxorubicin in tumors

The EPR effect (due to the size of DriveIn® nanoparticles), combined with active targeting by hyaluronic acid, should lead to the accumulation of DriveIn® nanoparticles in the tumor. This hypothesis was tested on two animal models of cancer with DriveIn®-docetaxel and DriveIn®-doxorubicin . In both cases, the results showed the preferential accumulation of DriveIn® in the tumors compared to the active product alone. (cf. Figure 27)

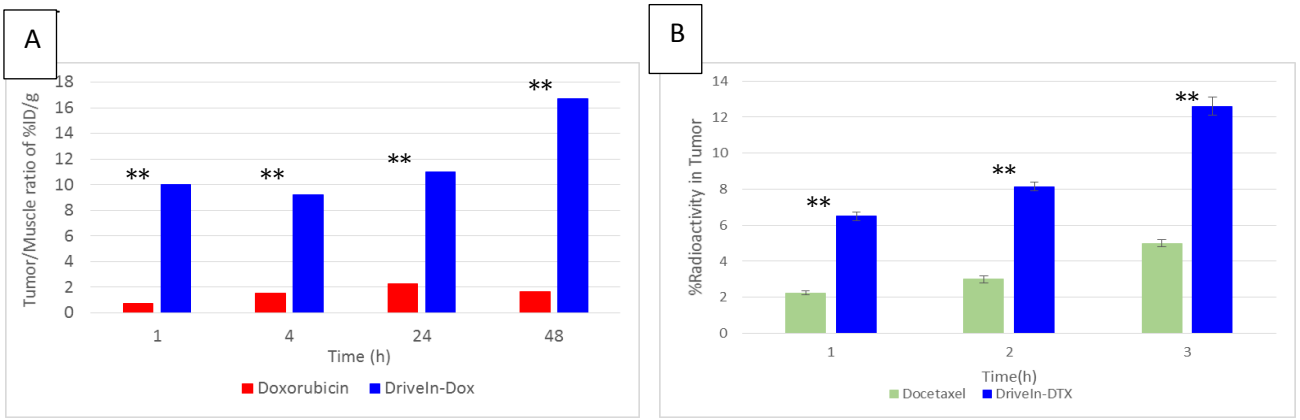


Figure 27 : Kinetics of the tumor/muscle ratio of DriveIn® assayed at different times after injection of the product in mice with cancers. A: EAT Balb-C mice, DriveIn®-doxorubicin vs. doxorubicin alone at 5 mg/kg (Dox). B: EAT (CD44+) mice; DriveIn®-docetaxel vs. docetaxel at 2 mg/kg. (: P < 0.05, **; P < 0.001).*

Improvement of efficacy in vivo

Improved targeting and uptake of the molecule transported should result in higher efficacy at the same dose, compared to the drug substance in its standard formulation. This increased efficacy has been shown for DriveIn®-doxorubicin in several murine models of cancer.

In initial work, Upadhyay et al7 injected DriveIn®-doxorubicin vs. doxorubicin alone in DMBA mice (model of breast cancer) at 5 mg/kg. The authors reported the decreased progression of tumors over 30 days, as well as the total size of tumors at 30 days in mice treated with DriveIn®-doxorubicin compared to doxorubicin alone (see Figure 29).

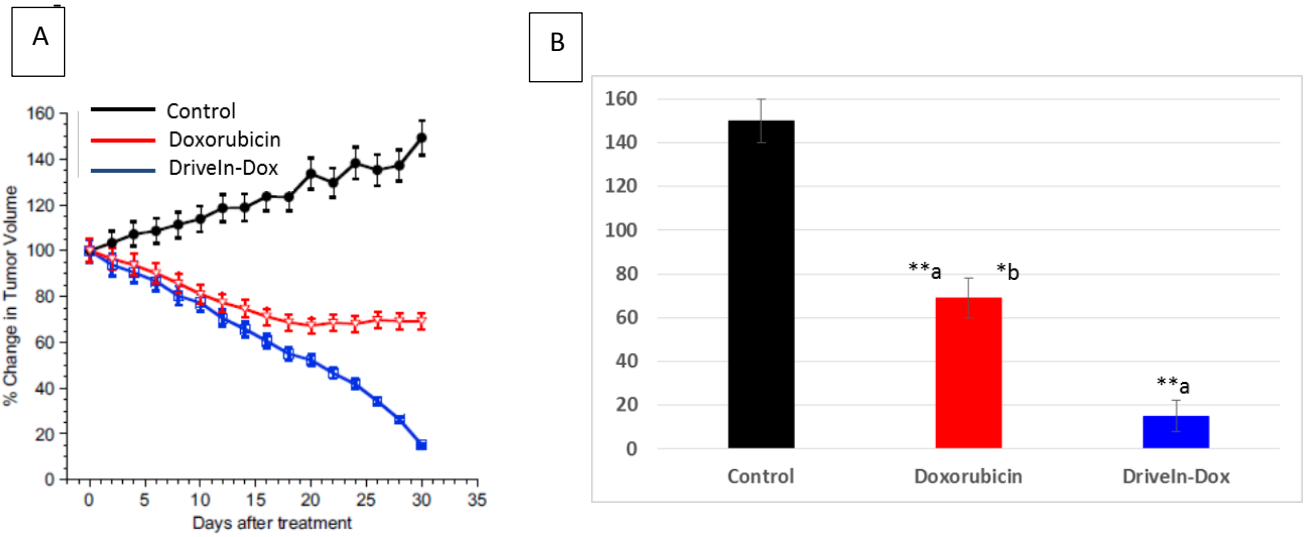


Figure 29: Reduced tumor progression and total tumor volume (A) at 30 days, and as a ratio compared to starting values (B) in DMBA mice after injecting doxorubicin and DriveIn®-doxorubicin at 5 mg/kg, 6 animals per group. (: P < 0.05; P < 0.001; a: vs. control; b. vs. DriveIn®-doxorubicin).*

In a second series of experiments, Upadhyay et al (2012) injected DriveIn®-doxorubicin vs. doxorubicin alone in EAT-Balb-C mice (murine model of an induced cancer) at 5 mg/kg. The authors reported a significant reduction in the growth of tumors over 30 days, as well as increased survival of mice treated with DriveIn®-doxorubicin compared to doxorubicin alone.)

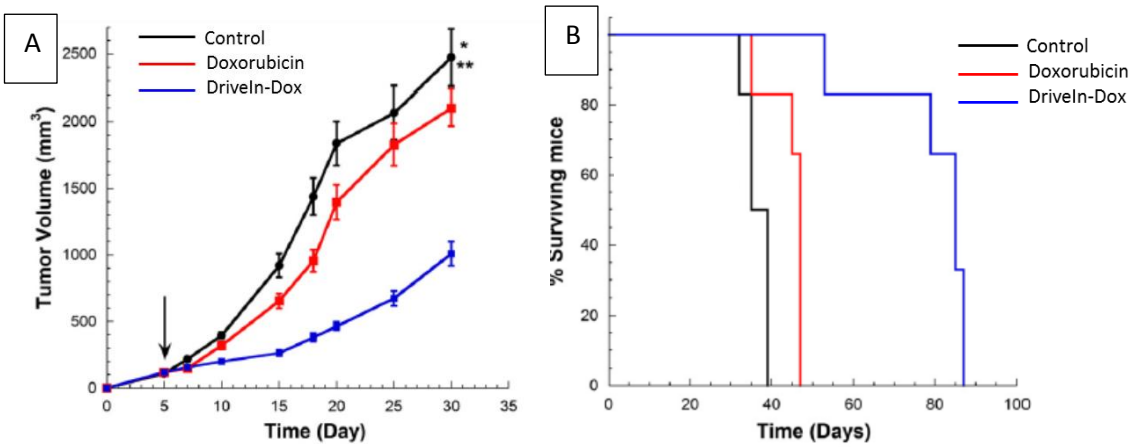


Figure 29 : Changes in tumor volume (A) and survival rate (B) in EAT-Balb-C mice after an injection of doxorubicin or DriveIn®-doxorubicin at 5 mg/kg (6 animals per group).

Adocia is currently continuing the preclinical development of the DriveIn® platform.

6.5.4 The competition

In order to increase the proportion of chemical molecules effectively reaching the tumor, the active targeting approach is useful. This approach was used for DriveIn® and by a small number of competitors. The most advanced nanoparticle approaches with active targeting are:

- **BIND** : an American biotechnology company that is developing a nanoparticle platform using copolymers. Its major product, BIND-014, is a pegylated nanoparticle containing docetaxel, targeting a prostate cancer receptor (PSMA). This product is currently under phase II clinical development for the treatment of prostate cancer and lung cancer. While still under preclinical development, BIND licensed the use of its platform for the development of proprietary molecules to three partners (2013): Pfizer, Amgen and Astra Zeneca, for total potential revenues of $705 million.
- **Merrimack** : this company has developed several pegylated liposomal formulations of chemotherapeutic molecules. The most advanced formulation, MM398, is a pegylated liposomal formulation containing irinotecan. It is in phase III for the treatment of pancreatic cancer, but this is not an actively targeted approach. Merrimack is also developing a pegylated liposomal formulation of doxorubicin that uses an mAb bound to the surface of the liposome to target HER2 receptors for the treatment of breast cancer (currently in phase I). Another product of this type is under preclinical development for an application that has not yet been divulged.
- **Cristal Therapeutics** is a young Dutch company that is developing both actively and passively targeted nanoparticles. A pegylated nanoparticle formulation of doxorubicin targeting EGFR is under preclinical.
- **NanoCarrier** is a Japanese drug delivery company that is developing nanoparticles composed of polymers.

6.6 A strategy based on several therapeutic innovations with an original and solid business model.

6.6.1 A strategy of medical innovation for the development of best-in-class products from therapeutic molecules authorized by the FDA and the EMA.

Adocia has designed a new family of polymers called BioChaperone®, whose exceptional properties improve the performance of a number of therapeutic molecules already on the market, in particular:

- by boosting their therapeutic efficacy;
- by attenuating their adverse effects (toxic effects), and
- by improving their compliance (reduced administration frequency, shorter treatment regimen times , etc.),
- by making possible the combined use of products incompatible until now because of their different pH.

Adocia's strategy involves continuing the development of each of its products until proof of concept is established. It is considered that proof of concept is established when experts in the field can have the scientific and medical conviction of the efficacy of the proposed technology. Depending on the nature of the product and the therapeutic area of application, proof of concept may be obtained from animal studies, but more generally from human clinical trials. Adocia plans to license its formulations of monoclonal antibodies based on animal studies but its PDGF-BB formulation for the treatment of diabetic foot ulcers only after having obtained probative results in a phase II clinical trial. The proof of concept for the treatment of diabetic foot ulcers cannot be established with an animal model and the large number of test on humans required to establish this proof are equivalent to a phase III trial.

In the few years, the company has developed several different, highly promising products for therapeutic applications as varied as the treatment of diabetic foot ulcers, insulin therapy, or oncology, with innovative formulations of monoclonal antibodies and the new DriveIn® technology.

6.6.1.1 An original and solid business model

Adocia has developed a B-to-B economic model having the following advantages:

- limited needs for financing: the cost of development of a product to obtain proof of concept is much lower than the cost of bringing a product to market ;
- a relatively short time to generate revenues: the company receives revenues from its partners well before the product reaches the market; and
- a risk of failure for any new formulation much lower than that of a new pharmaceutical molecule: the safety in use of the therapeutic protein used has already been established (authorized molecules).

All expenditures up to the time of establishment of this proof of concept are borne by Adocia while all costs of development will then be assumed by the partner. In the framework of the signature of a license contract, Adocia will receive an initial fee, the upfront payment, followed by payments in stages as scientific, technical or clinical milestones are reached, and finally by sharing revenues generated by the sale of products (royalties).

Adocia intends signing new joint work contracts, similar to previous joint development work with large pharmaceutical companies for the development of BioChaperone®/monoclonal antibodies complexes (refer to section 6.4.3 “Innovative formulation of monoclonal antibodies”). This enables the company to receive payments covering research and development costs. These contracts are consistent with the company's business structure, enabling it to make more profitable use of its proprietary

BioChaperone® platform and to confirm the relevance of the technological choice based on the properties of BioChaperone® polymers by demonstrating the interest of major players in the sector for this technology. In addition, if joint developments generate positive results, it is probable that these contracts will be transformed into license contracts with the same revenue structure (upfront payment, milestones and royalties).

This relatively non-capitalistic development has the advantage of enabling the company to receive revenues if license contracts are signed, without waiting for products resulting from its BioChaperone® technology to reach the market.

In addition, the company can give more focus to its competitive advantages resulting from its know-how in terms of the design of innovative therapeutic and drug delivery formulations. This will be made possible by joint work with multinational partners experienced in regulatory, clinical and marketing aspects for the sales of pharmaceutical products.

6.6.1.2 Technological developments optimizing the properties of all types of therapeutic molecules (hormones, growth factors, monoclonal antibodies) and facilitating their production

Adocia is developing specific applications using its proprietary BioChaperone® technological platform for therapeutic molecules having already shown their value in the treatments of the intended or similar indications, and that in most cases have been granted international Marketing Authorizations.

These developments are built around five orientations:

- maximizing the potential of the existing BioChaperone® platform in terms of physicochemical capacities;
- extending the collection of polymers to increase the number of therapeutic molecules that could be used with BioChaperone® technology;
- reformulating existing therapeutic molecules made possible by BioChaperone® technology in order to ultimately create technological breakthroughs, for example replacing intravenous injection of monoclonal antibodies by the subcutaneous route;
- creating best-in-class products providing a real pharmaceutical-economic advantage; and
- identifying new complexes responding to public health needs not yet fulfilled.

Work on on development of the collection of BioChaperone® polymers was originally guided by requirements of the American Food and Drug Administration (FDA) and the European Medicines Agency (EMA) concerning new pharmaceutical excipients, such as the absence of biological activity, the absence of toxicity, stability of products for several months, reproducibility of the manufacturing process of the product, precise documentation on impurities of the product and conducting clinical trials in compliance with standard operating procedures (SOP*) and requirements of the International Conference on Harmonization (ICH*).

In addition to these regulatory requirements, the industrial vision of the production of best-in-class products has led Adocia to add prerequisites to enable global marketing of its BioChaperone® technology: production of BioChaperone® polymers from natural molecules complying with the requirements of the European Pharmacopoeia* and The United States Pharmacopeia - National Formulary*, rapid synthesis of BioChaperone® polymers and a manufacturing process that can scaled up to industrial production, and finally production standards compatible with Good Manufacturing Practices* of the European Commission in the context of manufacturing drug products.

6.6.2 A management team having anticipated global public health challenges

In today's context of global markets, the pharmaceutical industry has not been spared and must face a number of economic, industrial and even ethical challenges. Adocia's management has anticipated pharmaceutical-economic changes via a strategy combining medical benefits and cost reduction with an offer suited for both developped countries and emerging nations, the latter providing genuine opportunities because of their growth and market size.

6.6.2.1 A strategy responding to changes in the pharmaceutical industry by combining medical benefits and cost reduction

Adocia's development of BioChaperone® and DriveIn® technological platforms was guided by the notion of proposing more effective and safer pharmaceutical products with competitive production costs and prices, using therapeutic proteins having already proven their value. In addition, most of them have been granted international Marketing Authorizations, thereby limiting the risks of failure during development.

Treatments can no longer be developed without taking their costs to consumers into account. This is because of the increased prevalence and incidence of the pathologies addressed by Adocia, as well as the growth and aging of the population in a political climate of controlling public health expenditures in developed nations and increasing demand from emerging nations. Primary health insurance and second carriers, whether public or private, require pharmaceutical companies to consider the costs of the products they propose. The fact of simply having been granted a Marketing Authorization is no longer sufficient and the reasoning applied during research and development must take economic and therapeutic aspects into account. The entities reimbursing medical expenditures are increasing their vigorous protests of the costs of medicines and services, explaining the partial or total reduction of certain reimbursements.

These political-economic issues are dealt with by improving the efficacy of therapeutic molecules used with BioChaperone® polymers enabling treatments and dosages to be changed, in particular with substantial reductions in dosages, the number of applications and/or treatment duration, similar to the treatment of diabetic foot ulcers, as well as reduced production costs because the manufacturing process is easily scaled up to the industrial level.

The explosion of generic drugs that will increase as many patents expire in the years to come61 and the increased use of biosimilar* products by companies in both developed nations and emerging economies also force large pharmaceutical companies to rethink the management of the life cycle of their flagship drugs, even in some cases their innovation policy in research and development, diversification and industrial partnership.

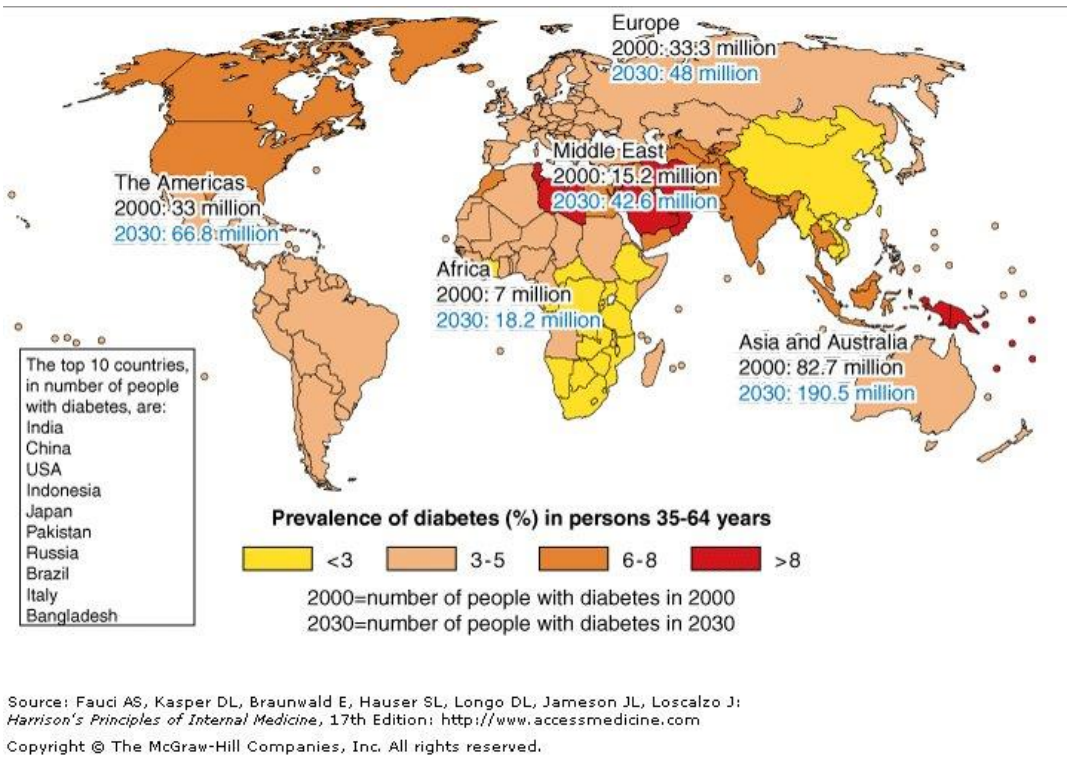
Obtaining a Marketing Authorization for a new pharmaceutical molecule is very long, requiring more than 10 years of research and development investment with a very high risk of failure related to toxicity, low or absent acceptability or adverse effects to humans not compensated by the therapeutic benefits provided. A response to issues of innovations by the pharmaceutical industry can thereby be furnished by new formulations of existing therapeutic molecules on the market and developed using BioChaperone® and DriveIn® technological platforms based on polymers having no intrinsic biological activity and that are registered with regulatory authorities as new excipients. Pharmaceutical companies will be able to continue proposing their therapeutic molecules with new formulations that are at least as effective as before but with new properties (shorter onset to action, sustained action, new routes and/or methods of administration) with shorter lead times, with lower development costs and with a lower probability of project failure).

Adocia can provide credible responses in the context of political, economic and regulatory pressure, the explosion of drugs and biosimilars, and globalization of the pharmaceutical industry:

- to issues of innovations for large pharmaceutical companies that must cope with the increased use of generic drugs and the expiration of many patents protecting their flagship products, by proposing new formulations of their therapeutic proteins with new properties and with efficacy at least equivalent to that of existing treatments; and
- to issues of reducing treatment costs by enabling a reduction in dosages, the number of applications and the duration of treatment, or by new routes and/or mechanisms of administration of treatments.

6.6.2.2 A strategy adapted to emerging nations

Although the demand for pharmaceutical products is increasing in emerging nations, access to healthcare and drugs on the other hand remains highly problematical, even critical in some countries. The World Health Organization has estimated[62] that more than 80% of mortalities due to chronic pathologies occur in countries with low or intermediate per capita income.



Source: Fauci AS, Kasper DL, Braunwald E, Hauser SL, Longo DL, Jameson JL, Loscalzo J: *Harrison's Principles of Internal Medicine*, 17th Edition: http://www.accessmedicine.com

Figure 25 : *Prevalence of diabetes in the world (from Fauci et al, Principles of Internal Medicine 7th Edition).*

In 2011, growth of the pharmaceutical products market in emerging nations (China +20%, India +15% or Brazil +11%) was much higher than the anticipated growth rate of the entire world market (+4.8% for a market estimated at $918.6 billion)[63]. Emerging nations will therefore play an increasingly more important role in the pharmaceutical industry. As an illustration, the contribution of the United States

[62] Prevention of chronic diseases: a vital investment, World Health Organization
[63] IMS Health France

to world growth of the pharmaceutical market was 27% between 2005 and 2010 and will be only 11% between 2010 and 2015, whereas in the same period China will increase from 12% to 26%[64].

No.	2004	2014
1	United States	United States
2	Japan	Japan
3	France	China
4	Germany	Germany
5	Italy	France
6	United Kingdom	Brazil
7	Canada	Italy
8	Spain	Canada
9	China	Spain
10	Brazil	India
11	Mexico	Russia
12	Australia	United Kingdom
13	South Korea	Venezuela
14	India	Turkey
15	Holland	South Korea
16	Belgium	Australia
17	Poland	Mexico
18	Turkey	Argentine
19	Greece	Poland
20	Russia	Greece

Table 13 : Major pharmaceutical markets, listed in order of the value of the market in constant dollars. Source: IMS Health France

This strong growth in emerging nations is explained by elevated standards of living and hygiene, access to healthcare by populations and also by the creation of many local companies producing generic drugs and biosimilars, even the creation of biotechnology companies. According to a 2009 study by Ernst & Young[65], turnover by the Indian pharmaceutical industry was estimated at $22 billion in 2008 of which $2.5 billion were in biotechnologies; the domestic market was €7.7 billion with an average annual growth rate of 14.6% between 2003 and 2008. The same study stated that India was the 4th (in number) among countries producing drugs and the 13th in value.

Adocia's strategy involves proposing pharmaceutical products intended to become best-in-class products at costs lower than those of existing products to these markets. This strategy is very well suited to meet the substantial needs of these emerging nations. This strategy could also develop with the support of a growing local pharmaceutical industry and the possibility of license contracts with local companies.

This explains why Adocia is conducting clinical trials in India for its most advanced product for the treatment of diabetic foot ulcers with BioChaperone®-Growth factor PDGF-BB complex, before conducting clinical trials in Europe and the United States.

[64] IMS Health France
[65] Capitalizing on the India opportunity: Helping French companies achieve business success in India, Ernst & Young, 2009

6.6.3 A model for development of pharmaceutical products with high added value

6.6.3.1 Experienced teams of scientists working on the development of innovative products

The Adocia team working on research and development of innovative pharmaceutical products developed with BioChaperone® and DriveIn® technological platforms accounts for almost 80% of company staff. Scientific management (refer to section 17.1.1 “Main key employeed”) is assured by about 20 PhDs in the varied and complementary fields of chemistry, physical chemistry, biology, medicine and veterinary science, each having solid experience in the management of technological innovation and partnerships with large industrial groups in the field of drug delivery technologies of therapeutic proteins or in the development of medical devices.

This team of scientists was behind the in-house development of the BioChaperone® technological platform, a genuine asset for the company since they have demonstrated their capacities for the coordinated, flexible and reactive management of complex, innovative, cross-discipline research and development programs.

6.6.3.2 Effective subcontracting of clinical trials

In order to maximize is economic model based on innovation and the creation of value, the company has decided to outsource preclinical and clinical trials with recognized and certified service providers after conducting quality audits. Adocia is working with:

- the International Toxicology Center for all toxicology studies on polymers in compliance with the rules defined by competent regulatory authorities (Good Laboratory Practices (GLP));
- Biomatech or the Claude Bourgelat Institute of the Lyon School of Veterinary Medicine in France, conducting preclinical studies on animals and that employ specialists in anesthesiology, surgery, endocrinology, pathology and animal breeding, with animal facilities consistent with study needs; and
- contract research organizations (CROs), companies specialized in conducting clinical trials in compliance with rules defined by competent regulatory authorities (Good Clinical Practices (GCP)).

Clinical trials of BioChaperone® insulins (refer to section 6.4.2.3. and 6.4.2.4 “Clinical trials conducted by Adocia and future clinical trials”) were conducted by PROFILE, a German CRO that provides a full range of clinical trial services in the areas of diabetes, endocrinology and cardiovascular diseases, for all phases (I to IV) in compliance with international quality standards (ICH-GCP and GLP). Adocia chose I.K.F.E. because of its experience in conducting clinical trials involving diabetes, with more than 200 trials thus far carried out.

For clinical trials on the treatment of diabetic foot ulcers with the BioChaperone®-growth factor PDGF-BB complex, the Indian partner of Adocia, Virchow Biotech that developed and markets a biosimilar of PDGF-BB, was the sponsor of the phase I trial/II in India in 11 centers specialized in treating this pathology. The phase III clinical study in India is ongoing and has been outsourced to the international CRO MAKROCARE, who is present in USA, in Europe, in Japan, in Singapore and India. Future phase III clinical trials in Europe and the United States will be sponsored by Adocia who will use the services of a global CRO (refer to sections 6.4.1.1.3 and 6.4.1.4 “The first phase II clinical trial in India and Future clinical trials”).

6.6.3.3 Outsourced production

Adocia is actively participating in the organization and supervision of the production of clinical batches. Its development model, however, has resulted in subcontracting the manufacturing of its products to:

- Virchow Biotech for BioChaperone®/PDGF-BB complexes ;
- The British company Aptuit, a Contract Manufacturing Organization (CMO) for BioChaperone® insulins.

In addition to regulations, authorizations and required standards, these companies also comply with Good Manufacturing Practices (GMP) validated with competent authorities and certification organizations.

For the needs of preclinical and clinical work, however, Adocia produces all BioChaperone® polymers in solution, primarily polymers of dextran manufactured by the Danish company Pharmacosmos and then transferred to the company DBI for freeze drying.

In the framework of marketing BioChaperone® polymers, they will be produced by CMOs selected by Adocia that use the same process as Adocia that was designed to comply with industrial requirements.

6.6.4 A strategy for dynamic management of intellectual property

The strategy for managing intellectual property developed by Adocia is intended to provide maximal protection of the company's innovations, in terms of both products developed and geography, in order to protect future markets in which these products could be sold.

This strategy for the protection of Adocia's innovations is a "locked door" to new players using a similar technology or to access to the company's markets. At the present time, 22 inventions have been protected by patent applications covering 22 distinct families. Adocia's portfolio is presently composed of almost 200 patents and patent applications.

6.6.4.1 Intellectual property protected at several levels

The intellectual property portfolio of Adocia has resulted from considerable in-house research and development. The company's industrial property protection policy covers the three areas of Adocia's innovation: the collection of BioChaperone® polymers, formulations of BioChaperone®/Therapeutic protein and the therapeutic applications of these formulations.

Patents protecting BioChaperone® polymers and small organic molecules

There are seven families of patents covering polymers (refer to section 11.2.2 Type and coverage of patents held by the company) and are intended to protect the entire collection of BioChaperone® polymers and small molecules, both concerning what these polymers have in common and the specific physical and chemical properties of each of them.

The proprietary BioChaperone® technological platform, the heart of Adocia's model, is intended for multiple applications and multiple indications. The therapeutic proteins selected for treatments of the pathologies targeted by Adocia, whether hormones, growth factors or monoclonal antibodies, with very different physicochemical characteristics, will be able to be combined with different specific BioChaperone® polymers.

Patents protecting BioChaperone®/therapeutic molecules complexes

There are three families of patents covering BioChaperone® polymers/therapeutic molecules complexes (refer to section 11.2.2 Type and coverage of patents held by the company) that cover the different types of therapeutic proteins that can be combined with BioChaperone® polymers: hormones, growth factors and monoclonal antibodies. These patents are intended to protect all the properties of therapeutic proteins provided by the combined use of a BioChaperone® polymer.

Patents protecting the scope of application of the BioChaperone® technological platform

There are eleven families of patents covering applications of the BioChaperone® technological platform (refer to section 11.2.2 Type and coverage of patents held by the company) and are intended to extend the company's innovations *via* the medical applications developed.

Patents protecting the scope of application of the DriveIn® technological platform

One family of patents covering applications of the DriveIn® technological platform has been deposited (refer to section 11.2.2 Type and coverage of patents held by the company) and are intended to extend the company's innovations *via* the medical applications developed.

Only these families of patents will be the subject of licensing contracts, in line with the economic model of partnerships developed by the company.

6.6.4.2 International coverage

Before the implementation on new regulations in United States on March 16, 2013, the patent application policy of Adocia involved an initial application in France, followed by patent applications in the United States as rapidly as possible. Since March 16, 2013, priority applications are only in France (it is no longer necessary to apply for an American patent in order to be recognized).

Twelve months after the French application, a demand for international extension *via* the Patent Cooperation Treaty (PCT) procedure is carried out. Among the 142 countries that can be covered by this procedure, each country is selected with respect to Adocia's commercial strategy for the patent. The three main geographical areas of patent protection defined by the company are :

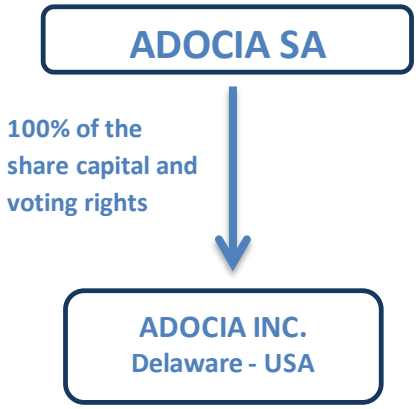
- the major European countries and the United States;
- followed by Canada, China, Japan, India, Australia and Israel; and
- finally countries such as Mexico, Brazil, Russia, South Africa, Singapore and South Korea.

The goal of the strategy of international patent protection (Europe/United States/emerging nations) is to obtain the first patents more rapidly in these target zones and to place each innovation in a strong position to obtain the most effective protection possible in all these countries.

7 ORGANIZATIONAL CHART

7.1 Organization of the Company

At the date of the issue of this reference document, the organizational chart is as follows:



7.2 Subsidiaries, branches and secondary establishments

The company was founded in February 2015 Adocia Inc., a subsidiary based in the state of Delaware, U.S.A, which has, as of the date of this reference document, two employees: one Medical Director and one marketing director. The objective is for the subsidiary to facilitate interaction with the US market and to lodge advocacy activities of the Company in the U.S.A.

8 REAL ESTATE, FACTORIES AND EQUIPMENT

8.1 Description of real estate

The company uses only the following premises:

- Its headquarter in Lyon: located at 115, avenue Lacassagne, 69003, Lyon, registered office of the Company is located in a building for innovative biotechnology firms (la "Pépinière"), on a total area of approximately 2.732m² for rent an annual amount of €439 thousand excluding charges and excluding taxes. The Company also entered into a lease of covered parking, in force since 13 October 2011, providing for the supply of twenty spaces reserved covered parking situated 115, Avenue Lacassagne, 69003 Lyon, on payment of a sum €9,600 TTC per year. The Company has recorded a charge rent (including service charges) amounting to €517 thousand for the year ended December 31, 2015.

To be noticed that, in late December 2013, the Company acquired 15 parking spaces for a total of €130 thousand.

With the aim to sustain its presence on this site, in the center of Lyon, the Company signed a preliminary sale agreement in January 2016 for the acquisition of this property of 7.120 m², the land on which the building is located and 43 parking spaces.

Upon signature of preliminary the sale agreement, the Company has the immediate use and enjoyment of the property.

The signing of the bill sale is expected in the coming weeks.

The “Métropole de Lyon” (city of Lyon) which owns the business enterprise zone, has no capital ties with any of the company’s managers and/or shareholders.

8.2 Other property, plant and equipment

The principal property, plant and equipment that the company holds is described in note 3.2 to the notes to the corporate financial statements prepared in accordance with IFRS, in Chapter 20.1 of this reference document.

8.3 Environmental issues, as required by Article R. 225-105-1 of the French Commercial Code

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. Its activities do not include industrial production or distribution, or significant discharges of effluents or greenhouse gases into the environment. Its activities do not require the use of the ground as a resource and employ few raw materials.

The company leases the laboratories and offices it occupies. It complies with the obligations the lease imposes on it, which concern primarily (see Article 10) compliance by environmentally sensitive sites (ICPE) with the reporting thresholds for 1432a and 1432b flammable substances.

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 and noise environmental impact of the business.

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

Despite the company's low environmental impact, from the outset, it has focused on environmental protection and appointed two persons to manage environmental aspects, one of whom, the HSQE manager, represents senior management.

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

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), and after their use in research operations, waste is recovered and stored under specific conditions until it is collected by a specialized company.

The water rejected after use is mainly coming from washing machines and from kitchen sinks located in various laboratories and common spaces of the company.

The Company has no regulatory obligation to make a follow-up of the solvents or volatile issues of organic compounds (COV) for the rejections in link to the use of solvents manipulated under extractors. The company has appointed a service provider that specializes in removing and recycling chemical waste. Before collection, which takes place two or three times a year, the company stores its waste in appropriate containers in dedicated premises (a storeroom).

In 2015, the quantity of hazardous laboratory waste sent to a specific center (packaging and soiled glass, chemical waste) totaled 23 tons. The company considers that the quantity of waste that it discharges into the city of Lyon's wastewater treatment system is low, as most waste is recovered during handling. The Company rejects no liquid effluent in waste water.

Furthermore, the company has initiated the following recycling actions:
- Sorting of plastics and caps;
- Sorting of paper and cardboard;
- Sorting of ink cartridges; and
- Sorting of batteries.

In 2015, the quantity of paper and cardboard removed totaled approximately 4.56 tons. The sorting and packaging is made by the Centre de tri of Vaux en Velin (69) and Bourgoin Jallieu (38) following the closure of the office of Decines (69) for a recycling in industry paper-maker.

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

- external resources, comprised of purchases of specific containers and expenses associated with services subcontracted to waste specialists for a total €26 thousand euros in 2015 ;
- 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 "integration training", during which the Safety-Environment department provides information on environmental practices that have been implemented. At such time, employees are provided with a waste management procedure.

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 soundproofing casing. Accordingly, the company deems that it has minimized the risk of noise pollution.

With respect to sustainable resource use, the company is concerned by the management of its water and energy consumption.

The company's consumption of municipal water is mainly for sanitary purposes, although it also uses municipal water to produce distilled water.

The building that the company occupies with other companies has no individual meters that enable it to precisely know how much water it consumes. The landlord bills water costs on the basis of the floor area that each tenant occupies. Based on the amount of expenses chargeback as part of its property expenses, the company has estimated its concumption of water.

In addition, the company buys bottled water for employee's personal consumption. Lastly, certain research operations require purified water, which is supplied in water canisters.

Consumption	**2 015**	**2 014**
bottled water	10	8
distilled water	12	9
water - consumer	6 807	5 437
water (m3)	**6 829**	**5 454**

With respect to energy, the company consumes electricity only. As is the case for water, there are no individual meters. Based on the amount invoiced as part of its property charges, the company estimates its kWh consumptions. Gas consumption exist but is minor.

consumption	**2 015**	**2 014**
electricity (kWh)	1 185 050	695 851

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. In certain premises, motion detectors that automatically turn off lights have been installed. The company has also adopted and is gradually implementing a plan to replace old generation light bulbs with low consumption light bulbs.

With respect to the environment and impact on climate change, the company considers that the quantity of greenhouse gases it emits in connection with its business is very limited. Its activities do not require combustion.
In light of the above factors and the company's limited impact, no provisions or guarantees for environmental risks have been recognized to date.

8.4 Information on societal commitments to promote sustainable development, as required by Article R. 225-105-1 of the French Commercial Code

8.4.1 Territorial, economic and social impact of the company's business

Because of its activity (research and development), the Company considers that its environmental impact is low. The activities of the Company generate no particular noise and visual pollution for its employees or for the waterside people.

Adocia has been based in Lyon since its creation, and it endeavors to be active and involved in its local area at various levels:

- In nine years, the company has hired over 100 persons, most of whom are 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 (seven at the end of December 2014) and a certain number of interns in order to train them (four over the year 2015). Furthermore, at its level, the company is attractive to and offers professional prospects for scientists, researchers and technicians in the life sciences.
- In 2015, the company's payroll expenses and social security contributions accounted for nearly 37% of total expenses.
    - 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 houses) or organizations specialized in conducting clinical trials, known as contact research organizations (CROs). These external expenses account for nearly 46% of the total expenses, and 79% of external expenses of the Company.
    - In this connection, at the local level, the company has created partnerships with the Lyon veterinary school and Biomatech for conducting its preclinical trials. It also uses the services of numerous consulting firms in the area (patents, finance, lawyers). The premises that it leases are owned by the city of Lyon.
- The process for the selection of suppliers complies with pharmaceutical regulations and takes into account criteria such as proximity, excellence and research ethics. Due to its size and the social and environmental stakes noted, the company does not audit its suppliers on CSR issues.

8.4.2 Fair practices

With respect to the risk of corruption, the company considers that it has set up mechanisms, relying on effective internal controls, that enable it to prevent this occurrence. Separating tasks associated with payments is one of the means put in place for avoiding possible errors or embezzlement.

Concerning the choice of suppliers, comparative quotations are systematically requested above a certain expenditure threshold. In connection with its research and development activities, the company is obliged to comply with standards in effect (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 Euronext-Paris stock exchange 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.

8.4.3 Public health issues

The health and safety of consumers is at the heart of the company's business: developing innovative medicine for everyone, everywhere.
The company develops drugs based on therapeutic molecules that have already been approved. Using its two proprietary technologies, BioChaperone® and DriveIn®, 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.

8.4.4 Actions taken to promote human rights

The company endeavors to comply with the laws in force 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 Chapter 17.7 of this reference document.

9 REVIEW OF THE COMPANY'S RESULTS AND FINANCIAL POSITION

Readers are invited to read this analysis of the company's financial position and results in conjunction with the financial statements prepared in accordance with IFRS for the fiscal years ended December 31, 2014 and December 31, 2015, as well as the notes to the consolidated financial statements prepared in accordance with IFRS, in Chapter 20.1 of this reference document, and all other financial information included herein. Readers may also review the description of research activities provided in Chapter 6 entitled "Overview of Activities".

The consolidated financial statements prepared under IFRS are presenteted in paragraph 20.1 of this reference document. Only corporate financial statements prepared under French Gaap are legitimately legal and are reproduced in annex of this reference document with the statutory auditor's reports.

9.1 Overview

ADOCIA is a biotechnology specialized in the development of innovative therapeutic protein formulations based on molecules already approved. It has high level of expertise in the field of insulin. The technological platform, called BioChaperone® intends to improve the therapeutic protein efficacy but also their ease of use for patients.
The outcome of this research and the commercial development of the results obtained is a long-term project. The company's financial statements show primarily research and development expenses, which, for the most part, have been financed by capital increases, Bpifrance reimbursable advances and grants, and the research tax credit.

Since the company's inception, and before its IPO, it has raised over €27 million through capital increases subscribed, in particular, by the company's founders, Messrs. Gérard, Olivier and Rémi Soula, and institutional investors (IdInvest, Amundi, Viveris, BioAm, SHAM and InnoBio). In 2012, the company was listed on the Euronext regulated market in Paris and raised over €27.4 million (excluding transaction expenses). In March 2015, it completed a private placement of nearly €32 million by issuing new shares for healthcare specialized investors, in particular from the US.

In 2009, the company recorded its first revenues when it concluded research and cooperation agreements. At the end of 2011, a major license agreement was signed with the Eli Lilly group, from which it received an up-front payment of €7.6 million in early 2012. In July 2013, the company announced the end of this cooperation agreement, thereby recovering its rights to develop ultra-fast-acting insulin analogs and giving it the possibility of conducting its own clinical trials to obtain "proof of concept".

Following the clinical results achieved in 2013 and during the year 2014, Adocia has convinced Eli lilly to renew their collaboration. On December 19, 2014 a licence agreement was signed, related to the development of an ultra-rapid insulin based on BioChaperone technology. ADOCIA received at end of December 2014 a non-refundable initial upfront-payment of USD 50 million (EUR 41 million).

The year 2015 was marked by intense activity in the framework of this partnership with the launch of three clinical studies on BioChaperone Lispro. In parallel to these trials with the U100 formulation, a formulation twice as concentrated U200 has been tested during a pilot bioequivalence study with the U100 formulation. The positive results of this test, published in December, allowed Adocia to receive a milestone payment of $10 million. This is the first milestone payment received under the license agreement that provides for a potential $520 million if the product reaches certain clinical development milestones, regulatory and certain sales targets.

The year 2015 was also intensive for projects financed on its own by Adocia.

Finally, in December 2015, the company celebrated its 10th anniversary during a day gathering employees, individuals and companies that have contributed to its success.

The company's financial statements have been prepared in accordance with the standards and interpretations published by the International Accounting Standards Board (IASB) and adopted by the European Union as of the date the financial statements were prepared. These financial statements as of December 31, 2015 were approved by the company's board of directors at its meeting held on March 15, 2016.

9.2 Comparison of the last two fiscal years

9.2.1 Components of the net income

The table below summarizes the company's income statement prepared in accordance with IFRS rules for the fiscal year ended December 31, 2015, and provides a comparison with fiscal year 2014:

(IFRS - EUR thousands)	**FY 2015 (12 months)**	**FY 2014 (12 months)**
Licencing revenues	19 888	383
Research and collaborative agreements	17 048	321
Revenue (a)	**36 936**	**704**
Research tax credit	6 768	3 461
Grants, public financing	1 050	(2)
Other revenues (b)	**7 818**	**3 459**
Operating income (a) + (b)	**44 753**	**4 163**
Research and development expenses	(28 625)	(17 006)
General and administrative expenses	(6 025)	(4 319)
Operating expenses	**(34 651)**	**(21 324)**
OPERATING INCOME / (loss)	**10 103**	**(17 161)**
FINANCIAL INCOME/ (loss)	**2 118**	**524**
Tax	333	(4 078)
NET PROFIT/ (loss)	**12 553**	**(20 715)**
Base earnings per share (€)	1,88	(3,33)
Diluted earnings per share (€)	1,80	(3,33)
GROUP NET PROFIT/LOSS	**12 553**	**(20 715)**

Operating income:

The operating income of the Company resulted from the licensing and research agreement and also from the public financing of research expenses. They amounted respectively to EUR 4.2 million and EUR 44.7 million, for the fiscal years ended December 31, 2014 and December 31, 2015, according to the following breakdown:

(IFRS - EUR thousands)	FY 2015 (12 months)	FY 2014 (12 months)
Licencing revenues	19 888	383
Research and collaborative agreements	17 048	321
Revenue (a)	**36 936**	**704**
Grants, public financing and research tax credits (b)	7 818	3 459
Operating income (a)+(b)	**44 753**	**4 163**

Revenue in 2015 amounted to EUR 37 million compared to EUR 0.7 million for the fiscal year ended 2014, representing an increase by EUR 36.3 million explained by the following items:

Licensing revenue in year 2015 amounted to EUR 19.9 million and included:

- Accounting amortization for EUR 10.7 million of the initial USD 50 million upfront payment received from Lilly in December 2014. In IFRS rules, this payment was recognized in licensing revenues linearly over the duration of the clinical development plan, as anticipated at the time of the signature of the agreement. Last year, due to the execution of the contract on December 18, 2014, this amortization had a slight impact on revenue (EUR 0.4 million).
- Milestone payment of USD 10 million, or EUR 9.2 million, received from Lilly following positive results of a pilot bioequivalence clinical study. This is the first milestone paid pursuant to the contract which includes a potential total amount of USD 520 million in development and commercial milestones.

Revenue from research and collaboration agreement during 2015 amounted to over EUR 17 million, mainly reflecting Lilly's financial coverage of all internal and external costs incurred by Adocia for the development of the licensed project. Last year, over the same period, revenue of EUR 0.3 million resulted solely from feasibility studies contracts related to the formulation of monoclonal antibodies. In 2015, these contracts continued and generated a total EUR 0.2 million in revenue.

Public funding for research expenditures consisted primarily of the French research and development tax credit. It amounted to EUR 6.8 million in year 2015, compared to EUR 3.5 million in year 2014. This significant change reflects increased activity supporting the development of our projects.

Additionally, the reimbursable advance of an initial EUR 2.25 million received from Bpifrance on a bone reconstruction project (osteoporosis) was cleared out during 2015. Consequent to the decision of a partial failure of the program in 2015, an amount of EUR 1.05 million was forgiven and recognized as a grant. The remaining amount of the advance which was not yet reimbursed (EUR 0.5 million) was paid by Adocia on September 30, 2015.

Operating expenses:

The table below gives a breakdown of the operating expenses by business function for the fiscal years ended December 31, 2015 and 2014:

EXPENSES BY FUNCTION (in € thousands)	12/31/2015	12/31/2014
Research and development expenses	(28 625)	(17 006)
General and administrative expenses	(6 025)	(4 319)
Operating expenses	**(34 651)**	**(21 324)**

Research and development expenses primarily include payroll costs of employees assigned to research and development operations, subcontracting costs (including preclinical and clinical studies), intellectual property rights expenses and costs of materials (reagents and other consumables) and pharmaceuticals products. These expenses amounted respectively to EUR 17 million and EUR 28.7 for

the fiscal year ended on December 31, 2014 and 2015. These expenses represent more than 82% of the total operating expenses for year 2015.

General and administrative expenses include expenses for employees not directly working on research and development, as well as expenses for services related to management, the business development of the Company and its subsidiary in the United States. General and administrative expenses amounted respectively EUR 4.3 million and EUR 6 million for the fiscal year ended on December 31, 2014 and 2015. The rise for the year 2015 is mainly due to the increase of the payroll expenses (including shares-based payments) and the general and administrative expenses of the American subsidiary created in February 2015.

The table below gives the breakdown of the operating expenses by nature of expenses for the fiscal years ended December 31, 2014 and 2015:

(IFRS - € thousands)	**FY 2015 (12 months)**	**FY 2014 (12 months)**
Purchases used in operations	1 133	961
Payroll expenses	12 690	11 025
External expenses	20 119	8 319
Taxes and contributions	240	622
Depreciation, amortization and provisions	468	397
Operating expenses	**34 651**	**21 324**

The cost of supplies and consumable materials amounted to EUR 1.1 million and increased by 18% compared to the previous year. This change results from the increase of purchase in connection with the intensification of clinical studies.

Personnel expenses increased by 15% between the two periods, reflecting, first, the increase in staff, and secondly, the Company's share-based compensation policy implemented for the benefit of all employees (in the context of the Company's 10th anniversary) and for the benefit of a part of R&D staff. These were recorded under IFRS at fair value of the equity instruments granted in the amount of 2.6 million euros over the year. In 2014, this amounted to 3.4 million euros.

Excluding these element that have no impact in French GAAP, nor on the cash position of the Company, payroll expenses totaled 10.1 million, up EUR 2.4 million (+31%) compared to 2014. This increase is explained mainly by recruitments made in 2015 in order to support the development of project. The averaged Full Time Equivalents (FTEs) went from 74.6 in average in 2014 to 93.9 FTE in 2015.

External expenses include essentially preclinical and clinical development costs, subcontracting expenses as well as intellectual property expenses.
These expenses increased by almost EUR 12 million, from EUR 8.3 million in 2014 to EUR 20.1 million in 2015. This change results from the intensification of the clinical development leading to the increase in sub-contracting related to:

- Preparation, production and release of clinical batches needed for the clinical studies that took place in 2015, and also for the studies provided early 2016,
- Management of the clinical studies conducted in year 2015, especially on the insulin products, and subcontracted to Profil GmbH (*Clinical research Organization*).

Taxes amounted to EUR 0.2 million, decreasing by EUR 0.5 million compared to last year, due to the reduction in the contribution tax on added value (CVAE) in 2015.

Net Financial result:

Net financial income totaled EUR 2.1 million in 2015, compared to EUR 0.5 million in 2014, representing a EUR 1.6 million increase. This situation is mostly due to net foreign exchange gains recognized during the year and also interests received on cash invested over the year 2015.

The Company's cash investment policy favors the liquidity, the total absence of capital risks and, as far as possible, guaranteed performance.

Income Tax expenses:

Last year, with EUR 41 million net sales recognized according to French GAAP, the Company had a net profit before tax of EUR 24.8 million. The deferred tax losses that could be carried forward on this profit were limited to a maximum amount of EUR 12.9 million. As a consequence, the taxable profit for 2014 amounted to EUR 11.9 million and led to the recognition of a total amount of tax of EUR 4.1 million, combined with an exceptional contribution of EUR 0.1 million.

In 2015, with a net fiscal loss amounting to nearly EUR 5 million, no income tax expense was recognized. The Company charged back a part of its net loss on the 2014 positive result, thus generating a tax receivable (carry back) of EUR 0.3 million.

The remaining deferred losses to be carried forward, after imputation of the fiscal year 2015, amounts to EUR 41 million. This loss carryforward is not time-barred. Since the company cannot determine with certainty when its cumulated deferred tax loss may be used, no deferred tax asset has been recognized for this loss.

Net Profit:

The net profit for the year 2015 amounted to EUR 12.6 million compared to a net loss of EUR 20.7 million for the year 2014. The profit per share stands at EUR 1.8 compared to a loss per share of EUR 3.3 last year.

9.2.2 Principal balance sheet items

Current assets:

Current assets totaled EUR 50.8 million and EUR 86 million on December 31, 2014 and 2015.

- The « cash and cash equivalents » item went from EUR 49.8 million as of December 31, 2014 to EUR 72.1 million as of December 31, 2015. This increase of more than EUR 22 million results from a private placement realized in March 2015 for EUR 30 million (net of fees), from payments made by Lilly under the research and collaborative development contract and from the receipt of a first USD 10 million first milestone payment in December.
- Other current assets went from EUR 0.7 million on December 31, 2014 to EUR 8.7 million on December 31, 2015. This increase of EUR 8 million is due primarily by the Company's tax change situation.

Indeed, for the year 2015, this item includes the Research Tax Credit which is generated with the expenses of the year and whose reimbursement request will be completed in 2016 for an amount of EUR 6.8 million. Last year, as the net income was positive, the Research Tax Credit has been fully set off against the income tax, the net residual debt amount thus disclosed as liability on the income tax item (and no longer in tax receivable).

Non-current liabilities:

Non-current liabilities comprised three items: "long-term financial debts", "long-term provisions" and "other non-current liabilities". The total amount of non-current liabilities at the end of fiscal years 2014 and 2015 totaled EUR 30.7 million and EUR 20.6 million, respectively.

- « The other non-current liabilities » include the long term part of the initial up-front payment received from Lilly for a total of USD 50 million (EUR 40.7 million). Under IFRS rules, this amount is recognized in licensing revenues linearly over the duration of the clinical development plan, as anticipated at the time of the signature of the agreement. Some of these EUR 40.7 million has been recognized in revenues in 2014 (for EUR 0.4 million) and in 2015 (for EUR 10.7 million). The remaining EUR 29.6 million amount is recognized in other current liabilities (short term part of EUR 10.8 million) and in other non-current liabilities (long term part of EUR 18.8 million).
- « The long term financial debts » correspond to reimbursable advances granted by Bpifrance and COFACE. The balance sheet value of these advances is measured at their amortized cost in accordance with IFRS rules for the fiscal year ended 2014 and 2015 for an amount of EUR 0.7 million.
- « Long-term provisions » mainly comprise provisions for retirement benefits, which totaled EUR 0.4 million for the fiscal year 2014 and EUR 1 million for the fiscal year 2015.

Current liabilities:

Current liabilities amounted to EUR 19.3 million for the fiscal year 2014 and EUR 20.4 million for the fiscal year 2015. They included:

- Current suppliers liabilities for EUR 2.6 million in 2014 and EUR 5.5 million in 2015,
- Short-term financial debt for EUR 0.1 million in 2015 compared to EUR 1.6 million in 2014 ; this item included in year 2014 reimbursable advance received from Bpifrance which was ended during the year 2015 with an amount recognized in grant (EUR 1.05 million) and an amount reimbursed (EUR 0.5 million),
- Other current liabilities for EUR 15 million in year 2014 and 2015, of which EUR 10.8 million correspond to the short term portion of the amortization of the up-front payment received from Lilly.

10 CASH AND EQUITY

10.1 Information on the company's equity, liquidities and sources of financing

Readers are invited to review notes 3.9 and 3.10 of the notes to the consolidated financial statements prepared in accordance with IFRS for the fiscal years ended December 31, 2014 and December 31, 2015, which are presented in Chapter 20.1 of this reference document.

10.1.1 Equity financing :

Net changes in equity are, to a large extent, explained by the losses recognized in fiscal years 2014 and 2015.

The company received a total of about €87 million in the form of capital increases between its creation and the filing date of this reference document:

- €11,999,999.97 was raised in a first round of equity financing carried out in October 2007 and supplemented in December 2007,
- €9,023,548.80 was raised in connection with a capital increase carried out on November 2, 2009,
- €4,976,665.44 was raised in connection with various exercises of stock warrants in fiscal years 2009 and 2010;
- €27,362,288.08 was raised from the company's stock exchange listing in February 2012, which was carried out by an initial public offering in France and an institutional placement in France and certain other European countries, which, in each case, concerned new shares,
- €31,964,991.80 was raised end of March 2015, through a private polacement of 621,887 Company's shares from private investors specialized in health, in particular American, which concerned new shares.

	Share capital						
(in € thousands)	Number of shares	Amount	Paid-in capital	Reserve	Net profit / (loss)	Other comprehensive income (OCI)	Total equity
Balance at 12/31/2013	**6 211 876**	**621**	**48 810**	**-26 136**	**-4 293**	**128**	**19 130**
Profit for the year 2014					-20 715		-20 715
gain (losses) on actuarial adjustments on defined pension liabilities						-69	-69
translation adjustment							0
Comprehensive income for the period					**-20 715**	**-69**	**-20 783**
allocation of profit for the year 2013				-4 293	4 293		0
increase in capital							0
costs of capital increases							0
Exercise of equity instruments (warrants)	4 200	0	0			12	12
Share-based payment				3 328			3 328
Liquidity Contract - Elimination of treasury shares			288	531			819
Total shareholder relations	**4 200**	**0**	**287**	**-435**	**4 293**	**12**	**4 158**
Balance at 12/31/2014	**6 216 076**	**622**	**49 097**	**-26 571**	**-20 715**	**71**	**2 505**
Profit for the year 2015					12 553		12 553
gain (losses) on actuarial adjustments on defined pension liabilities						-629	-629
translation adjustment							0
Comprehensive income for the period					**12 553**	**-629**	**11 924**
allocation of profit for the year 2014				-20 715	20 715		0
increase in capital	621 887	62	31 903				31 965
costs of capital increases			-2 152				-2 152
Exercise of equity instruments (warrants)	8 400	1	33				34
Share-based payment				2 903			2 903
Liquidity Contract - Elimination of treasury shares			-211	84			-127
Total shareholder relations	**630 287**	**63**	**29 573**	**-17 728**	**20 715**	**0**	**32 623**
Balance at 12/31/2015	**6 846 363**	**685**	**78 670**	**-44 299**	**12 553**	**-558**	**47 052**

10.1.2 Debt financing

As of the filing date of this reference document, the company has received non-interest bearing reimbursable assistance for its research from Bpifrance and Coface, for a total amount of €3.6 million. As of December 31, 2015, the amount still owed on these advances was €0.9 million.

For additional details on the reimbursable advances, readers may also review Chapter 22.1 of this reference document.

In addition, the company uses other types of financing vehicles to finance purchases of laboratory equipment. As of December 31, 2015, future obligations under these finance leases totaled €89.000.

10.1.3 Off-balance sheet commitments

The company's off-balance sheet commitments as of the filing date of this reference document are described in note 7 of the notes to the corporate financial statements prepared under French GAAP, which are presented in Chapter 20.3 of this reference document.

10.2 Cash flows

The table presented below shows changes in the net cash between the fiscal years ended December 31, 2014 and December 31, 2015:

(IFRS - € thousands)	**FY 2015 (12 months)**	**FY 2014 (12 months)**
Net cash flow generated by operating activities	(6 216)	30 560
Net cash flow in connection with investment transactions	(1 304)	(174)
Net cash flow in connection with financing transactions	29 782	
CHANGES IN NET CASH	**22 262**	**30 386**
Cash and cash equivalents at the start of the year	49 800	19 415
Cash and cash equivalents at year-end	72 062	49 800

10.2.1 Cash flows from operations

For the fiscal year 2015, the net cash flow dedicated to operations is amounted to €6.2 million. It includes reimbursements by Lilly internal and external expenses incurred by the project Adocia BioChaperone Lispro and the first milestones payment under license agreement (€ 9.2 million received in December 2015). Adjusted for the latter, the consumption of cash required for the operation amounted to € 15.4 million in 2015.
Last year, the payment by Eli Lilly of the initial up-front payment of €41 million (USD 50 million) set in the licencing agreement signed on December 18, 2014 has helped generated a positive cash-flow of €30.6 million.

10.2.2 Cash flow from investments

The cash needed for the capital expenditure of the Company amounted to €0.8 million in 2015. During 2015, the Company increased its investment in equipment and facilities to support its growth.

10.2.3 Cash flows from financing transactions

In 2015, net cash flow from financing operations resulted primarily from the private placement that has generated a cash flow of almost €30 million (net of costs), partially offset by the repayment of balance of the repayable advance to Bpifrance for €0.5 million.

10.3 Restrictions on the use of equity

None.

10.4 Future sources of financing required

With nearly €72 million in cash and cash equivalents at December 31, 2015 The Company believes have the resources to finance its operating expenses for at least the next 24 months from the filing date of this reference document.
The amount repayable advances Bpifrance amounting to €0.8 million at the end of December 2015 (see paragraphs 22.1, 22.2 and 22.3 of this reference document for details on these reimbursable advances), the net cash of the Company amounts to €71.2 million.

11 INVENTIONS, PATENTS, LICENSES, TRADEMARKS AND DOMAIN NAMES

11.1 Innovation policy

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

These inventions concern innovative therapeutic treatments based on combinations of its proprietary technologies (BioChaperone® and DriveIn®) with therapeutic agents (proteins, cytotoxic agents) approved in Europe and the United States. Inventions based on combinations of therapeutic proteins with small proprietary or non-proprietary molecules have also been made. In 2013, the Company also pursued the development of a new invention involving nanoparticles that comprise a cytotoxic agent and a copolymer (DriveIn® technology).

Since it was founded, Adocia has created inventions in several therapeutic domains, such as the healing of chronic wounds and the treatment of diabetes with insulin therapy. With its DriveIn® technology, Adocia is now also active in the oncology field.

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, the training of employees, and its work methods.

Furthermore, the inventions that Adocia develops are cross-disciplinary and cover various scientific, chemical, physicochemical, analytical and biological fields. To meet this challenge, teams of experts have been formed in each discipline. The various teams are coordinated during regular working meetings held for each project. In addition, every two weeks, each management-level scientist presents a briefing, in the form of a bimonthly report, on scientific advances.

Mr. Gérard Soula has significant research and innovation management experience, with over 30 years' experience in this field. Mr. Olivier Soula, Vice-President and R&D Director, has 10 years of experience in R&D management, first with Flamel Technologies and then with Adocia.

Adocia has set up an attractive compensation policy for inventions in order to promote innovation within the company. An internal memorandum explains the conditions under which employees who develop inventions are entitled to the additional compensation prescribed by the French Industrial Property Code, and provides for payment of attractive lump-sum fixed compensation when a priority patent application is extended or a patent is issued in Europe or the USA, as well as variable compensation that increases in accordance with sales generated by the relevant invention.

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

11.2 Patents and patent applications

11.2.1 Industrial property protection policy

The success of the company depends at least in part on its capacity to protect its inventions, primarily by obtaining and renewing patents in Europe, the United States and the rest of the world. An active policy is continued to protect products under clinical development (offensive strategy) and also to protect alternative solutions (alternative strategy), and also to consider defensive solutions (defensive

strategies). Patent applications are qualified as (i) protection of core business, (ii) protection of alternative solutions and (iii) defensive applications.

Since March 16, 2013, priority applications are only in France since it is no longer necessary to apply for an American patent in order to be recognized. Before the new regulation became effective 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.

The patent portfolio is analyzed periodically and applications for inventions no longer under development and that cannot be transferred are abandoned for reasons of cost control.

An invention declaration form has been created to describe the invention in question and designate the inventor(s), mentioning their respective contributions.

Also, direct extensions in USA are filed simultaneously to PCT extensions in order to have direct and faster american proceedings.

The company's patents filed or in the course of being filed are the property of the company because their inventors are employees, except for Mr. Gérard Soula for whom all rights to his inventions (i) have been ceded to the company as stipulated in the accord signed by the principal shareholders of the company on December 15, 2009, which stated that the said accord shall be null and void when stocks are traded on the Euronext in Paris on February 20, 2012 and (ii) since that date, are ceded to the company in compliance with a contract for the transfer of intellectual property rights between the company and Mr. Gérard Soula. In the case of company employees, each labor contract contains a clause covering inventions and so all inventions legally belong to the company as stipulated in article L.611-7 of the Intellectual Property Code. In addition, transfer agreements are systematically signed for each invention every time a State regulation applies.

At the present time, 30 inventions are protected by patent application filings for 30 disctinct families. Adocia's portfolio therefore contains more than 150 patents and patent applications belonging to the company, most of which (106) are still being examined by patent authorities.

11.2.2 Type and coverage of patents and patent applications held by the company

The core of the company's patent portfolio involves patents and patent applications protecting BioChaperone® molecules (polymers, oligomers and small organic molecules) that can interact with therapeutic proteins/peptides to improve their properties. The following table lists the patents and patent applications in the name of Adocia that protect families of polymers, oligomers or of small organic molecules (table updated on 31 december 2015)

Families protecting polymers and small organic molecules		
Family	**1st Priority***	**Title**

* The priority date of a patent is the date of the first application in France and/or the United States (or *via* PCT for family 39). Patents are granted for 20 years from their application date (the date when national, European or international applications were deposited, with the stipulation that European and international patent applications must be deposited within 12 months of the priority patent application). Furthermore, when products are registered (a Marketing Authorization is granted) patents may receive a maximum extension of their protection of 5 years and 6 months (corresponding to being granted a Complementary Certificate of Protection and a 6 month extension for pediatric uses).

F03	09/26/2006	Dextran functionalized by hydrophobic amino acids
F13	10/06/2008	Polysaccharides with functional carboxyl groups substituted with a derivative of a hydrophobic alcohol
F29	12/23/2009	Anionic polysaccharides functionalized by a derivative of a hydrophobic acid
F30	04/08/2010	Polysaccharides with functional carboxyl groups substituted with hydrophobic derivative with a spacer at least trivalent
F35	05/10/2011	Functionalized oligosaccharides
F43	11/13/2012	Substituted anionic compounds composed of a skeleton on a small number of sugar units

The second aspect of the company's portfolio concerns patents and patent applications protecting complexes formed between BioChaperone® polymers and proteins of interest. These molecular complexes can be demonstrated using a variety of methods. The formation of complexes improves the useful properties of the protein. Patents and patent applications in the name of Adocia protecting families of complexes are listed in the following table (table updated on 31 december 2015):

Families protecting complexes		
Family	**1st Priority***	**Title**
F01	09/26/2005	Amphiphilic-PDGF polymer complex
F05	07/27/2007	Complex between an amphiphilic polymer and an osteogenic protein belonging to the family of BMPs
F12	09/26/2008	Complex composed of a polysaccharide and an HBP

Patents and patent applications protecting formulations of BioChaperone® polymers or small molecules with therapeutic proteins or complexes are the third aspect of Adocia's portfolio. In addition, all products under clinical development are covered by patents/patent applications.

Patents and patent applications in the name of Adocia protecting formulations are listed in the following table (table updated on 31 december 2015) :

Families protecting formulations		
Family	**Priority***	**Title**
F18	11/19/2008	New form of administration of complexes of osteogenic proteins
F21	03/27/2009	Formulation of fast acting recombinant human insulin
F33	08/10/2011	Solution for injection at pH 7 comprising at least one basal insulin whose pI is between 5.8 and 8.5
F36	08/09/2014	Stable pharmaceutical composition comprising PDGF
F37	01/09/2012	Solution for injection at pH 7 comprising at least one basal insulin whose pI is between 5.8 and 8.5 and a substituted co-polyamino acid
F39	09/18/2012	Stable pharmaceutical composition containing an aqueous solution of an antibody derived from a therapeutically active protein
F40	08/10/2012	Process for lowering the viscosity of solutions of proteins at high concentrations
F42	09/10/2012	Aqueous solution of a protein at high concentration with reduced viscosity
F44	11/13/2012	Formulation of fast acting insulin comprising a substituted anionic compound

F45	11/02/2011	Formulation of fast acting insulin comprising an oligosaccharide
F46	02/12/2013	Solution for injection at pH 7 comprising at least one basal insulin whose pI is between 5.8 and 8.5 and a carboxylated anionic compound and hydrophobic moieties
F47	02/12/2013	Solution for injection at pH 7 comprising at least one basal insulin whose pI is between 5.8 and 8.5 and an anionic polymer rendered hydrophobic
F50	14/05/2014	Formulation of fast acting insulin comprising a substituted anionic compound and a polyanionic compound
F51	14/05/2014	Composition of fast acting insulin comprising a substituted anionic compound and a polyanionic compound
F52	14/05/2014	Aqueous composition comprising at least a protein, a solubilizing agent, its preparation and its uses
F54	11/16/2015	Composition of fast acting insulin comprising a substituted anionic compound and a polyanionic compound
F56	11/16/2015	Composition of fast acting insulin comprising an anionic compound
F57	11/19/2015	Composition of fast acting insulin comprising an anionic compound
F58	12/28/2015	Composition of fast acting insulin comprising an anionic compound

Finally, patents and patent applications protecting nanoparticles containing a cytotoxic agent and a copolymer (Drive*In*® technology) is a fourth and new aspect of the Adocia portfolio. The patents/ patent applications in the name of Adocia protecting families of nanoparticles are found below (table updated on 31 december 2015):

Families protecting nanoparticles		
Family	**Priority***	**Title**
F48	12/24/2013	Nanoparticles containing a HA-PLA copolymer
F55	06/25/2015	Nanoparticles containing a HA-PLA copolymer

Adocia is currently active in four therapeutic domains:

- wound healing, in particular for the treatment of diabetic foot ulcers: Adocia polymers enable a notable improvement in treatments with PDGF-BB. BioChaperone®-PDGF-BB has been the subject of a phase II clinical trial and a phase III trial will be conducted;
- treatment of diabetes with:

* The priority date of a patent is the date of the first application in France and/or the United States (or *via* PCT for family 39). Patents are granted for 20 years from their application date (the date when national, European or international applications were deposited, with the stipulation that European and international patent applications must be deposited within 12 months of the priority patent application). Furthermore, when products are registered (a Marketing Authorization is granted) patents may receive a maximum extension of their protection of 5 years and 6 months (corresponding to being granted a Complementary Certificate of Protection and a 6 month extension for pediatric uses).

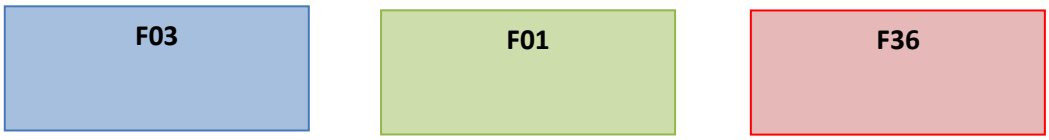
  - fast acting insulins administered before each meal. BioChaperone® polymers and small organic molecules reduce the time to onset of action of these fast acting insulins, whether human insulin or fast acting insulin analogs and
  - the combination of the best slow acting insulin, insulin glargine, with a fast acting insulin;

- therapeutic treatments with monoclonal antibodies;
- the treatment of cancers with nanoparticles formed by a cytotoxic agent and a copolymer.

Therapeutic agents (proteins, cytotoxic agents) used in these programs may have been the subject of patents filed by third parties. Some of these therapeutic agents are in the public domain whereas others are still covered by valid patents. The protection status of therapeutic agents is described in the description of each program (see below). For therapeutic agents still protected by a patent, no product resulting from the company's program can be marketed by a third party other than the holder of the said patent, or without its authorization, before the therapeutic agent enters the public domain.

The following diagrams show the different levels of patent protection implemented by Adocia around each of its flagship research programs.

11.2.2.1 Program for wound healing of chronic lesions



Patent for polymers | Patent for complexes | Patents for formulations

The aim of this program is to develop treatments to improve wound healing of chronic lesions such as diabetic foot ulcers. The therapeutic compositions under development include:

- a BioChaperone polymer® covered by the scope of patents and patent applications of family 03 of the company;
- a skin regeneration protein, PDGF-BB.

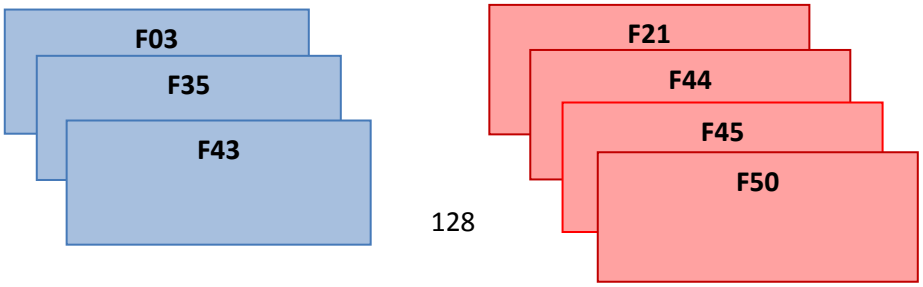
The polymer provides the protein with exceptional properties resulting from the formation of a complex: stability of the protein at room temperature for at least 3 months, resistance to enzymes in the wound and increased biological activity. The compositions resulting from this program are covered by a triple patent protection, i.e. families F03 (patents and patent applications for polymers) , patents and patent applications for complexes resulting from F01 and patent applications from formulations resulting from F36.

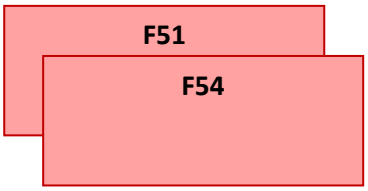
A United States and European patent have been granted for the family F01 of complexes, in particular protecting the lead complex of the program under development. A United States patent was also granted for family 03 of polymers whose scope covers the lead BioChaperone® and an intention to grant the european patent has been issued for this same family. The patent application on the lead formulation of the development program has been recently extended by PCT filing.

Concerning protein PDGF-BB, a product patented by a third party, most patents involving this protein have been in the public domain since 2010.

11.2.2.2 Program of treatment of diabetes with insulin

11.2.2.2.1 *Insuline à Action Rapide*





Patents for polymers and oligomers

Patents for formulations

The aim of this program is to develop formulations containing fast-acting recombinant human insulin or its analogs. These formulations use special BioChaperone® polymers covered by the scope of patents and patent applications of families F03 and F35, or special small organic molecules covered by the scope of the company's patents and patent applications of family F43 to accelerate passage of insulin into the blood, thereby significantly reducing the time to onset of action. The formulations resulting from this program are covered by a double protection from the company's patents and patent applications for polymers (families F03 and F35), patent applications for small organic molecules (family F43) and patents and patent applications for formulations (families F21, F44, F45, F50,F51, F54, F56, F57 and F58).

Patents and patent applications on formulations of the F21 family cover formulations implying the use of the BioChaperone polymers. The patent applications on formulations of the F44 and F50 families cover formulations implying the use of BioChaperone oligomers. The patent applications on formulations of the F51, F54 and F56 families cover formulations implying the use of BioChaperone small molecules.

Families F57 and F58 cover formulations implying the use of particular small organic molecules.

A United States and a European patent have already beengranted for family 03 of polymers.

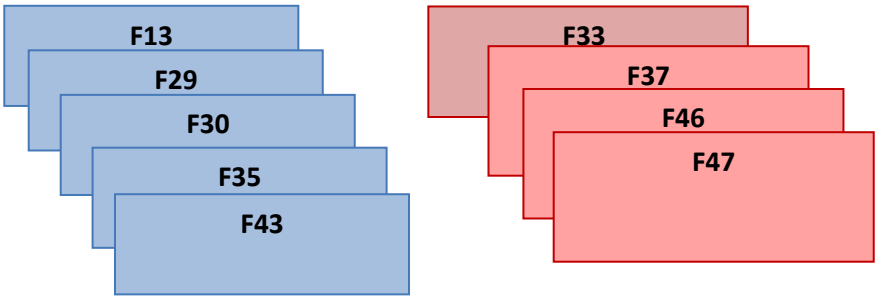
A US patent has been recently granted for the F21 family on formulations, and an intention to grant a European patent has been recently issued.

A United States patent has been granted in april 2015 for the F35 family of polymers.

The human insulin is already in the public domain. Concerning the marketed fast acting analogs, they are three:

- Humalog® (insulin lispro), patented by Eli Lilly, that entered the public domain in 2013;
- NovoLog® (insulin aspart), patented by Novo Nordisk, that entered the public domain in December; and
- Apidra® (insulin glulisine), patented by Sanofi that will enter the public domain in 2017.

11.2.2.2.2 *Combination of a slow acting insulin with a fast acting insulin*



Patents for polymers or oligomers

Patents for formulations

The aim of this program is to develop insulin formulations for the combined administration of a fast acting prandial insulin and the most efficient basal insulin, insulin glargine, as a single injection of the product. Until the present, this type of combination was not possible because the products had to be formulated at different pH value. The use of the formulations proposed by Adocia resolves this issue of compatibility and thereby enables diabetic patients to reduce the number of daily insulin injections.

These formulations are covered by a double protection from patents and patent applications:

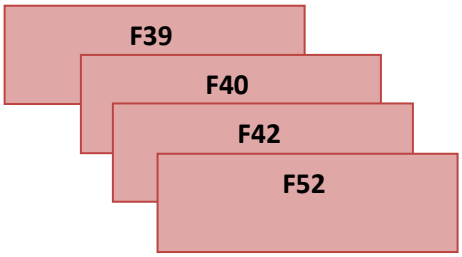
- for polymers (families F13, F29, F30 et F35) and oligomers Biochaperone (family F43) of the company, that now make it possible to mix insulin glargine with commercial prandial insulins;
- for formulations (families F33, F37, F46 and F47) of the company. The patents and patent applications on formulations of families F33, F37 and F47 cover formulation implying the use of BioChaperone polymers. Patent applications on formulation of family F46 cover formulations implying the use of BioChaperone oligomers and small organic molecules.

A United States patent and a European patent have been granted for the family of F13 products, in particular for the protection of the principal product of the program under development.

In family F33, protecting more particularly the formulations being developed, a United States patent has been granted in july 2015 and an intention to grant a European patent has recently been issued.

Insulin glargine is currently the subject of a patent held by Sanofi. Most patents and their extensions expired in 2015. Regarding fast acting insulins, the patent expiration dates are listed in the "fast acting insulin" part (see above).

11.2.2.3 Program of formulations of monoclonal antibodies



Patents for formulations

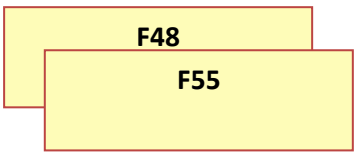
The aim of this program is to develop stable pharmaceutical compositions of monoclonal antibodies (mAb) and/or compositions with lower viscosity in solution at high concentrations. The compositions

proposed by the company involve small organic molecules enabling highly concentrated solutions of monoclonal antibodies to be prepared, while maintaining physical and chemical stability and reducing their viscosity. The stable pharmaceutical compositions created with this program are protected by the family of patent applications for formulations (family F39 and F52 of the company). Pharmaceutical compositions with reduced viscosity prepared with this program are protected by the family of patent applications for formulations (families F40 and F42 of the company).

A granting notification has been issued on 7th December 2015 for the F40 United States patent application.

Most monoclonal antibodies are proprietary proteins still protected by third party patents.

11.2.2.4 Nanoparticles program



Patent for nanoparticles

The aim of this program is to develop nanoparticles containing a cytotoxic agent and a copolymer for the treatment of cancers. The first nanoparticles obtained with this program are protected by patent application F48 of the company. These nanoparticles contain a cytotoxic agent (doxorubicin, docetaxel) and a specific copolymer.

A patent application has been filed in june 2015 for family F55. This application covers specific nanoparticles.

11.2.2.5 Programme de régénération osseuse

Patent for polymers | Patent for complexes | Patent for formulations

The aim of this program is to develop pharmaceutical formulations containing a growth factor from the family of BMPs, in particular intended for regeneration of bone tissues in vivo. The formulations proposed by the company involve special BioChaperone® polymers that form complexes with the growth factor of the family of BMPs: they improve its solubility at physiological pH and its stability. The formulations resulting from this program are covered by a triple patent protection of families F13 (patent for polymers), F5 (patent for complexes) and F18 (patent for formulations) of the company.

This growth factor belonging to the family of BMPs has been patented by a third party and most of the patent protecting the product expired in 2012.

The company has abandoned this program.

11.2.3 Patents currently in use

At the present time, no patent is in use.

11.2.4 Geographic coverage

Patent coverages are examined with respect to the importance of inventions and three predetermined strategies have been implemented by the company involving the choice of countries in which the national phase of PCT applications are in force (no later than 30 months after depositing 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 eventually Brazil, Canada, , Japan, , Australia and/or Israel;
- Strategy 3 for the core of the business: United States, Europe, Canada, China, Japan, India, Australia, Israel, Mexico, Brazil, Russia (or Eurasia), South Africa, Singapore and South Korea.

These predetermined strategies are decision-making tools enabling the company to be reactive depending on results obtained and contacts made with partners, and also enable budget control when starting the national phase. The following table lists the countries in which the company's inventions are protected by a patent/patent application. "X": patent application deposited, "D": patent granted (delivered), "w": patent application withdrawn or abandoned and "V": “European patent delivered and validated in specific countries member of the European Patent Convention (EPC)”.

Patents protecting polymers and small organic molecules				**Countries covered**															
Family	**Priorities***	FR	US	PCT	EP	AU	CA	CN	EA	IL	IN	JP	BR	KR	MX	RU	SA	SG	ZA
F03	PCT/IB2006/002666 (26/09/2006) FR07.02316 (29/03/2007)	D	D	x	V	D	x	D		D	x	D	x	D	D	D		D	D
F13	FR08.05506 (06/10/2008)	w	D	x	V	D	x	D		x	x	D	x	x	D	D		D	D

* The priority date of a patent is the date of the first application in France and/or the United States. Patents are granted for 20 years from their application date (the date when national, European or international applications were deposited, with the stipulation that European and international patent applications must be deposited within 12 months of the priority patent application). Furthermore, when products are registered (a Marketing Authorization is granted) patents may receive a maximum extension of their protection of 5 years and 6 months (corresponding to being granted a Complementary Certificate of Protection and a 6 month extension for pediatric uses).

F29	PCT/IB2009/007899 (23/12/2009) FR10.01439 (07/04/2010)	D	x	x	x														
F30	PCT/IB2010/02970 (19/11/2010) FR10.01474 (08/04/2010) FR10.00537 (02/09/2010)	D	D	x	x			D			x	x	x			x			
F35	FR11.58885 (30/09/2011) FR 11.54039 (05/10/2011)	D	D	x	x														
F43	FR12.60808 (13/11/2012) FR12.60855 (11/14/2012) FR13.51199 (02/12/2013)	D	x	x	x	x	x	x	x	x	x	x	x	x	x		x	x	x
Patents protecting complexes				**Countries covered**															
Family	**Priorities****	FR	US	PCT	EP	AU	CA	CN	EA	IL	IN	JP	BR	KR	MX	RU		SG	ZA
F01	FR05.09803 (26/09/2005)	w	D	x	V	D	D	x		D	x	D	x	D	D	D		D	D
F05	FR07.05536 (27/07/2007)	w	D	x	x	w	w	w		w	w	w	w	w	w	w		w	w
F12	FR08.05321 (26/09/2008)	w	D	x	x	w	w	w		w	w	w	w	w	w	D		w	w

Patents protecting formulations				**Countries covered**														
Family	**Priorities***	FR	US	PCT	EP	AU	CA	CN	EA	IL	IN	JP	BR	KR	MX	RU	SA	SG	ZA
F18	FR09.03803 (31/07/2009)	D	D	x	x	w	w	w		w	w	w	w	w	w	w		w	w
F21	FR09.01478 (27/03/2009)	D	D	x	x	w	w	w		w	w	w	w	w	w	w		w	w
F33	FR11.577291 (10/08/2011) FR11.62445 (12/23/2011)	D	D	x	x	x	x	x		x	x	x	x	x	D	x		D	x
F36	FR14.58417 (08/09/2014)	x		x															
F37	FR12.50224 (09/01/2012)	x	D	x	x			x			x		x						
F39	PCT/IB2012/054 950 (18/09/2012)		x	x	x														
F40	FR12.57775 (10/08/2012)	D	x	x	x														
F42	FR12.58494 (10/09/2012)	D	x	x	x														
F44	FR12.60855 (14/11/2012) FR12.60808 (11/13/2012)	x	x	x	x	x	x	x	x	x	x	x	x	x	x		x	D	x
F45	US13/287793 (02/11/2011)		x	x	x														
F46	FR13.51199 (12/02/2013)	D	x	x	x														
F47	FR13.51200 (12/02/2013)	D	x	x	x														
F50	FR14.54315 (14/05/2014)	x	x	x															
F51	FR14.54313 (14/05/2014)	w	x	x															
F52	FR14.54314 (14/05/2014)	x																	
F54	PCT/EP2015/076 727 (11/16/2015))			x															
F56	FR15.61017 (16/11/2015)	x																	
F57	FR15.61168 (11/19/2015)	x																	
F58	FR15.63380 (12/28/2015)	x																	
Patents protecting nanoparticles				**Countries covered**														
Family	**Priority***	FR	US	PCT	EP	AU	CA	CN	EA	IL	IN	JP	BR	KR	MX	RU	SA	SG	ZA
F48	FR13.63550 (24/12/2013)	x		x															
F55	FR15.55866 (06/25/2015)	x																	

A United States patent and a european patent have been delivered for the family of F13 products, in particular protecting the principal product of the program for development of the combination of a slow acting insulin with a fast acting insulin.

For family F33 covering more particularly formulations in development, an intention to grant a European patent has been issued and a United States patent has been granted.

A United states patent and a European patent have already been granted for family F01 of complexes, in particular protecting the principal the principal complex of the program for development of wound healing of chronic lesions.

Regarding the fast insulin program, several US and EP patents have already been issued.

Five new patent applications have been filed in 2015 (at 31 december), four or them are relative to formulations and one of them is relative to nanoparticles.

11.2.5 Litigations

No claims or litigations are declared.

11.3 Cooperation agreements and licenses granted by or to the company

11.3.1 Cooperation agreements

11.3.2

In November 2007, the company signed cooperation agreements with various major pharmaceutical groups.

The company did not assign the intellectual property rights in its technology pursuant to any of the agreements it signed. Furthermore, no implicit license can arise from any of the cooperation agreements that the company has concluded with its partners, as this is a prerequisite for Adocia before it signs any cooperation 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 concern an assessment of the BioChaperone® technology vis-à-vis active pharmaceutical principles that are already marketed or are under pharmaceutical development.

Trials are conducted either in the company's laboratories or in the partner's laboratories, and the costs of such trials are paid by the company's partners.

Because the company's partners have demanded confidentiality about the existence itself of these agreements, neither the field of cooperation nor the identity of the partners can be disclosed in this reference document.

On December 14, 2011, the company signed a licensing and cooperation agreement with the US pharmaceutical group Eli Lilly and Company (hereinafter "Eli Lilly"). In July 2013, Adocia and Eli Lilly decided to terminate the licensing and cooperation agreement. This enabled Adocia to recover its rights to develop ultra-fast-acting insulin analogs.

11.3.3 Licenses granted by Adocia

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 Humalog fast-acting insulin analog in conjunction with the BioChaperone® technology ("BioChaperone® Humalog"). The company granted Eli Lilly exclusive worldwide rights to BioChaperone® for the purpose of developing, manufacturing and marketing BioChaperone® Humalog. This agreement covered all potential indications for BioChaperone® Humalog. The license rights granted were based on the F03 and F21 families of patent applications and patents. In July 2013, Adocia and Eli Lilly decided to terminate the licensing and cooperation agreement. This enabled Adocia to recover its rights to develop ultra-fast-acting insulin analogs.

On December 19, 2014, Adocia et Eli Lilly announced an alliance by signing a licensing agreement related to the development of an ultra-rapid insulin Humalog (commercila product from Eli Lilly Lispro) with the BioChaperone ® (« BioChaperone Lispro »).

Within this contract, Adocia et Eli Lilly will developp BioChaperone Lispro with the aim to optimize gliucose levels during and after meal. Potential benefits of BioCHaproen Lispro include greater flexibility in the timing of insulin injections, lower variability of post-meal blood elevations, lower rates of hypoglycemia and better averall glucose

Under the terms of the agreement, Lilly is responsible for future development, manufacturing, and commercialization of BioChaperone Lispro. The total up-front and milestone payments could reach up to $570 million. Adocia received a total upfront fee of $50 million and may receive the potential future payments of up to $280 million if the product reaches certain development and regulatory milestones, and sales milestones up to $240 million. Adocia may also receive tiered sales royalties. Lilly shall also reimburse Adocia for certain research and development expenses during the terms of the agreement. A concentrated formulation of BioChaperone Lispro is also part of the agreement.

Adocia retains the right to develop and license its insulin programs unrelated to prandial ultra-rapid insulin. Patents licensed to Eli Lilly relate to ones included in F03, F021, F43 and F44.

11.3.4 Acquisition d'une licence exclusive sur une nanotechnologie (DriveIn®)

On December 9th, 2013, Adocia signed an exclusive and worldwide license agreement with the CNRS, Bordeau I University, Bordeau Polytechnic Institute and Aquitaine Science Transfert (SATT Aquitaine) on a technology, called DriveIn. This license is granted to the Company until the end of the protection of the last patent of the licensed patent family, a priori until October 30, 2029 (20 years from the filing of the PCT application), under condition of their grant, being precised that the patent applications are under examination.

As part of this agreement, Adocia obtained the right to operate, directly or indirectly, the patent application filed by Mr. Sébastien Lecommandoux and held by the signatory companies of this agreement (and owners of such patents), and in the field of human or animal health, excluding the applications in the fields of cosmetics, dermatology non-therapeutic dermatology, and dietary supplements

The patent application licensed to Adocia covers a nanoparticulate technology of drug delivery. This application covers innovative polymers comprising hyaluronic acid, a natural and hydrophilic polymer, and a hydrophobic polymer based on amino-acid. It also covers nanoparticular systems formed by these polymers, such as vesicles. The patent application is under examination and Adocia took in charge the prosecution and the fees due.

As a counterpart of the acquired rights, Adocia did agree to pay an annual fee based on a percentage of the turnover which would be realised by Adocia, directly or indirectly.

Adocia wants to adopt a dual strategy to develop this technology. On one hand, ADOCIA anticipates developping proprietary nanoparticles based on doxorubicine and docetaxel, two of the most used anticancer cytotoxic agents which could highly beneficiate from a better entrance in the solid tumor cells. On the other hand, ADOCIA intends to propose to pharmaceutical companies its DriveIn technology for optimising the eficacy of proprietary molecules.

11.4 Trademarks, trademark applications and domain names

The company holds inter alia the following trademarks and trademark applications:

- « ADOCIA », which has been registered in classes 1, 5 and 42, in France, in the European Union, in China, in Japan, in the Unites States, and in India;
- « BioChaperone », which has been registered in classes 1, 5 and 42, in France, in the European Union, in China, in Japan, and in the Unites States, and which has been filed in these same classes in India ;
- « Hinsbet », which has been registered in classes 1 and 5, in France, in the European Union, in China, in Japan, in the Unites States, and in India;
- « Betin », which has been registered in classes 1 and 5, in France;
- « Transidex », which has been registered in classes 1, 5 and 42, in France;
- « Drive*In* » et « Drive-*In* », which has been registered in classes 1,5 and 42 in France. « DRIVEIN », has been also registered in class 1,5 and 42 in the European union, in the United States, in Australia, in China, in South Korea, in Japan, in Mexico, and in Russian Federation, and which has been filed in these same classes in Canada, in India, and in Israel.

The company registers its trademarks by filing national, EU or international applications. In general, trademark registrations are granted for a period of 10 years and are renewable indefinitely. The laws of certain countries may impose specific requirements for the validity of trademarks, such as requiring that the trademark be actually used.

The company defends its trademark rights by filing oppositions against the registration of identical or similar trademarks by third parties. The company filed an opposition in France against an application by THL Concept SARL to register “Adoxia” as a trademark. That opposition became moot when the products and services against which the opposition had been field were withdrawn. On the other hand, the opposition that the company filed in India against the application of M/S Ajanta Pharma Limited to register “Audacia” as a trademark is still pending.

In France, Astellas Pharma Inc. filed an opposition against the company’s application to register “Betins”. The company withdrew its registration application, filed a new application to register “Betin”, and undertook not to use that trademark for products and/or services in connection with the treatment of urological diseases.

11.4.1 Domain names

The company currently holds the six domain names listed below:

- adocia.com, adocia.fr, adocia.eu, adocia.net, adocia.biz ;
- biochaperone.com

12 TRENDS

See section 6.3 entitled "The markets" of this reference document, which describes the epidemiological data for the pathologies targeted by the BioChaperone® technological platform, as well as, for certain pathologies, the expected evolutions and market size.

In the first months of the yea 2016, the information below has been provided by the company:

12.1 Press release of January 29, 2016

Lyon and Indianapolis, January 29, 2016 – Adocia (Euronext Paris: ADOC) and Eli Lilly and Company (NYSE: LLY) announced today the initiation of a Phase 1b clinical trial evaluating BioChaperone Lispro, an ultra-rapid formulation of insulin lispro licensed to Lilly. This formulation uses Adocia's proprietary technology, BioChaperone®, which is designed to enable the acceleration of insulin absorption.

The study, under the Adocia-Lilly partnership, aims to compare the pharmacokinetic and pharmacodynamic profiles of BioChaperone Lispro to that of Humalog® (insulin lispro rDNA origin) in 15 healthy Japanese subjects placed under euglycemic clamp.

"Japan, like other Asian countries, is confronted with a rapidly growing diabetes epidemic, and patients are in need of new treatment options," says Simon Bruce, Adocia's Chief Medical Officer. "This study should serve to allow the inclusion of Japanese patients with diabetes in the phase 3 program, in line with our objective to prepare for a global registration plan for the product."

In this double-blind, randomized, three-period crossover study, 15 healthy Japanese subjects placed under euglycemic clamp will receive three single dose administrations, separated by 1 to 14 days. Each subject will be randomly allocated to receive either three single doses of BioChaperone Lispro U100 (0.1, 0.2 and 0.4 U/kg) or one single dose of Humalog U100 (0.2 U/kg) and two single doses of BioChaperone Lispro U100 (0.1 and 0.2 or 0.2 and 0.4 U/kg) on three separate dosing visits.

Objectives also include the assessment of safety and tolerability of BioChaperone Lispro in these subjects.

This study will be sponsored by Adocia and performed by Profil Neuss in Germany.

This trial (EUDRACT 2015-004829-13) is registered and appears on clinicaltrials.gov

12.2 Press release of February 16, 2016

Lyon, France, February 16, 2016 - ADOCIA (Euronext Paris: FR0011184241 – ADOC) announces today its revenue and cash position for the full year 2015.

Cash position and indebtedness

At December 31, 2015, cash and cash equivalents amounted to EUR 72 million compared to EUR 49.8 million on December 31st 2014.

This increase of EUR 22.3 million is primarily attributed to a capital increase of approximately EUR 30 million (net of fees) completed in March 2015 with healthcare-focused investors. Cash position at the end of the year also included a USD 10 million milestone payment (EUR 9.2 million) from Eli Lilly following positive results of a bioequivalence pilot study comparing BioChaperone U200 to BioChaperone U100.

Over the full year 2015, the net amount of cash needed to finance operations amounted to EUR 15.3 million, compared to EUR 10.6 million over the same period last year.

Financial debts at the end of December 2015 totaled EUR 0.8 million. They consisted essentially of reimbursable advances received from the French agency for innovation Bpifrance Financement related to our insulin projects.

Annual revenue details for 2015

In millions of euros – IFRS rules	**2015**	**2014**	***Var. value***
Licensing revenue	19,9	0,4	*+ 19,5*
Research and collaborative development contracts	17,0	0,3	*+ 16,7*
Revenue (a)	**36,9**	**0,7**	***+ 36,2***
Grants, public funding and tax credit research (b)	7,8	3,5	*+4,3*
Operating income (a)+(b)	**44,7**	**4,2**	***+40,5***

Consolidated operating income at December 31, 2015 increased significantly to EUR 44.7 million compared to EUR 4.2 million in the same period in 2014.

Revenue of nearly EUR 37 million at December 31, 2015 resulted primarily from the collaborative and licensing agreement signed with Lilly at the end of 2014 for the development of an ultra-rapid insulin analog formulated with Adocia's proprietary Biochaperone technology.

Licensing revenue for the full year 2015 amounted to EUR 19.9 million and included:

- The technical amortization for EUR 10.7 million of the initial USD 50 million payment received in December 2014. In IFRS rules this payment is linearly amortized over the duration of the program as anticipated at the time of the signature of the agreement.

  In 2014, due to execution of the contract on December 18, 2014, this amortization had a slight impact on revenue (EUR 0.4 million).

- A milestone payment of USD 10 million, or EUR 9.2 million, received from Lilly following positive results of a pilot bioequivalence study. This is the first milestone payment paid pursuant to the contract, which includes a total potential for USD 520 million in development and commercial milestones.

Revenues from the research and collaboration agreement amounted to EUR 17 million, reflecting Lilly reimbursement of all internal and external costs related to development of the licensed project.

In 2014, revenue of EUR 0.3 million resulted solely from on-going research and collaborative contracts related to the formulation of monoclonal antibodies. In 2015, these collaborations continued and generated a total EUR 0.2 million in revenue.

Other operating income consisted of a Research Tax Credit ("Crédit Impôt Recherche") for EUR 6.8 million in 2015 compared to EUR 3.5 million in 2014. This significant change reflects increased activity supporting the development of our projects.

Additionally, the reimbursable advance of an initial amount of EUR 2.25 million obtained from Bpi on a bone reconstruction project (osteoporosis) was cleared out during 2015. Consequent to the decision of a "partial failure" of the program in 2015, an amount of EUR 1.05 was forgiven and recognized as a grant. The remaining amount of the advance which was not yet reimbursed (EUR 0.5 million) was paid by Adocia on September 30, 2015.

“Adocia strengthened its cash position through its active partnership with Eli Lilly and its fundraising carried out in March 2015. With 72 million euros and a strict and controlled management of its expenses, the Company intends to pursue its ambitious development plan”comments Valérie Danaguezian, Financial Director of Adocia.

Detail of revenue per quarter

	2015				2014			
In millions of euros - IFRS	**Q4**	**Q3**	**Q2**	**Q1**	Q4	Q3	Q2	Q1
Licensing revenue	11,8	2,7	2,7	2,7	0,4	-	-	-
Research and collaborative development contracts	6,2	3,5	4,1	3,2	0,1	0,1	0,1	0,1
Revenue	**18,0**	**6,2**	**6,8**	**5,9**	**0,4**	**0,1**	**0,1**	**0,1**

12.3 Press release of March 14, 2016

Lyon and Indianapolis, March 14, 2016 – Adocia (Euronext Paris: ADOC) and Eli Lilly and Company (NYSE: LLY) announced today positive topline results from a Phase 1b clinical trial under the Adocia-Lilly partnership evaluating BioChaperone Lispro, an ultra-rapid formulation of insulin lispro licensed to Lilly. This formulation uses Adocia’s proprietary technology BioChaperone, designed to accelerate insulin absorption.

This study was the first outpatient 14-day study comparing the effect of multiple daily injections of BioChaperone Lispro and Humalog® (insulin lispro rDNA origin) on post-prandial glycemic control relative to solid standardized meals in 36 patients with type 1 diabetes. The study also investigated the effects of different timing of administration, with treatments being injected either at mealtime, 15 minutes before, or 15 minutes after the start of a solid meal. Whereas commercialized fast-acting insulin analogs are usually injected before the meal, an ultra-rapid insulin aims to allow injection at the time of the meal, or even after the start of a meal, while maintaining a reduction in the magnitude of glycemic excursions.

“We are extremely pleased to confirm that BioChaperone Lispro consistently delivered superior post-prandial control compared to Humalog, especially after a real-life solid meal. BioChaperone Lispro proved to offer a robust performance throughout the study period,” said Simon Bruce, MD, PhD, Adocia’s Chief Medical Officer. “We also saw excellent preliminary safety results in the outpatient setting, with no observed difference between the treatments.”

In this double-blind, randomized, crossover study, 36 patients with type 1 diabetes used individualized doses of either BioChaperone Lispro or Humalog as the short acting insulin in their multiple daily injection regimen, over two periods of 14 days. At the beginning and the end of each period, patients were subject to a meal tolerance test in the clinic to compare post-prandial blood glucose profiles after identical bolus injections immediately before the meal of either BioChaperone Lispro or Humalog relative to a solid standard meal. At the beginning of the study, when injected at the time of meal, BioChaperone Lispro demonstrated a statistically significant 31 percent reduction in blood glucose excursion over the first two hours compared to Humalog. After 14 days of treatment for each treatment, BioChaperone Lispro also demonstrated a statistically significant 42 percent reduction in blood glucose excursion over the first two hours compared to Humalog, when injected at the time of

the meal. This last result demonstrates the robustness of the performance of BioChaperone Lispro on a two week period.

"This was an important study and provides our first experience with repeat doses of this ultra-rapid insulin formulation in an outpatient setting," said Thomas Hardy, M.D. Ph.D., Senior Medical Director, Lilly Research Laboratories. "We are encouraged by these results and look forward to seeing the results of additional, ongoing studies."

Both BioChaperone Lispro and Humalog were similarly well tolerated throughout the 14 days. No new or unexpected safety findings were observed and no local reactions were seen on the site of administration for either treatment.

The registry on clinicaltrials.gov for this trial (NCT02528396) has been updated.

12.4 Press release of March 16, 2016

Lyon, France, March 16, 2016 - ADOCIA (Euronext Paris: FR0011184241 – ADOC) announces today its financial results for 2015. The financial statements were approved by the board of directors on March 15th, 2016 and will be submitted to the shareholders for approval at the next general meeting on June 21st, 2016.

"2015 was marked by several clinical successes for our projects. These good results coincide with our 10th anniversary and reflect the maturity of our company. Beyond the development of our projects, Adocia has become a center of excellence in diabetes-focused innovation, thanks to its research team including more than 40 Ph.Ds. The incorporation of a subsidiary in the USA also allows us to access the best global experts as well as the US financial place." commented Gérard Soula, President and CEO of Adocia. "Today, we have adequate financial resources to work serenely for several years and we are confident in the value of our products, based on the clinical results obtained."

A conference call will be held on Thursday March 17, 2016 at 6 PM (CET)
Dial in number: (+33) 1 70 77 09 27

An audio file and a transcript in English will be available on the website of the Company
www.adocia.com

Financial Highlights

The following table summarizes the financial statements under IFRS for the years ended December 31, 2015 and December 31, 2014:

(IFRS - € thousands)	FY 2015 (12 months)	FY 2014 (12 months)
Revenue	36 936	704
Grants and research tax credit	7 818	3 459
Operating income	**44 753**	**4 163**
Research and development expenses	(28 625)	(17 006)
General and administrative expenses	(6 025)	(4 319)
Operating expenses	**(34 651)**	**(21 324)**
OPERATING INCOME / (loss)	**10 103**	**(17 161)**
FINANCIAL INCOME	**2 118**	**524**
Tax	333	(4 078)
NET INCOME / (loss)	**12 553**	**(20 715)**

The consolidated financial statements on 31 December 2015 as well as detailed explanations on the evolution of accounts are presented in the Appendix.

The results of the Company for 2015 are characterized by:

- **A strengthened cash position of EUR 72 million**, compared to EUR 49.8 million as of December 2014, as a result of the EUR 30 million increase (net of fees) in capital realized in March 2015 from a private placement and the receipt of a USD 10 million (EUR 9.2 million) milestone payment from Eli Lilly and Company (Lilly) in December.

  In 2015, the net cash needed to finance operations amounted to EUR 15.3 million compared to EUR 10.6 million last year.

- **A positive net result of EUR 12.6 million**, compared to EUR 20.7 million net loss for 2014, mainly constituted by :
  - Revenue close to EUR 37 million in 2015 (compared to EUR 0.7 million in 2014) which primarily results from the research and collaborative contract signed with Eli Lilly.
    - EUR 10.7 million for amortization of the initial payment (non-cash) received in December 2014 upon signing of the contract,
    - EUR 9.2 million related to milestone payment for BioChaperone Lispro U200,
    - EUR 17 million for the financial coverage by the partner of project-related expenses,
  - Other operating income of EUR 7.8 million, of which EUR 6.8 million in research tax credit ("Crédit d'impôt recherche") calculated on 2015 expenses,
  - Operating expenses of EUR 34.7 million (compared to EUR 21.3 million in 2014) of which 82% are dedicated to research and development activities.

    The increase in expenses is mainly related to an increase in external expenses by EUR 11.8 million between 2015 and 2014, in order to support the preparation and the conduct of clinical trials over the year.

    The EUR 1.6 million increase in staff costs between 2014 and 2015 resulted from staff recruitment and staff costs (including payments in shares).
  - A fiscal tax loss (by French standards) leading to the absence of taxes.

"In 2015, we controlled our expenses, 82% of which were dedicated to R&D, while we actively developed our projects and strengthened our organization. Besides, the strong growth in revenues as well as the private placement reinforced our cash position to reach close to 72 million euros as of end of December. This strong cash position allows us to continue this positive momentum to support the growth of the Company" commented Valerie Danaguezian, Chief Financial Officer of Adocia.

Key events in 2015:

➢ Intensive activity within the Lilly partnership

2014 ended with the signing of a major license agreement with Eli Lilly for the development of BioChaperone Lispro, an ultra-rapid insulin lispro formulation using the with BioChaperone® technology.

2015 was marked by an intense activity within this partnership, including the launch, on January 20th, of a clinical trial measuring the effect of ultra-fast insulin BioChaperone Lispro on glycemic control after the meal. After the publication, end of June 2015, of positive results from this trial, three additional trials were launched in the second half year:

- a phase 1b study of repeated administration of BioChaperone Lispro in type 1 diabetic patients,
- a phase 1b study of repeated administration of BioChaperone Lispro in type 2 diabetic patients,
- a phase 1b clinical trial realized in patients with type 1 diabetes using a pump.

Topline positive results from the first study were published on Monday, March 14, 2016 and the results of the two other studies are expected during the first half of 2016

In parallel with the U100 formulation, a formulation twice as concentrated, U200, was compared to the U100 formulation in a pilot bioequivalence study.The positive results from this trial, published in December, triggered a USD 10 million milestone payment from Lilly to Adocia. This is the first milestone payment received under the license agreement that provides for a total potential USD 520 million, if the product reaches certain clinical and regulatory milestones as well as certain sales targets.

➢ Major clinical progress throughout the product portfolio

The year 2015 was also marked by significant progress in the projects developed by Adocia on its own:

- BioChaperone Combo, the unique combination of long-acting insulin glargine and fast-acting insulin lispro. Two clinical trials were launched in 2015: the first one in 28 patients with type 1 diabetes comparing BioChaperone Combo with Humalog Mix 75/25, the second one in 24 patients with type 2 diabetes, comparing BioChaperon Combo with Humalog Mix 75/25 and separate injection of Lantus® and Humalog®.

  Positive results obtained on these studies confirmed the value of BioChaperone Combo compared to both the premix and basal bolus regimens. Adocia actively pursues the clinical development of the product with new clinical trials expected to launch in 2016.
- BioChaperone human insulin (HinsBet): the results of the phase 2a clinical study published in February 2015 showed that HinsBet acted significantly faster than Humulin® and as fast as Humalog in the first hour, which is critical for glycemic control. Based on these results, the Company pursued the development and prepared the launch of a new study planned in the beginning of 2016.
- BioChaperone PDGF-BB: the phase 3 clinical trial was ongoing throughout 2015 with the enrollment and the treatment of 252 patients. Results are expected during the first half of 2016.

Besides, the Company continued to collaborate with major pharmaceutical companies by performing feasibility studies on innovative formulation of monoclonal antibodies and pursued its research activities on the Drive*In* platform.

➢ **A strengthening of the organization and the sustainability of its facility**

From an organizational perspective, Adocia entered a new phase in its development with the recruitment of 25 people in France and the creation of a subsidiary in the United States. Hiring mainly focused on R&D positions to support the development of projects. The US subsidiary is composed of a General Manager, Steve Daly, and a Chief Medical Officer, Dr. Simon Bruce.

In 2015, the Company expanded its premises and fitted nearly 700 m² of additional laboratory and office space, resulting to a 2 709 m² facility altogether.

With the aim to sustain its presence on this site, in the center of Lyon, the Company signed a preliminary sales agreement in January 2016 for the acquisition of this property of 7,120 m². The purchase price was fixed at 5 million euros, excluding VAT and registration fees. The Company plans to finance this acquisition by bank loan. The signing of the bill sale is expected in the coming weeks.

Perspectives for 2016:

Regarding the project in partnership with Lilly, BioChaperone Lispro, we expect during 2016 the results of the studies initiated in 2015 (phase 1b clinical study in patients with type 1 diabetes using an insulin pump and phase 1b clinical study of repeated administration in patients with type 2 diabetes) and January 2016 (phase 1 study evaluating BioChaperone Lispro in healthy Japanese subjects). Further development remains confidential.

Regarding BioChaperone Combo, Adocia intends to intensify the development and to push the product up to the entry in phase 3. In 2016, two clinical studies are planned on the first semester:

- a phase 1b/2a on type 2 diabetic patients treated with basal insulin in order to evaluate the performance of BioChaperone Combo injected once daily at steady-state,
- a phase 1b/2a on type 2 diabetic patients in order to compare the control of post-meal blood glucose of BioChaperone Combo compared to a premix.

Regarding HinsBet, a first clinical phase 1b/2a study in patients with type 1 diabetes is planned, aiming to measure the glycemic control at mealtime. This study is expected to start in the coming weeks.

Regarding the diabetic foot ulcer wound healing project, Adocia is pursuing a dual strategy. In India, the results of the ongoing phase 3 clinical study are expected mid-2016. In Europe and the United States, the aim is to prepare during the second half of 2016 two clinical phase 3 studies with a PDGF compliant to European and American quality standards, cGMP.

Lastly, Adocia is actively exploring new opportunities to use its BioChaperone platform in various therapeutic areas.

12.5 Press release of March 21, 2016

Lyon, March 21st, 2016 – Adocia (Euronext Paris: FR0011184241 – ADOC), a clinical stage biopharmaceutical company focused on developing innovative formulations of existing therapeutic proteins, today announced the formation of its new Global Diabetes Medical Advisory Board (MAB) consisting of well-respected endocrinologists from the US and EU.

The MAB will serve as an ongoing key strategic resource to ADOCIA for the development of its expanding diabetes portfolio. In the near term, MAB engagement will focus on the development of BioChaperone Combo, a unique combination of the basal insulin glargine and the prandial insulin lispro, currently in phase 2.

“We are extremely proud and honored to welcome these world-leading experts in diabetes to our Medical Advisory Board,” said Olivier Soula, Deputy General Manager and R&D Director of ADOCIA. “The specific background and extensive experience of each member brings invaluable insight to ADOCIA. We are particularly looking forward to further demonstrating the value of BioChaperone Combo and optimizing the next clinical studies to advance this key program into later clinical stage development.”

The inaugural nine-member board will be chaired by Dr. Jay Skyler, Professor of Medicine, Pediatrics & Psychology at the University of Miami, Miami, Florida (USA).

“I am delighted to take the role of Chairman to ADOCIA’s Diabetes Medical Advisory Board and be part of the development of their exciting innovative products”, said Dr Jay Skyler, Professor at the University of Miami. “I am especially pleased by the depth of experience and leadership in the diabetes field represented at the board, and I look forward to contributing to the development of BioChaperone Combo, a potentially promising treatment option for many diabetic patients requiring intensive insulin therapy.”

The inaugural members of ADOCIA’s Medical Advisory Board include:

Dr Jay Skyler, MD, Chairman of ADOCIA’s Diabetes Medical Advisory Board. Dr Skyler is a Professor of Medicine, Pediatrics & Psychology at the University of Miami (USA), in the Division of Endocrinology, Diabetes & Metabolism in the Department of Medicine, of which he was the Director from 2000 to 2004; and Associate Director for Academic Programs in the Diabetes Research Institute.

Dr Vanita Aroda, MD, is a Physician Investigator at MedStar Health Research Institute (MHRI), Hyattsville (USA). Dr. Aroda also serves as Scientific Director of the MedStar Community Clinical Research Center.

Dr. Bruce Bode, MD, is a Clinical Associate Professor in the Department of Medicine at Emory University, Atlanta (USA) and a diabetes specialist with Atlanta Diabetes Associates.

Dr John Buse, MD, PhD, is a professor at the University of North Carolina, School of Medicine in Chapel Hill (USA) where he serves as the Director of the Diabetes Care Center, Chief of the Division of Endocrinology and Executive Associate Dean for Clinical Research.

Dr. William Cefalu, MD, is the executive director of Louisiana State University’s Pennington Biomedical Research Center (USA). He also holds the George A. Bray Endowed Super Chair in Nutrition.

Dr. Dan Einhorn, MD, is the President of Diabetes and Endocrine Associates as well as Clinical Professor of Medicine at the University of California, San Diego (USA). He also serves as Medical Director of the Scripps Whittier Diabetes Institute.

Dr. Vivian Fonseca, MD, is Professor of Medicine, Tullis–Tulane Alumni Chair in Diabetes, Section of Endocrinology at Tulane University Health Sciences Center (USA).

Dr. Chantal Mathieu MD, PhD, is currently Director of the Endocrinology Clinic at the University Hospital of Leuven (Belgium). She also serves as Professor of Endocrinology at the University of Leuven.

Prof. Denis Raccah, MD, PhD, is currently Professor at the Assistance Publique des Hôpitaux de Marseille (APHM) and Director of the Department of Nutrition, Metabolic Diseases and Endocrinology at the Sainte Marguerite Hospital and the Conception Hospital (Marseille, France).

13 PROFIT FORECASTS OR ESTIMATES

The company does not plan to make any profit forecasts or estimates.

14 ADMINISTRATIVE, MANAGEMENT, SUPERVISORY AND EXECUTIVE MANAGEMENT BODIES

14.1 Officers and directors

Until October 24, 2011, the company was incorporated as a société par actions simplifiée (simplified joint stock company).

The shareholders' meeting held on October 24, 2011 approved the conversion of the company into a société anonyme (corporation) with a board of directors, and adopted new corporate governance rules.

A summary description of the main provisions of the company's articles of incorporation and bylaws and of the internal rules and regulations of the specialized committees is provided in this reference document, in section 21.3 "Articles of incorporation and bylaws" and section 16.3 "Specialized committees – Corporate governance".

14.1.1 Members of the board of directors

As of the filing date of this reference document, the members of the company's board of directors are:

Name	Office	Main functions within the company	Main functions outside the company	Starting and ending dates of terms of office
Mr. Gérard Soula	Chairman of the board of directors	Chairman Chief Executive Officer	None	Appointed director by the shareholders' meeting held on October 24, 2011. Reniewed by the shareholders' meeting on June24, 2014 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, 2016. Reniewed as chairman of the board of directors and chief executive officer by the board of directors' meeting held on March 21, 2014 for the duration of his term of office as director
Mr. Olivier Soula	Vice-President, Director	R&D Director VP	None	Appointed director by the shareholders' meeting held on October 24, 2011. Reniewed by the shareholders' meeting on June24, 2014 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, 2016. Reniewed as vice-president by the board of directors' meeting held on March 21, 2014for the duration of his term of office as director

Mr. Olivier Martinez	Director	None	Investment Manager, Bpifrance Investissement (formerly CDC Entreprises)	Appointed director by the shareholders' meeting held on October 24, 2011. Reniewed by the shareholders' meeting on June24, 2014 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, 2016
Bpifrance Investissement (formerly CDC Entreprises), represented by Mr. Laurent Arthaud	Director	None	Vice-President, Bpifrance Investissement (formerly CDC Entreprises)	Appointed director by the shareholders' meeting held on October 24, 2011. Reniewed by the shareholders' meeting on June24, 2014 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, 2016
Ms. Dominique Takizawa	Director (*)	None	Secretary General, Institut Mérieux	Appointed director by the shareholders' meeting held on October 24, 2011. Reniewed by the shareholders' meeting on June24, 2014 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, 2016
Ms. Ekaterina Smirnyagina	Director (*)	None	Investment Manager, Capricorn Venture Partners	Appointed director by the shareholders' meeting held on June 18, 2013 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, 2015

* Independent Board members

The business address of the chairman and chief executive officer and of the vice-president is the address of company's registered office.

The business addresses of the other directors are shown below:

- Mr. Olivier Martinez, Bpifrance Investissement, 6-8 Boulevard Haussmann, 75009 Paris
- Mr. Laurent Arthaud, Bpifrance, 6-8 Boulevard Haussmann, 75009 Paris
- Ms. Dominique Takizawa, Institut Mérieux, 17 Rue Bourgelat, 69002 Lyon
- Ms. Ekaterina Smirnyagina, Capricorn Venture Partners, De Jonge Saint Jacob, Lei 19/1-B-3000 Leuven, Belgium

These persons have gained expertise and management experience in the various salaried and management positions they have previously held (see section 14.1.3 “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, during the five years preceding the date of this reference document, no corporate officer or board of director member:

- has been convicted of fraud;
- has been associated in his/her capacity as corporate officer or director with any bankruptcy, receivership or liquidation;
- has been deprived of the right to hold management positions in companies; and
- has been publicly and officially accused or penalized by any statutory or regulatory authority.

14.1.2 Other corporate offices

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	Director Member of the supervisory board Member of the management committee Director Censeur Censeur	POXEL GENTICEL FAB PHARMA ALIZE PHARMA INNATE PHARMA CERENIS THERAPEUTICS
Mr. Laurent Arthaud	Member of the supervisory board Director Member of the supervisory board Director Director	KURMA PARTNERS TxCell EMERTEC GESTION SA CELLECTIS SA
Ms. Dominique Takizawa	Permanent representative and member of audit committee Director and chair of the audit committee Director, chair of the audit committee and member if the investment committee Director et audit committee Director Director Director et vice president Director Director	TRANSGENE (**) MERIEUX NUTRISCIENCES (USA) (**) APRIL GROUP (FRANCE) ABL Inc. (USA) (**) ElsaLys (**) Platine (**) Lyon Place Financière Lyon Pôle Bourse
Ms. Ekaterina Smirnyagina	Director Director Director	Nexstim Oy (FINLANDE) iSTAR Medical SA (BELGIQUE) ConfoTherapeutics NV (BELGIQUE)

(*) None of the companies mentioned has capital ties with Adocia

(**) Institut Mérieux group

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

Name	Office held	Company
Mr. Gérard Soula	Chairman of the board of directors and chief executive officer Director	BIODEX LIFE CYCLE PHARMA A/S
Mr. Olivier Soula	Director	BIODEX
Mr. Olivier Martinez	Director Member of the supervisory board	CERENIS THERAPEUTICS CYTHERIS
Mr. Laurent Arthaud	Director Member of the supervisory board Chairman	SCYNEXIS INC BIOAM GESTION ORGANIBIO
Ms. Dominique Takizawa	Director Director	MACSF EPARGNE RETRAITE AVESTHAGEN (INDE)
Ms. Ekaterina Smirnyagina	Director Director Director	Innate Pharma SA Cerenis Therapeutics SA Kiadis Pharma NV (Pays Bas)

14.1.3 Biographies of the directors

Gérard Soula PhD, 71 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 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, 46 years old, holds a doctorate in polymer physical chemistry, and is a graduate of ENSIC Mulhouse. He also earned an MBA from IAE in Lyon.
He began his career with Flamel Technologies, where he stayed for eight years and was inter alia nanotechnologies research manager. He directed the development of Medusa, a therapeutic protein sustained release platform, and successfully conducted clinical studies for three such projects. He is co-holder of nearly 40 patents.

Olivier Martinez PhD, 45 years old, Senior Investment Manager within the Innovation Division of Investment Bpifrance.
From 1992 to 1997, Olivier Martinez was a student researcher with Institut Pasteur, and then with Institut Curie, in the field of cellular biology. After receiving training in management, he joined the life sciences group of Gemini Consulting where, for two years, he worked on projects in the pharmaceutical and health sectors. In 2000, he joined Bioam Gestion as project manager, and was appointed investment manager and member of the management board in 2004. When Bioam Gestion was taken over by CDC Entreprises

in July 2010, Olivier Martinez joined the life sciences team of CDC Entreprises, which manages the InnoBio and Bioam funds, and advises the Strategic Investment Fund (FSI) on its investments in biotechnology firms. CDC Entreprises and the FSI are now divisions of Bpifrance, the French public investment bank. Olivier Martinez 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, 53 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 November 2006, he joined CDC Entreprises as vice-president 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, 59 years old is secretary general of Institut Mérieux since 2006. She joined Merieux Group in 2001 and has been involved in its strategic development, especially in merger and acquisition transactions and relationships with other shareholders and investors. She also managed the IPO of bioMerieux. Previously, she held chief financial officer position for different companies: Pasteur Merieux Connaught (since renamed Sanofi Pasteur), Rhône Merieux/Mérial ….etc. She is a board member of several subsidiaries of Merieux Group: Mérieux NutriSciences Corporation (USA), ABL Inc (USA) and is at Transgène Board. She is also Board member and Chairman od the Audit Committee of the April group.
Dominique Takizawa is a graduate of the HEC Business School and holds DECF (Diplôme d'Etudes Comptables et Financières).

Ekaterina Smirnyagina, 49 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. From 2002 to 2012, she worked for Alta Partners, an investment fund company in San Francisco that specializes in the health field. Since then, she has held the position of manager with the Capricorn Partners investment fund in Belgium.

14.2 Conflicts of interest at the level of the company's management bodies and executive management

The chairman and the directors are direct or indirect shareholders of the company (see Chapter 18 "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 14.1 "Officers and directors" of this reference document has agreed to any other restriction on the sale of their equity interest in the company, except the collective commitment of preservation of

the Adocia securities, say pact " Dutreil ", concluded by Gérard Soula, Olivier Soula, Rémi Soula and Laure Soula in application of provisions of the article 787 B from the general code of the taxes.

To the company's knowledge, there is no actual or potential conflict of interest between the duties to the company and the private interests and/or other duties of the persons who are members of the company's management bodies, management staff or executive management, as listed in section 14.1 "Officers and directors" above.

15 COMPENSATION AND BENEFITS

15.1 Compensation of corporate officers

The company was originally incorporated as a société par actions simplifiée (simplified joint stock company) which was governed by a chairman, board of directors and audit committee. It was converted into a société anonyme (corporation) by a resolution adopted by the general shareholders' meeting held on October 24, 2011.

The information in this chapter has been prepared with reference to the Corporate Governance Code for midcaps and small-caps published in December 2009 by MiddleNext. All tables contained in the Positions and recommendations AMF n°2014-14 and n°2009-16 are presented below.

15.1.1 Table summarizing compensation, stock options and bonus shares granted to each corporate officer (table 1)

(in euro) **Gérard Soula** - Chairman and Chief Executive Officer	**FY 2015**	**FY 2014**
Compensation owed for the fiscal year	633 389	570 268
Value of pluriannual variable compensation granted during the fiscal year	*2 220 440*	*620 000*
Value of stock options granted during the fiscal year	*NA*	*NA*
TOTAL	**2 853 829**	**1 190 268**

(in euro) **Olivier Soula** - Vice-President	**FY 2015**	**FY 2014**
Compensation owed for the fiscal year	431 282	360 302
Value of pluriannualvariable compensation granted during the fiscal year	*None*	*1 395 000*
Value of stock options granted during the fiscal year	*NA*	*NA*
TOTAL	**446 040**	**1 755 302**

15.1.2 Table summarizing compensation paid to each corporate officer (table 2)

The tables below show the compensation owed to the corporate officers for the fiscal years ended December 31, 2014 and December 31, 2015, as well as the compensation such persons received during those same fiscal years.

(in euro) **Gérard Soula** - Chairman and Chief Executive Officer	FY 2015		FY 2014	
	Amouts owed (1)	**Amounts paid (2)**	**Amouts owed (1)**	**Amounts paid (2)**
Fixed compensation	300 001	300 001	236 899	236 899
Variable compensation *	225 000	225 000	225 000	50 000
Extraordinary compensation *	*100 000*	*100 000*	*100 000*	*None*
Directors' fees	*N/A*	*N/A*	*N/A*	*N/A*
Non-cash benefis *	8 388	8 388	8 369	8 369
TOTAL	**633 389**	**633 389**	**570 268**	**295 268**

(in euro) **Olivier Soula** - Vice-President	FY 2015		FY 2014	
	Amouts owed (1)	**Amounts paid (2)**	**Amouts owed (1)**	**Amounts paid (2)**
Fixed compensation	208 182	208 182	158 402	158 402
Variable compensation *	120 000	120 000	120 000	40 000
Extraordinary compensation *	*100 000*	*80 000*	*80 000*	*None*
premium invention	*3 100*	*500*	*1 900*	*1 900*
Directors' fees	*N/A*	*N/A*	*N/A*	*N/A*
Non-cash benefis *	*N/A*	*N/A*	*N/A*	*N/A*
TOTAL	**431 282**	**408 682**	**360 302**	**200 302**

(1) for the fiscal year (2) 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 part, a variable part and an exceptional part:

- The fixed part is the reference compensation of the officer to compensate his responsibility, his level of experience, his technical and managerial skills.
- The variable part is bound to the achievements. It is calculated according to the fixed wage and can reach up to 100 % in case of achievement of all the defined qualitative objectives which can be bound to the signature of license agreement, to the development of collaborations, to the launch of clinical trials, to the signature of feasibilities contract, to the level of cash, and more generally, to the development and the growth of the Company.
- The exceptional part aims at paying a particularly exceptional performance having a major positive impact on the development of the Company, as, as regards for 2014, the signature of a major license agreement with Eli Lilly, that includes in particular a not refundable up-front payment of $50M.

15.1.3 Table summurazing director's fees and other compensation received by non-executive corporate officers (table 3)

Directors' fees and other compensation received by non-executive corporate officers

Non-executive corporate officers	Amounts paid in fiscal year 2015	Amounts paid in fiscal year 2014
Mr. Olivier Martinez – Director		
Directors' fees (*)	0	0
Other compensation	0	0
Kurma Partners, represented by Mr Thierry Laugel - Director**		
Jetons de présence (*)	0	0
Autres rémunérations	0	0
BPI France Investissement, represented by Mr. Laurent Arthaud - Director		
Directors' fees (*)	0	0
Other compensation	0	0
Ms. Dominique Takizawa - Director		
Directors' fees (*)	26,000	24,000
Other compensation	0	0
Ms. Ekaterina Smirnyagina - Director		
Directors' fees (*)	16,000	14,000
Other compensation	0	0
TOTAL	**42,000**	**38,000**

*Only Ms. Dominique Takizawa and Ms. Ekaterina Smirnyagina received directors' fees in 2015 because the company's board of directors decided to grant directors' fees to independent directors only.

15.1.4 BSPCE granted during the year to each executive corporate officer (Table 4)

Executive officier of Officer name	Number and date of plan	Value of options based on method used for the consolidated accounts	Number of shares granted during the year	Exercise Price	End of exercise period
Gérard Soula	Plan 2015 dirigeants CA du 16/12/2015	2.220.440	40.000	74,60€	Déc. 2025

15.1.5 Stock options or stock exercised during the year by each corporate officer (Table 5)

None

15.1.6 Share granted to each corporate officer (table 6)

Executive officer or officer Name	Number and date of plan	Number of options granted during the year	Value of options based on method used for the consolidated accounts	Final acquisition date	Date of availability	Performance criteria
Olivier Soula, Deputy General Manager	Plan 2015 dirigeants Board dated 16/12/2015	5 ,000	383,700	12/16/2016	12/16/2017	Ues (cf note 15.1.10)

15.1.7 Share granted free become available for each corporate officer (table 7)

None

15.1.8 History grants of stock options or purchase of shares for each executive (table 8)

	BSA12-2013
Date of shareholders' meeting	June 18, 2013
Date of chairman's decision	December 13, 2013
Number of BSAs authorized	20,000
Number of BSAs issued	20,000
Total number of shares that may be subscribed (1)	20,000
Of which the number that may be subscribed by corporate officers	20,000
Name of non-corporate officer beneficiaries	Dominique Takizawa Ekaterina Smirnyagina

Earliest BSA exercise date	(1)
BSA expiration date	December 13, 2023
BSA issue price	0.588
BSA exercise price	€5.88
Exercise conditions	(1)
Number of shares subscribed as of the filing date of the reference document	0
Aggregate number of lapsed or canceled BSAs as of the filing date of the reference document	0
BSAs remaining as of the filing date of the reference document	20,000
Total number of shares that may be subscribed as of the filing date of the reference document	20,000

(1) BSA$_{12\text{-}2013}$ are exercisable (i) in respect of Ms Dominique Takizawa, in whole at any time from 1 January 2014 for a period of 10 years and (ii) in respect of Ms Ekaterina Smirnyagina, up to third from 1 January 2014, and an additional third from 1 January 2015 and in full from 1 January 2016

15.1.9 Subscription or purchase options granted to the each executive officer and options exercised by them (table 9)

	BSPCE dirigeants 2014	**BSPCE** dirigeants 2015
Date of shareholders' meeting	24/6/2014	12/11/2015
Date of chairman's decision	25/9/2014	16/12/2015
Number of BSCE authorized	65,000	40,000
Number of BSPCE issued	65,000	40,000
Total number of shares that may be subscribed (1)	65,000	40,000
Of which the number that may be subscribed by corporate officers	65,000	40,000
Name of non-corporate officer beneficiaries	Gérard Soula Olivier Soula	Gérard Soula
Earliest BSA exercise date	Immediate vesting following achievement of criteria, validated	Immediate vesting following achievement of criteria, validated

	by the Board on 12/23/2014	by the Board on 12/16/2015
BSCE expiration date	9/24/2024	12/16/2025
BSPCE issue price	free	free
BSCE exercise price	34.99€	74.60€
Exercise conditions	-	-
Number of shares subscribed as of the filing date of the reference document	0	0
Aggregate number of lapsed or canceled BSCE as of the filing date of the reference document	0	0
BSPCE remaining as of the filing date of the reference document	65,000	40,000
Total number of shares that may be subscribed as of the filing date of the reference document	65,000	40,000

15.1.10 Subscription or purchase options granted to the ten non-officer employees responsibilities and options exercised by them (table 10)

Stock options or options to purchase stock granted to the ten non-officer employees during the year and options exercised by them	Total allocated shares / shares subscribed or purchased	Weighted average price	Plan SO 2015 n°1	Plan SO 2015 n°2
Options granted during the year	24,000	58.22€	20,000	4,000
Options exercised during the year	*none*	*none*	*none*	*none*

15.1.11 History of bonus shares granted executives officers and non-executive directors (Table 11)

	Plan 2015 dirigeant
Date of chairman's decision	12/16/2015
Total number of free shares granted	5,000
Beneficiaries	Olivier Soula
Final acquisition date	12/16/2016
Date of availability	12/16/2017
Shares exercised at the end of December 2015	0

Total number of shares granted or expired	*Néant*
Free shares remaining at the end of December 2015	5,000

Criteria defined and validated by the Board are the following: 50% related to value creation on the partnership with Lilly, and in particular the U200 project, 20% related to value creation on BC Combo, 10% related to the launch of new projects and 20% linked to the 2015 revenue.

15.1.12 Breakdown of compensation and other benefits granted to corporate officers (table 11)

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
Gérard Soula Chairman and chief executive officer		X		X		X		X
Term of office starting date:	Board of director's meeting of October 24, 2011, renewed by Combined General Meeting of June 24, 2014							
Term of office ending date:	Ordinary general shareholders' meeting convened to vote on the financial statements for the fiscal year ending December 31, 2016							
	Yes	No	Yes	No	Yes	No	Yes	No
Olivier Soula Vice-President	X			X		X		X
Term of office starting date:	Board of director's meeting of December 19, 2012, renewed by Combined General Meeting of June 24, 2014							
Term of office ending date:	Ordinary general shareholders' meeting convened to vote on the financial statements for the fiscal year ending December 31, 2016							

15.2 Amounts that the company has provisioned for payment of pensions, retirement allowances and other benefits to corporate officers

As of December 31, 2015, the company recognized provisions of €82,005 for the payment of retirement benefits to Olivier Soula.

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

15.3 Bonus shares, stock warrants and stock options granted to corporate officers

15.3.1 $BSA_{12\text{-}2013}$ stock warrants award of December 13, 2013

Pursuant to the authority delegated by the general shareholders' meeting held on June 18, 2013, the board of directors granted 20,000 stock warrants ($BSA_{12\text{-}2013}$) to certain directors on December 13, 2013. The $BSA_{12\text{-}2013}$ stock warrants were reserved to two independent directors, i.e., who were neither managers nor employees of the company, and who were in office at that time, as follows;

- 10,000 stock warrants to Ms. Dominique Takizawa;
- 10,000 stock warrants to Ms. Ekaterina Smirnyagina.

The table detailing the characteristics of $BSA_{12\text{-}2013}$ in paragraph 15.1.8 of this reference document.

15.3.2 Allocation of company stock warrants (BSPCE) of September 25, 2014

Making use of the authorization granted at the General Meeting of 24 June 2014, the Board of Directors of September 25, 2014 decided to issue 100,000 "BSPCE 2014 Exectutives" for the benefit of three founders of the Company, Gérard Soula, Olivier and Rémi Soula Soula..

The allocation of $BSPCE_{\text{2014 Executives}}$ concerned :

- Mr. Gérard Soula, President and CEO up to 20,000 BSPCE ;
- Mr. Olivier Soula, R&D Director and Deputy General Manager up to 45,000 BSPCE.
- Mr. Rémi Soula, Director of Business Developpement and Scientific Advisor up to 35,000 BSPCE.

The table detailing the characteristics of BSPCE in paragraph 15.1.9 of this reference document.

15.3.3 Allocation of company stock warrants (BSPCE) of December 16, 2015

Making use of the authorization granted at the General Meeting of 12 November 2015, the Board of Directors of December 16, 2015 decided to issue 40,000 "BSPCE 2015 Executives" for the benefit of Gérard Soula, President and CEO of the Company.

The table detailing the characteristics of BSPCE in paragraph 21.1.8 of this reference document.

15.3.4 Allocation of bonus share of December 16, 2015

Making use of the authorization granted at the General Meeting of 12 November 2015, the Board of Directors of December 16, 2015 decided to issue 5,000 shares "Plan AGA 2015 Executives" for the benefit of Olivier Soula, R&D Director and Deputy General Manager.

The table detailing the characteristics of these bonus shares in paragraph 21.1.7 of this reference document.

15.4 Summary of transactions by managers and the persons referred to in Article L. 621-18-2 of the French Monetary and Financial Code (Code monétaire et financier) in the company's shares during the past fiscal year

Persons concerned	Nature of the transaction	Date of transaction	transaction amount (in euro)
Bpifrance Investissement	Cession	09/03/2015	326,436.66
Bpifrance Investissement	Cession	08/28/2015	28,143
Bpifrance Investissement	Cession	08/27/2015	87,526.50
Bpifrance Investissement	Cession	08/18/2015	641,398.68
Bpifrance Investissement	Cession	08/18/2015	797,780.62
Bpifrance Investissement	Cession	08/17/2015	177,092
Bpifrance Investissement	Cession	08/14/2015	79,065.91
Bpifrance Investissement	Cession	08/13/2015	387,694.41
Bpifrance Investissement	Cession	08/06/2015	1,098,998.98
Bpifrance Investissement	Cession	08/06/2015	6,948,993.25
Bpifrance Investissement	Cession	08/05/2015	455,533.01
Bpifrance Investissement	Cession	08/05/2015	455,533.01
Bpifrance Investissement	Cession	07/29/2015	923,099.82
Bpifrance Investissement	Cession	07/29/2015	923,099.82
Bpifrance Investissement	Cession	07/28/2015	651,571.76
Bpifrance Investissement	Cession	07/28/2015	651,571.76
Bpifrance Investissement	Cession	07/27/2015	252,826.39
Bpifrance Investissement	Cession	07/27/2015	252,826.39
Bpifrance Investissement	Cession	07/24/2015	598,237.19
Bpifrance Investissement	Cession	07/24/2015	598,237.19
Bpifrance Investissement	Cession	07/23/2015	557,439.04
Bpifrance Investissement	Cession	07/23/2015	557,439.04
Bpifrance Investissement	Cession	01/28/2015	139,306.11
Bpifrance Investissement	Cession	01/27/2015	556,342.73
Bpifrance Investissement	Cession	01/26/2015	527,799.28
Bpifrance Investissement	Cession	01/19/2015	200,316.71
Bpifrance Investissement	Cession	01/12/2015	352,770.93
Bpifrance Investissement	Cession	01/12/2015	196,698.60
Bpifrance Investissement	Cession	01/09/2015	100,812.19
Olivier Soula	Cession	01/09/2015	599,691.00
Rémi Soula	Cession	01/09/2015	299,500.00

16 FUNCTIONING OF SUPERVISORY AND MANAGEMENT BODIES

16.1 Management of the company

Pursuant to a resolution adopted by an extraordinary general shareholders' meeting held on October 24, 2011, the company was converted from a société par actions simplifiée (simplified joint stock company) into a société anonyme (corporation). A detailed description of the composition of the board of directors is provided in section 14.1 "Officers and directors".

During the fiscal year ended December 31, 2015, the company's board of directors met twelve (12) times. The average attendance rate for board of directors members was 93%.

Executive management of the company

Pursuant to a decision adopted on October 24, 2011, the board of directors chose to combine the functions of chairman and chief executive officer. As a result thereof, as regards third parties, the company is represented by Mr. Gérard Soula, in his capacity as chairman of the board of directors and chief executive officer.

Since December 19, 2012, he has been assisted in these duties by a vice-president, Mr. Olivier Soula.

16.2 Information on contracts between corporate officers and the company

There is no service contract between the members of its board of directors and its officers to the Company.

16.3 Board of administration and specialized committees – Corporate governance

16.3.1 Board of directors

16.3.1.1 Composition

The composition of the board of directors and information about its members is provided in Chapter 14 "Administrative, management, supervisory and executive management bodies" and Chapter 21.2 "Articles of incorporation and bylaws" of this reference document.

Rules of procedure were adopted on October 24, 2011, which cover inter alia the role and composition of the board, the rules of conduct and the obligations incumbent on the members of the company's board of directors. Each board of directors member undertakes inter alia to maintain his/her independence of analysis, judgment and action and to actively participate in the work of the board. Directors must inform the board of any conflicts of interests that may arise. In addition, the rules of procedure explain the laws 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.

The company deems that it already has two independent directors, Ms. Dominique Takizawa and Ms. Ekaterina Smirnyagina, within the meaning of the Corporate Governance Code for midcaps and small-caps, as published in December 2009 by MiddleNext and approved as a code of reference by the AMF. Ms. Dominique Takizawa and Ms. Ekaterina Smirnyagina meet the definition of independent directors because they:

- are not employees or officers of the company, nor employees or officers of any of its subsidiaries, and have not held such position or office within the past three years;

- are not major customers, suppliers or bankers of the company, and the company does not account for a significant share of their business operations;
- are not major shareholders of the company;
- do not have close family ties with any corporate officer or major shareholder; and
- have not been auditors of the company within the past three years.

Nevertheless, recruiting one or more additional independent directors is under consideration by the company as part of its process to improve its corporate governance following the listing of the company's shares on the Euronext regulated market in Paris.

16.3.2 Specialized committees

The company has two specialized committees, the audit committee and the compensation committee.

16.3.2.1 Audit committee

16.3.2.1.1 *Composition*

Pursuant to a decision of the board of directors adopted on June 6, 2008, the company set up an audit committee for an indefinite period. The committee members adopted rules of procedure, as described below.

To the extent possible, the audit committee is comprised of at least two members appointed by the board of directors on the basis of a recommendation of the compensation committee. The audit committee members are chosen from among the members of the board of directors and, to the extent possible, two-thirds of its members should be independent directors, one of whom should have specific financial or accounting expertise, although all members should have a minimum understanding of financial or accounting matters.

As of the filing date of this reference document, the audit committee members are:

- Ms. Dominique Takizawa, an independent director who has financial and accounting expertise; and
- Mr. Olivier Martinez.

Ms. Dominique Takizawa chairs this committee.

Ms. Takizawa is the member of the board who has "specific financial or accounting expertise" due to her experience of nearly 25 years in the pharmaceutical industry and the senior management positions she has held with Sanofi Pasteur, Biomérieux and Institut Mérieux.

16.3.2.1.2 *Duties*

The role of the audit committee, acting independently of the company's management, is to assist the board of directors and ensure that the financial statements are accurate, that internal controls are adequate, that information provided is pertinent, and that the statutory auditors fulfill their duties.

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 roles 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 senior financial managers). The committee has the right to directly, independently and confidentially consult with the statutory auditors.

16.3.2.1.3 *Operation*

The audit committee meets at least twice a year, in accordance with a schedule set by the chair, to review the annual, semi-annual and, if applicable, quarterly financial statements, pursuant to an agenda prepared by its chair and sent to the audit 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 chairman of the company's board of directors.

The audit 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 administrative and financial manager and the principal senior financial managers).

The audit committee is entitled to interview the statutory auditors. It may meet with them outside the presence of any company representative.

16.3.2.1.4 *Reports*

The audit 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 over the past fiscal year.

If in the course of its work, the audit committee becomes aware of any material risk that it does not consider is being handled appropriately, the chair must immediately inform the chairman of the board of directors.

16.3.2.2 Compensation committee

16.3.2.2.1 *Composition*

The compensation committee was set up on June 6, 2008. Its members adopted rules of procedure, which are described below. If possible, the committee is composed of at least two members of the board of directors appointed by the board of directors.

No board of directors member who holds a management position within the company may be a member of the compensation committee.

As of the filing date of this reference document, the compensation committee members are:

- Ms. Ekaterina Smirnyagina, independent member, and
- Mr. Laurent Arthaud.

Mr. Laurent Arthaud chairs this committee.

16.3.2.2.2 *Duties*

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 board of directors members. The committee proposes compensation amounts and structures, in particular the rules for calculating the variable component of compensation, taking into account the company's strategies, objectives and performance, as well as market practices, and
  - bonus share plans, stock subscription or purchase options, and any other similar incentive plan, in particular benefits granted to specific members of the board of directors;
- reviewing the total amount of directors' fees and the method for distributing them among the members of the board of directors, as well as the requirements for obtaining reimbursement of expenses that board of directors members may incur,
- preparing and submitting to the board of directors any reports that may be required by the rules of procedure; and
- making any other recommendation concerning compensation that may be requested of it by the board of directors.

In general, the compensation committee provides advice and makes appropriate recommendations in connection with the above matters.

16.3.2.2.3 *Operating procedures*

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.

16.3.2.2.4 *Reports*

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.

16.4 Statement on corporate governance

To promote transparency and public disclosure, the company has initiated a review of all of its corporate governance practices.

To comply with the requirements of Article L. 225-37 of the French Commercial Code (*Code de commerce*), the company has adopted as a code of reference the Corporate Governance Code for midcaps and small-caps published in December 2009 by MiddleNext.

The company complies with all recommendations of the Corporate Governance Code for midcaps and small-caps and, in particular, it meets the following objectives:

- the board of directors includes at least two independent members, as it has five members in total;

- the audit committee, whose current composition is in accordance with Article L.823-19 of the French Commercial Code, also complies with the recommendations of the Corporate Governance Code for midcaps and small-caps, which provide that the audit committee should have at least two independent members.

However, as of the date of this reference document, the company does not comply with:

- the 13th recommendation of the code published by MiddleNext, insofar as the number of 4 meetings per year called for specialized committees in the recommendation is not deemed necessary by the society in relation to its size and role of day each of these committees;

- the 14th recommendation of the code published by MiddleNext, which recommends that the board of directors apportion directors' fees on the basis of directors' attendance and the time they

devote to their duties, as the company's board of directors has decided to grant directors' fees to independent directors only (see section 15.1.3 of this reference document) ; and

- the 15th recommendation of the code published by MiddleNext,since the Company has not yet established procedures for assessing the work of the Board, it being specified that it intends to do so in 2015.

16.5 Chairman's report on internal control

As required by Article 222-9 I of the AMF's General Regulation, and in accordance with Article L. 225-37 of the French Commercial Code, the chairman of the board of directors presents an annual report on the composition of the board, the conditions under which the board prepares and organizes its work, and the internal control and risk management procedures set up by the company. The chairman's report for 2015 can be found in Appendix I of this reference document.

In the course of its expansion, with respect to internal control, the company follows the risk management and internal control systems implementation guide for small-caps and midcaps published by the AMF on July 22, 2010.

16.6 Information required by Article L. 225-100-3 of the French Commercial Code

16.6.1 Shareholder structure of the company

See Chapter 18 of this reference document.

16.6.2 Restrictions imposed by the articles of incorporation and bylaws on exercising voting rights and share transfers or similar clauses of which the company is aware, as required by Article L. 233-11 of the French Commercial Code

Not applicable.

16.6.3 Direct or indirect equity stakes in the company of which the company is aware, as required by Articles L. 233-7 and L. 233-12 of the French Commercial Code

See Chapter 18 of this reference document.

16.6.4 List of holders of any securities with special control rights and a description of such right

The company is not aware of the existence of any special control rights.

16.6.5 Control mechanisms included in any employee share plan in which the control rights are not exercised by the employees

The company has not set up any employee share plan that may contain control mechanisms in which the control rights are not exercised by the employees.

16.6.6 Shareholder agreements of which the company is aware that may impose restrictions on share transfers and exercising voting rights

Not applicable.

16.6.7 Rules governing the appointment and replacement of board of directors members and amendments to the articles of incorporation and bylaws

The rules governing these matters are set out in the articles of incorporation and bylaws and are in compliance with the law.

16.6.8 Powers of the board of directors, in particular the power to issue or redeem shares

The general shareholders' meeting held on May 27, 2015 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 redemption 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 section 18.1, 18.2 and 21.1.4 of this reference document).

16.6.9 Agreements entered into by the company that will be amended or terminated in the event of a change of control of the company

Not applicable.

16.6.10 Agreements that provide for compensation to board of directors members or employees if they resign or are terminated without just cause or if their employment ends due to a takeover bid

Not applicable.

17 EMPLOYEES

17.1 Human resources

17.1.1 Main key employees

The company's main managers 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, with the exception of the corporate officers (Messrs. Gérard and Olivier Soula), who are discussed in section 14.1.3 "Biographies of the directors" in this reference document:

Dr. Rémi Soula: Business Development Manager and Scientific Advisor

Rémi Soula holds a doctorate in polymer chemistry from CPE Lyon. He did a post-doctorate at Max-Planck Institute in Berlin. He began his career with Flamel Technologies as a senior researcher where, over the course of three years, he acquired solid experience in the synthesis of new polymers. He is a co-holder of 30 patents and has co-authored six scientific publications.

Ms. Valérie Danaguezian: Chief Financial Officer

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. She then joined the Aventis Pasteur group in Lyon where, for 12 years, she was initially in charge of the group's financial consolidation, and then headed the group's research and development expenditures management control system. Thereafter, she joined Flamel Technologies as administration and financial officer. Valérie Danaguezian 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.

Ms. Géraldine Favre Soula: Human Resources Director

Géraldine Favre Soula holds a Master 2 in human resources management (Université de Droit et de Sciences Politiques, Dijon) after having obtained a Master 1 in human resources from Institut de Gestion Sociale. She started her career at Bouygues as vocational training manager, before joining Pasteur Mérieux (Sanofi Pasteur) and Alptis Gestion where she worked as HR generalist. She then joined Flamel Technologies as Human Resources Manager where she spent 9 years, during the course of which the workforce increased from 50 to 300 employees, and where she created an HR department and built HR teams in 2 different sites (Lyon and Bordeaux). She has been working at Adocia since its creation.

Dr. Martin Gaudier : Scientific Director

Martin Gaudier holds an engineering degree from Ecole Polytechnique and a doctorate in structural biology and protein biochemistry. He did his dissertation in the field of structural virology, and then a four-year post-doctorate at Cancer Research UK in London on protein-DNA interactions. He has co-authored eight scientific publications and is a co-holder of two patents.

Dr. José Correia : Head of the Preclinical and Clinical Department, HSQE Manager and Project Manager

José Correia holds a doctorate in biomaterials engineering from the University of Paris-Nord. He was chairman and chief executive officer of Biodex from 2002 to 2006, where he managed chemical and

pharmaceutical development for nine years. He is a co-holder of four patents and has co-authored three scientific publications.

Dr. Bertrand Alluis: Head of the Analysis Department and Project Manager

Bertrand Alluis holds a doctorate in chemistry. He did his dissertation at the CNRS polyphenols laboratory at the University of Lyon I, and studied the complex and antioxidant powers of flavonoids. He spent three years with Diatos S.A. in the field of oncology and vectorization as head of the therapeutic chemistry department. Thereafter, he joined Flamel Technologies where, for three years as senior researcher, he specialized in the development and validation of analytical methods used to characterize proteins and the formulation thereof with polymers. He is a co-holder of one patent and has co-authored four scientific publications.

Dr. David Duracher: Head of the Pharmaceutical Development and Physical Chemistry Departments

David Duracher holds a doctorate in polymer physical chemistry. His dissertation, which was financed by BioMérieux, was in the field of biomedical diagnostics, at the interface between the science of polymers and biology. After a post-doctorate at the Key Centre for Polymer Colloids at the University of Sydney and two years' experience in the field of biochips with Apibio, he worked for Flamel Technologies on sustained release formulations for therapeutic proteins. He is a co-holder of five patents and has co-authored sixteen publications.

Dr. Grégory Meiffren: Director of the Biology Department and Project Manager

Grégory Meiffren is a graduate of the Ecole Normale Supérieure, Lyon and Doctor of Cellular Biology. He carried out his thesis on the transduction pathways of immune cells in various pathologies at the Centre d'Etudes et de Recherches en Virologie et Immunologie in Lyon and also collaborated with the Dana-Farber Cancer Institute and the Brigham and Women's Hospital in Boston. He is co-author of 6 scientific publications.

Dr. Richard Charvet : Director of the Chemistry Department

Richard Charvet earned a doctorate in organic chemistry and polymers from North Carolina State University, Raleigh, in the United States. He did a two-and-a-half year post-doctorate at Erato Nanospace Project in Tokyo, and then spent one year at the University of Wuppertal. Thereafter, he joined the National Institute for Materials Science (NIMS) in Tsukuba, Japan, as an associate researcher studying organic photoconductive nanostructures formed by supramolecular self-assembly. He is a co-holder of two patents and has co-authored fourteen scientific publications.

17.1.2 Number and breakdown of employees

At the end of the periods under review, the company's workforce experienced the following changes:

Breakdown of employees	**12/31/2015**	**12/31/2014**
R&D	89	63
SG&A	20	17
Total number of employees	**109**	**80**

As of December 31, 2015, the company had 109 workers (both full-time and part-time), including 1 blue-collar employee, 50 technicians and 58 management-level employees. Of these employees, 40 hold a doctorate in science, medicine or pharmacy, i.e., more than one-third of the company's employees.

17.1.3 Employee representatives

The company had two employee representatives, one incumbent and one alternate, who were elected on December 15, 2011 for a four-year term. At the end of 2012, the company reached the statutory number of workers for setting up a single employee representative body (*délégation unique du personnel*) and a health, safety and working conditions committee (CHSCT), which were set up in March 2013 (see section 17.7 below)

17.2 Financial instruments conferring equity rights in the company granted to the top ten employees who are not corporate officers

17.2.1 Bonus shares(AGA)

The table below shows the number of bonus shares that have been granted:

	Dates of the Boards decided to award				
	01/23/2008	06/06/2008	12/15/2009	03/05/2010	12/07/2010
Number of shares granted	42 000	5 600	5 600	5 600	5 600
Shares cancelled	2 100	0	0	0	0
Acquired and available shares	39 900	5 600	4 200	2 800	2 800
Exercised stock	11 600		410	200	0
Acquired and remaining available shares	28 300	5 600	3 790	2 600	2 800
Shares acquired under conservation	0	0	1 400	2 800	2 800
Actions attribuées mais non encore acquises	0	0	0	0	0
End of acquisition period	*completed*	*completed*	*completed*	*completed*	*completed*
End of retention period	*completed*	*completed*	1 400 stock : dec. 2016	1 400 stock : march 2016 1 400 stock : march 2017	1 400 stock : dec 2016 1 400 stock : dec 2017

	Date of the Boards decided to award			TOTAL
	12/10/2015	12/16/2015	12/16/2015	
Number of shares granted	39 150	5 000	12 600	**121 150**
Shares cancelled	0	0	0	**2 100**
Acquired and available shares	0	0	0	**55 300**
Exercised stock	0	0	0	**12 210**
Acquired and remaining available shares	0	0	0	**43 090**
Shares acquired under conservation	0	0	0	**7 000**
Actions attribuées mais non encore acquises	39 150	5 000	12 600	**56 750**
End of acquisition period	39 150 stock : dec 2017	5 000 stock : dec 2016	3 150 stock : dec 2016 3 150 stock : dec 2017 3 150 stock : dec 2018 3 150 stock : dec 2019	
End of retention period	No retention period considering the vesting period of 2 years	5 000 stock : dec 2017	3 150 stock : dec 2017 3 150 stock : dec 2018 3 150 stock : dec 2019 3 150 stock : dec 2020	

17.2.2 Business founders' stock warrants (BSPCE):

Pursuant to a delegation of authority granted by the ordinary and extraordinary general shareholders' meeting held :

a) on June 18, 2013, the board of directors, at its meeting of December 13, 2013, decided to grant, free of charge, a total of 50,400 business founders' stock warrants to certain company employees, entitling them to subscribe for 50,400 new shares with a par value of €0.10

Pursuant to that decision, the board of directors set up:

- **2013 Business founders' stock warrants plan no. 1**, which grants 28,000 business founders' stock warrants to employees whose employment contract with the company or promotion predates January 1, 2013;
- **2013 Business founders' stock warrants plan no. 2**, which grants 22,400 business founders' stock warrants to employees whose employment contract with the company or promotion is subsequent to January 1, 2013, or to any other employee pursuant to a specific proposal of the company's management.

Each beneficiary may exercise, at a price of €5.76 per warrant, one-fourth of the business founders' stock warrants on January 1 of each year, with the first tranche becoming exercisable on January 1, 2014 (plan no. 1) or January 1, 2015 (plan no 2). Business founders' stock warrants must be exercised within ten years from the date they are granted, i.e., no later than December 13, 2023. At the end of the ten-year period from the date the business founders' stock warrants are issued, business founders' stock warrants that have not been exercised will lapse and cease to confer the right to subscribe for shares in the company.

b) on June 24, 2014, the board of directors, at its meeting of September 25, 2014, decided to grant, free of charge, a total of 119,600 business founders' stock warrants to certain company employees, entitling them to subscribe for 119,600 new shares with a par value of €0.10

Pursuant to that decision, the board of directors set up:

- **2014 Business founders' stock warrants plan no. 1**, which grants 14,000 business founders' stock warrants to employees whose promotion is subsequent to January 1, 2014.
- **2014 Business founders' stock warrants plan 2014 no. 2**, which grants 5,600 business founders' stock warrants to employees whose employment contract with the company predates January 1, 2014;
- **2014 Business founders' stock warrants plan 2014 for managers**, which grants 100,000 business founders' stock warrants to officers or management function upon a employment contract.

Each beneficiary may exercise, at a price of €34.99 per warrant, one-fourth of the business founders' stock warrants on January 1 of each year, with the first tranche becoming exercisable on January 1, 2015 (plan 2014 no. 1, Managers Plan 2014) or January 1, 2016 (plan no 2). Business founders' stock warrants must be exercised within ten years from the date they are granted, i.e., no later than September 25, 2024. At the end of the ten-year period from the date the business founders' stock warrants are issued, business founders' stock warrants that have not been exercised will lapse and cease to confer the right to subscribe for shares in the company.

An exception to the exercise conditions specified above, each beneficiary of the "Managers Plan 2014", may exercise in anticipation, all the business founders' stock warrants he holds under certain conditions: in case of a signature of a significant contract with pharmaceutical Companies, which would guarantee an initial payment (up-front payment) of at least 30 million excluding VAT and would provide for payment by step (milestone payments) of at least 200 million excluding VAT; the realization of this condition must be validated by the Board of Directors. The early exercise of BSPCE could not be possible before a minimum period of 30 calendar days following the information of the signature of major contract to the stock market.

The Board of Directors at its meeting set on December 23, 2014, acknowledged the signature on December 18, 2014 of the license agreement with Eli Lilly, and validated accordingly the conditions required to accelerate calendar for "2014 Managers BSPCE". The "2014 Managers BSPCE" may be exercised at any time until their expiration date.

As of the filing date of this reference document, the company has received all subscription forms from eligible employees for the entire BSPCE plans.

17.2.3 Stock options :

a. On March 31, 2015, pursuant to a delegation of authority granted by the ordinary and extraordinary general shareholders' meeting held June 18, 2013, the Board of Directors decided to grant stock options to two employees Adocia Inc. A total of 20,000 common shares of stock options granted was well, each employee receives 10,000 common stock options.

For each beneficiary, the stock options are exercisable at a price of 55.64 euros per quarter, every year on January 1, with a first tranche exercisable from 1 January 2016. The options may be exercised at the expiration of a ten-year period which commences in the day of grant, or before March 31, 2025. At the end of the period of ten years following the issuance of stock options, the options have not been exercised will lapse and no longer be able to exercise the right to subscribe for shares of the Company.

b. On December 16, 2015, pursuant to a delegation of authority granted by the ordinary and extraordinary general shareholders' meeting held November 12, 2015, the Board of Directors decided to grant stock options to the two employees Adocia Inc. A total of 4,000 common shares of stock options granted was well.

For each beneficiary, the stock options are exercisable at a price of 71.12 euros, per quarter, every year on January 1, with a first tranche exercisable from 1 January 2017. The options may be exercised at the expiration of a ten-year period which commences in the day of grant, or before December 16, 2025. At the end of the period of ten years following the issuance of stock options, the options have not been exercised will lapse and no longer be able to exercise the right to subscribe for shares of the Company.

17.3 Equity interests and stock options held by corporate officers

The direct and indirect equity interests of board of directors members and the number of securities that confer equity rights in the company that they hold as of December 31, 2015 are shown below:

Name	Number of shares held directly	Number of shares held by tied entities (1)	% of the company's capital	Securities
Mr. Gérard Soula	898,463	0	13.1%	60,000
Mr. Olivier Soula	307,490	0	4.5%	50,000
Bpifrance Investissement represented by Mr. Laurent Arthaud [2]	0	738,639 [3]	10.8%	Néant
TOTAL	**1,944,592**		**-**	**110,000**

[1] "Tied entities" means entities with which the member has capital or contractual ties (such as delegated management authority) or ties pursuant to articles of incorporation provisions.
[2] Bpifrance Investissements is the management company for the Innobio fund and for sub-fund II of the Bioam 1b fund, which hold a 10.8% stake in the company (9.1% and 1.6%, respectively).
[3] Not including bearer shares, if any.

17.4 Equity interests held by employees

As of the filing date of this reference document, the company's employees (including Olivier Soula and Rémi Soula) held 650,250 [70] shares, i.e., 9.49% of the company's capital and 13.40% of its voting rights.

17.5 Discretionary profit sharing agreement (*intéressement*)

Not applicable

17.6 Employee savings

ADOCIA has implemented various employee savings schemes. True optimization of social policy tools of the company, these devices can meet various objectives, including strengthening the link between employee performance and business results, retain and motivate employees.

- mandatory profit sharing agreement (called "participation") implemented by an Agreement signed December 11, 2013 between the management and the employees represented by the Delegation of Unique Personnel. This system is mandatory for more than 50 employees, it enables the distribution of a portion of the profits made by the company. This agreement was the subject of an Amendment No. 1 dated July 28, 2014 signed under the same conditions. This amendment is intended to allow the payment of interest on a savings plan (PEE) and / or a collective pension savings plan (PERCO).

  The agreement covers all employees receive a minimum of three months seniority in the company at the closing date of the fiscal year. The amount allocated to all beneficiaries employees is called Special Reserve Participation, whose calculation methods comply with the statutory formula.

  At 31 December 2015, no participation was due as a consequence of the net 2015 fiscal loss of the Company.

- A Company Savings Plan (PEE) and collective retirement savings plan (PERCO) concluded July 28, 2014 between the management and the employees represented by the Delegation of Unique Personnel. Both plans aim to enable company employees with at least three months' (determined on the date of the first payment for optional voluntary payments) to participate, with the help of it, the constitution of a collective portfolio of securities and tax benefits that attach these forms of collective savings. The P.E.R.C.O. also offering an additional funding mechanism for retirement.

- The Time Savings Account (CET) set up by an agreement signed June 30, 2014 between the management and the employees represented by the Delegation of Unique Personnel. This device is not legally binding, it is a deliberate choice of Adocia company to enable the company staff with at least three months' service who wishes, to accumulate rights to be to build a long-term time savings, either to provide flexibility in taking leave or to consider savings by the transfer of rights from CET to a P.E.E or a P.E.R.C.O.

17.7 Employment information required by Article R. 225-105-1 of the French Commercial Code

17.7.1 Employment

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

- attract, retain and motivate the most competent talent necessary to enable development of the company's ambitious 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.

17.7.2 Workforce

At the end of December 2015, the company had 109 workers (both full-time and part-time) of which 107 are located In France and 2 are based in the US subsidiary Adocia Inc. The companyhas a total of 1 blue-collar employee, 50 technicians and 58 management-level employees. Of these employees, 94 are on permanent employment contracts and 15 are on fixed-term employment contracts (7 on apprenticeship contracts, 8 on fixed-term contracts entered into due to temporary increases in business. The 2 employees located in the US subsidiary are included in the indicator called “Employees” as of December 2015, but are permanently excluded from all others indicators(not managed by th France HR).

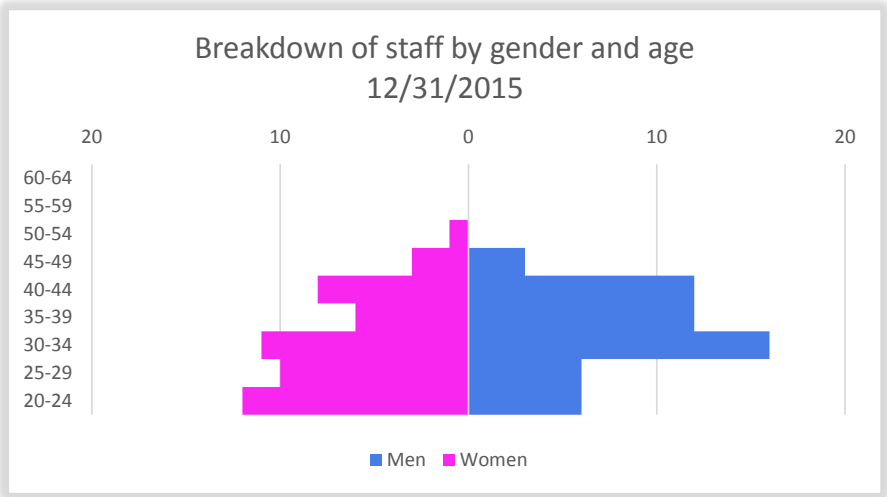
The company’s leading managers have broad experience in technological innovation management and in partnerships with major biopharmaceutical groups, as well as in drug delivery of therapeutic proteins and in the development of medical devices. All employees of the holding are based in Lyon, at the company’s registered office at 115 Avenue Lacassagne. Employees of the US subsidiary are located in California.

At the end of December 2015, the company employed 40 researchers who hold a doctorate in science, medicine or pharmacy, i.e., over one-third of all.

As of December 31, 2015, close to 80% of the workforce was assigned directly to research and development, with the remaining employees performing support functions, such as accounting, administrative services, quality control, intellectual property and human resources.

As of December 31, 2015, the average age of the French company’s employees was 33. The feminization rate was 47%.

The graph below shows the distribution of employees by age and sex:



17.7.3 Personnel movements in 2015

Number of hires and departures over the last three years:

	2013	2014	2015
Total recruitments	16	27	54
Total number of outputs	13	20	23

The 23 departures in 2015 were mainly related to :

- fixed term contract (56%) of which 46% of study contracts,
- resignations (22%),
- termination of the trial period driven by employer (13%)

No dismissal procedure has been initiated during this year.

Thanks to a highly selective hiring policy and a very high level of demand the integration success rate is over 81% (3 termination of the trial period at employer's initiative for fixed term contracts and 5 terminations of excluding study contrcats or replacement).

The Company has to be competitive and attractive to attract and retain top talent. She practices thus an ambitious remuneration policy which is reflected in particular by a payroll of 410 thousand euros (French GAAP) for 2015 and significant annual increases. Thus, over the last three years, average general and individual increases were within a 3% to 10% range (excluded top management), plus bonuses on the basis of collective and individual performances.

The award increases and / or bonuses is based on objective criteria and individual merit. Professional equality is thus granted to employees regardless of race, sex, color, religion, disability, family status, sexual orientation, age and ethnicity.

17.7.4 Work organization

The employment contracts of the French employees are reffering to the Collective Agreement of Pharmaceutical Industries.

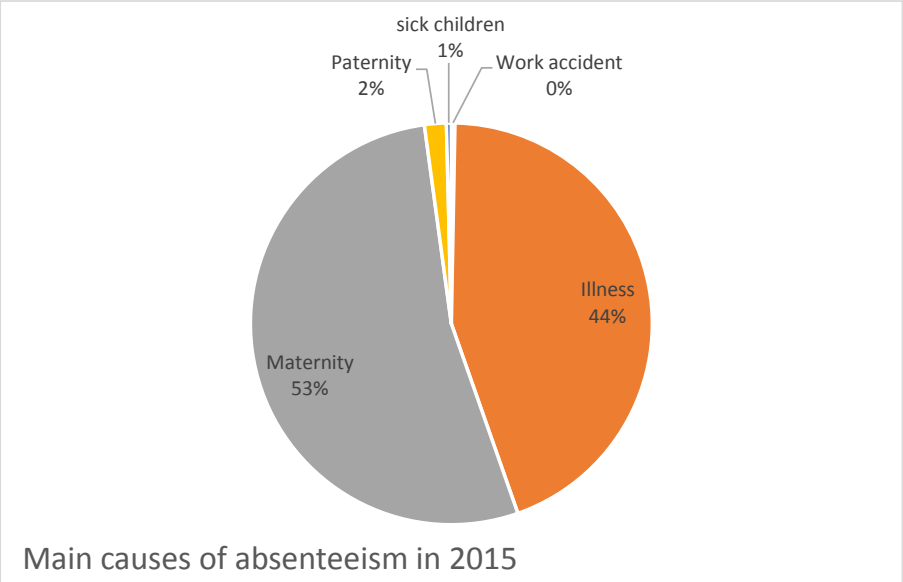
Those employed by th US subsidiary are under American laws.

July 22, 2010 the Company concluded with the staff representatives agreed on the organization of working time, the details of which were provided in a spirit of flexibility and flexibility needed to research. This agreement was approved by the National Joint Committee of the pharmaceutical industry 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. The standard working time for technicians is 35 hours per week, which may be increased, in which case employees are entitled to offsetting days off.

In 2015, 12 employees worked part time, of which 6 within a parental leave contract. All theseemployees choose to work part-time to deal with family responsibilities. In 2015, the main reasons for absences were illness and maternity or paternity leaves.
The number of days of absence due to sickness, work accident and sick child for 2015 is 1,024 days, meaning an absenteeism rate of 2.61%. The planned absences such as maternity leave or paternity leave are not included in the calculation.

The absenteeism rate is impacted in 2015 by one employee in a long disease.



Main causes of absenteeism in 2015

17.7.5 Labor relations

In 2012, the company reached the statutory number of workers for setting up a single employee representative body, which the company set up in 2013. This single representative body combines the powers of employee representatives and of the works council in a single elected body, and assigns the duties of the works council to the employee representatives. In 2015, the single representative body is comprised of:

- 2 incumbent members and 1 alternates for the non-management group (resignation in 2015 of a member due to his departure from the company);

- 1 incumbent member for the management group (resignation in 2015 of a member due to his departure from the company).

The company ensures that the rights and freedoms of the representatives of employee representative bodies are scrupulously respected, and that these representatives enjoy the same career perspectives 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 and quality industrial relations policy by maintaining an ongoing and constructive labor-management dialogue.

The company complies with the fundamental conventions of the International Labor Organization on respect for the 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.

17.7.6 Health and safety

The company has a two-person Health, Safety and Environment department. About a dozen persons in the company's various departments have received first aid at work training. 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.

In 2013, the Company proceeded to the election of representatives of the CHSCT. Following the resignation of two members, a new election was held current 2014 to appoint two new representatives.

At the end of December 2015, this organization is composed of 3 members, of which 2 are representing the non-management group and 1 the management group. 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 his/her home and workplace (round trip).

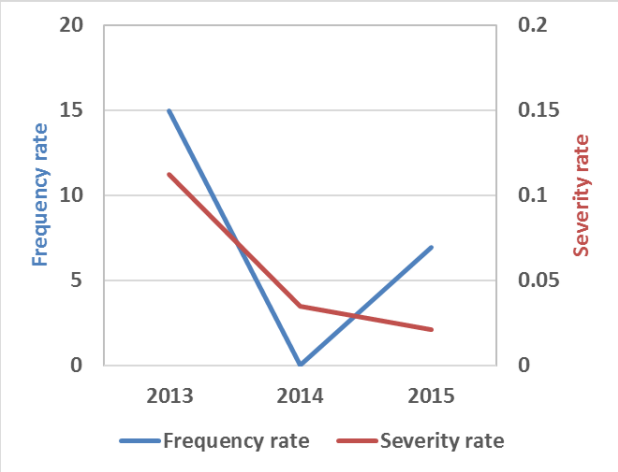
The company recorded 25 minor incidents, 52% of which involved needle sticks and cuts to hands. Compared to the average workforce in 2015, the rate of work accidents per employee is 0.24.

One accident has resulted in work stoppage in 2015. It was an accident on the way to work that led to 3 working days off work.

As a consequence, in 2014, the frequency and severity rates of workplace accidents were 0 and 0.03, respectively. In 2013, two accidents had resulted in work stoppage, frequency rate and severity rate amounted to 14.95 and 0.11 respectively.These rates are calculated using the following formulas:

- Frequency rate = (number of workplace accidents and commuting accidents resulting in medical leave / hours worked) x 1,000,000
- Severity rate = (number of days lost due to temporary disabilities as a result of a workplace accident or commuting accident / hours worked) x 1,000,000

	2013	2014	2015
Frequency rate	14,95	0	6.94
Severity rate	0,11	0,03	0.02



No occupational or work-related illness was reported in 2015 or during the previous three fiscal years. An occupational illness means an illness due to a person's exposure to a risk in connection with his/her employment position. The company has not been informed of any permanent disability in this fiscal year or prior fiscal years.

The company pays for a medical examination for all employees, with varying frequencies depending on the nature of employees' positions. Laboratory personnel undergo a medical examination, including a blood test, at least every 18 months, and administrative personnel are examined at least every two years.

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

17.7.7 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 to new tools and materials, regulatory monitoring. Moreover, each year, all employees receive general training for all staff together on a theme of reflection which the conductive line is the same for several years "better self-knowledge, better knowledge of others."

The total number of training hours totaled 1,598.50 hours for the year 2015. Of this volume of training hours: 49% correspond to formations undergoing a training agreement and delivered by a body outside, the remaining 51% correspond to internal training or training therefore do not fall within the training Plan.

Number of employees trained in 2015	**Men**	**Women**	**Total**
Executive	35	25	60
Non Executive	19	31	50
Total	54	56	110

Number of employees trained in 2015	
Research and developement	88
Support functions	22
TOTAL	**110**

Moreover, to develop individual skills and to maintain a high level of expertise, the company encourages all researchers to attend international conferences and seminars. On 2015, Adocia participated in 21 conferences and scientific seminars (involving 38 participants).

17.7.8 Equality in the workplace

To promote the recruitment of disabled workers, the company has taken steps to hire disabled workers, in particular holding meetings with CAP Emploi, the national placement network for disabled persons. Despite these actions and the fact that all positions are open to disabled persons, the company has

received few applicants (problem of skills not matching the position profile). At the end of December 2014, the company had no employees in its workforce recognized as having disabled worker status.

The company uses a disabled workers' assistance center to provide it with various services.

17.7.9 Gender equality action plan

After having consulted the single employee representative body in December 2013, an action plan was scheduled to take 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 the following three points:

- Workforce: The Company will continue to hire its employs on the basis of objective expertise criteria and individual merit, keeping in mind the equality between male and female.
- 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.
-

18 MAJOR SHAREHOLDERS

18.1 Change in the company's capital structure over the past three years on an undiluted basis

	Situation at December 31, 2015			Situation at December 31, 2014			Situation at December 31, 2013		
	Number of shares	% of capital	% of voting rights	Number of shares	% of capital	% of voting rights	Number of shares	% of capital	% of voting rights
Soula Family	**1 525 933**	**22,3%**	**31,8%**	**1 540 933**	**24,8%**	**32,0%**	**1 550 933**	**25,0%**	**29,7%**
Gérard Soula	898 463	13,1%	18,8%	898 463	14,5%	18,6%	898 463	14,5%	16,9%
Olivier Soula	307 490	4,49%	6,32%	317 490	5,11%	6,60%	317 490	5,1%	6,2%
Rémi Soula	302 490	4,42%	6,32%	307 490	4,95%	6,40%	317 490	5,1%	6,2%
Laure Soula	17 490	0,3%	0,4%	17 490	0,3%	0,4%	17 490	0,3%	0,3%
Financial investors	**1 166 639**	**17,0%**	**24,4%**	**1 831 650**	**29,5%**	**38,1%**	**2 916 042**	**46,9%**	**53,5%**
Innobio *(Bpifrance Investissement)*	625 923	9,1%	13,1%	700 020	11,3%	14,6%	700 020	11,3%	13,6%
Fonds BioAM *(Bpifrance Investissement)*	112 716	1,6%	2,4%	286 256	4,6%	6,0%	341 820	5,5%	6,7%
Subtotal BPIfrance investissement	*738 639*	*10,8%*	*15,4%*	*986 276*	*15,9%*	*20,5%*	*1 041 840*	*16,8%*	*20,3%*
Fonds IdInvest	0,00	0,00	0,00	0,00	0,00	0,00	683 710	11,0%	13,3%
Fonds Amundi	0,00	0,00	0,00	0,00	0,00	0,00	179 890	2,9%	3,5%
Fonds Viveris	67 439	1,0%	1,4%	364 754	5,9%	7,6%	364 754	5,9%	6,9%
Oréo Finance	40 561	0,6%	0,8%	81 561	1,3%	1,7%	191 343	3,1%	2,2%
Famille Deléage	0	0,0%	0,0%	17 090	0,3%	0,4%	68 360	1,1%	1,3%
SHAM (1)	320 000	4,7%	6,7%	381 969	6,1%	7,9%	386 145	6,2%	6,0%
Key employees	**40 270**	**0,65%**	**0,76%**	**50 090**	**0,8%**	**0,9%**	**49 000**	**0,8%**	**0,7%**
Scientific committees (stock warrants)	700	0,0%	0,0%	0	0,0%	0,0%	0	0,0%	0,0%
administrator (stock warrants)	0	0,0%	0,0%	0	0,0%	0,0%	0	0,0%	0,0%
Treasury shares	**4 185**	**0,06%**	**0,0%**	**2 323**	**0,0%**	**0,0%**	**40 326**	**0,6%**	**0,0%**
other shareholders *	**4 108 636**	**60,0%**	**43,1%**	**2 791 080**	**44,9%**	**29,1%**	**1 655 575**	**26,7%**	**16,2%**
Total	**6 846 363**	**100,0%**	**100,0%**	**6 216 076**	**100,0%**	**100,0%**	**6 211 876**	**100,0%**	**100,0%**

* Including any shares held in bearer form by the company's long-standing financial investors, as well as shares held by investors from the private placement realized in March 2015 (KKR having declared a threshold).

(1) SHAM : Société Hospitalière d'Assurance Mutuelles

As of the filing date of this reference document, the company had no knowledge of any significant changes in its shareholding structure after December 31, 2015.

Threshold crossing Mr. Rémi Soula

In a letter received January 6, 2015, supplemented in particular by a letter received January 9, 2015, Rémi Soula said, by way of adjustment, having crossed downwards, December 24, 2014, following a sale of shares ADOCIA on the market, the threshold of 5% of the Company's capital and that it held on that date and to date, ADOCIA 307,490 shares representing 614,980 voting rights, ie 4.95% of capital and 6.38% of voting rights (1).

On this occasion, the family group crossed Soula **has no threshold** and said hold on January 9, 2015, 1,540,933 shares representing ADOCIA 3,072,653 voting rights, ie 24.80% of capital and 31.90% of voting rights (1), as follows:

	Shares	%	Voting rights	% Voting rights
Gérard Soula (2)	898 463	14,46%	1 787 713	18,56%
Olivier Soula	317 490	5,11%	634 980	6,59%
Rémi Soula	307 490	4,95%	614 980	6,38%
Laure Soula	17 490	0,28%	34 980	0,36%
Total	**1 540 933**	**24,80%**	**3 072 653**	**31,90%**

(1) On the basis of a capital composed of 6,213,276 shares representing 9,632,145 voting rights, pursuant to the second paragraph of Article 223-11 of the General Regulations:

(2) Including his wife, Sylvie Soula.

Threshold crossing Mr. Olivier Soula

In a letter received January 15, 2015, supplemented in particular by a letter received January 16, 2015, Rémi Soula said, by way of adjustment, having crossed downwards, January, 2015, following a sale of shares ADOCIA on the market, the threshold of 5% of the Company's capital and that it held on that date and to date, ADOCIA 307,490 shares representing 614,980 voting rights, ie 4.95% of capital and 6.38% of voting rights [(1).]

On this occasion, the family group crossed Soula **has no threshold** and said hold on January 9, 2015, 1,525,933 shares representing ADOCIA 3,042,653 voting rights, ie 24.55% of capital and 31.24% of voting rights [(1)], as follows:

	Shares	%	Voting rights	% Voting rights
Gérard Soula [(2)]	898 463	14,45%	1 787 713	18,35%
Olivier Soula	307 490	4,95%	614 980	6,31%
Rémi Soula	302 490	4,87%	604 980	6,21%
Laure Soula	17 490	0,28%	34 980	0,36%
Total	**1 525 933**	**24,55%**	**3 042 653**	**31,24%**

[(1)] On the basis of a capital composed of 6,216,076 shares representing 9,740,990 voting rights, pursuant to the second paragraph of Article 223-11 of the General Regulation .
[(2)] Including his wife, Sylvie Soula.

Threshold crossing of the company ACG Management

In a letter received January 19, 2015, supplemented in particular by a letter received January 21, 2015, the limited company ACG Management [(1)] (6 aisles Turcat Mery, 13008 Marseille), acting on behalf of funds it manages, declared that it crossed downward, January 14, 2015, the threshold of 5% of the capital of the Company and hold, on behalf of said funds, 277,420 shares representing ADOCIA 554,840 voting rights, ie 4.46% of the capital and 5.70% of voting rights [(2)].

This threshold crossing results from a sale of Adocia shares on the market.

[(1)] Formerly Viveris Management. The company ACG Management is controlled at the highest level by Mr. Wladimir Mollof and states act independently of the person who controls, within the requirements of Articles L. 239-9 II of the Commercial Code and 223-12 and 223-12 -1 General Regulation.
[(2)] On the basis of a capital composed of 6,216,076 shares representing 9,740,990 voting rights, pursuant to the second paragraph of Article 223-11 of the General Regulation .

Threshold crossing of the company ACG Management

In a letter received January 22, 2015, the limited company ACG Management [(1)] (6 aisles Turcat Mery, 13008 Marseille), acting on behalf of funds it manages, declared that it crossed downward, January 19 2015, the threshold of 5% of the voting rights and hold, on behalf of said funds, 238,192 shares representing ADOCIA 476,384 voting rights, ie 3.83% of capital and 4.89% of voting rights [(2)].

This threshold crossing results from a sale of Adocia shares on the market.

[(1)] Formerly Viveris Management. The company ACG Management is controlled at the highest level by Mr. Wladimir Mollof and states act independently of the person who controls, within the requirements of Articles L. 239-9 II of the Commercial Code and 223-12 and 223-12 -1 General Regulation.
[(2)] On the basis of a capital composed of 6,216,076 shares representing 9,740,990 voting rights, pursuant to the second paragraph of Article 223-11 of the General Regulation .

Threshold crossing of the family group Soula

In a letter received February 20, 2015, the family group Soula said, by way of adjustment, having crossed over March 31, 2014, following a decrease in the total number of voting rights of the Company, the threshold 30% of the voting rights and held on that date, ADOCIA 1,550,933 shares representing 3,092,653 voting rights, ie 24.96% of capital and 30.92% voting rights [(1)], divided as follows :

	Shares	%	Voting rights	% Voting rights
Gérard Soula [(2)]	898 463	14,46%	1 787 713	17,87%
Olivier Soula	317 490	5,11%	634 980	6,35%
Rémi Soula	317 490	5,11%	634 980	6,35%
Laure Soula	17 490	0,28%	34 980	0,35%
Total	**1 550 933**	**24,96%**	**3 092 653**	**30,92%**

The declarant said hold on February 20, 2015, 1,525,933 shares representing 3,042,653 voting rights, ie 24.55% of capital and 32.61% of the voting rights [(3)], as follows:

	Shares	%	Voting rights	% Voting rights
Gérard Soula [(2)]	898 463	14,45%	1 787 713	19.16%
Olivier Soula	307 490	4,95%	644 980	6,59%
Rémi Soula	302 490	4,87%	604 980	6,48%
Laure Soula	17 490	0,28%	34 980	0,37%
Total	**1 525 933**	**24,55%**	**3 092 653**	**32,61%**

[(1)] On the basis of a capital composed of 6,213,276 shares representing 10,003,158 voting rights, in implementing paragraph 2 of article 223-11 of the General Regulation.
[(2)] Including his wife, Sylvie Soula.
[(3)] On the basis of a capital composed of 6,216,776 shares representing 9,329,515 voting rights, pursuant to the second paragraph of Article 223-11 of the General Regulation.

Threshold crossing company KKR & Co.LP :

In a letter received March 30, 2015, the KKR & Co. LP, (9 West 57th Street, Suite 4200, New York 10019, USA) reported having crossed over March 26, 2015 indirectly through the companies in its group, the threshold of 5% of the capital of the Company and indirectly holding 389,105 shares representing as many voting rights, representing 5.68% of capital and 3.93% of voting rights [1] distributed as follows:

	Shares	%	Voting rights	% Voting rights
KKR GMO II Holdings L.P [2]	369 650	5,40%	369 650	3,74%
KKR Partners II (International) L.P [3]	19 455	0,28%	19 455	0,20%
Total KKR & Co. L.P.	**389 105**	**5,68%**	**389 105**	**3,93%**

On this occasion, the KKR Holdings LP II GMO company had individually increase the same threshold.
These threshold crossings resulting from a capital increase of the Company following the lifting of realized funds via a private placement of new shares [4].

1 On the basis of a capital composed of 6,840,763 shares representing 9,893,718 voting rights, pursuant to the second paragraph of Article 223-11 of the General Regulation.
2 Controlled at the highest level by the company KKR & Co. LP.
3 Controlled by the company KKR PI-II GP Limited, acting as general partner, itself controlled at the highest level by the company KKR & Co. LP.
4 See in particular statement released by the company March 27, 2015.

Crossing the threshold Sham company:

Mails received by April 10, 2015, the Hospital Insurance Mutual Company (18 rue Edouard Rochet, 69372 Lyon cedex 08) said, by way of adjustment, it had fallen, March 26, 2015, the threshold of 5% ADOCIA capital of the company and hold at that time and to this day, ADOCIA 320,000 shares representing 640,000 voting rights, ie 4.68% of capital and 6.47% of the voting rights of the Company [1].
This threshold crossing results from a private placement of the Company in late March [2].

[1] On the basis of a capital composed of 6,840,763 shares representing 9,893,718 voting rights, pursuant to the second paragraph of Article 223-11 of the General Regulation.
[2] See in particular statement released by the company March 27, 2015.

Crossing the threshold Bpifrance Investment Company

In a letter received July 29, 2015, the Investment Company Bpifrance (1) (27-31 avenue du Général Leclerc - 94710 Maisons Alfort Cedex), acting on behalf of funds Bioam 1a Innobio compartment II and Innobio which it manages, said , by way of adjustment, having crossed downwards, July 23, 2015, the 20% threshold of the voting rights and hold, on that date, for the behalf of said funds, ADOCIA 1,084,665 shares representing 1,897,401 voting rights, ie 15.85% of capital and 19.60% of the voting rights distributed as follows:

	Shares	%	Voting rights	% voting rights
Bioam 1bis Compartiment II	274,573	4.03%	388,289	4.01%
Innobio	809,092	11.82%	1,509,112	15.59%
Total	**1,084,665**	**15.85%**	**1,897,401**	**19.60%**

(1) Jointly controlled at the highest level to 50% by Caisse des Dépôts et Consignations and 50% by EPIC BPI Group
(2) On the basis of a capital composed, on that date, of 6,842,163 shares representing 10,313,114 voting rights, pursuant to the second paragraph of Article 223-11 of the General Regulation

This threshold crossing results from the bearer of shares ADOCIA previously benefiting from double voting, as well as a sale of ADOCIA shares on the market.

Crossing the threshold Bpifrance Investment Company

In a letter received July 30, 2015, the Caisse des Depots et Consignations (CDC) (56 rue de Lille, 75356 Paris) said having crossed downwards, July 28, 2015, indirectly through Bpifrance Participations SA, which it controls through the company Bpifrance Group SA (1), and CDC Entreprises Valeurs moyennes the 20% threshold of the voting rights of Adocia company and indirectly held 1,117,223 Adocia shares representing 1,929,959 rights voting or 16.33% of the capital and 19.94% of voting rights in this company (2), as follows:

	Shares	%	Voting rights	% voting rights
CDC	0	0	0	0
Bpifrance Participations	0	0	0	0
CDC Entreprises Valeurs moyennes	65,732	0,96%	65,732	0,68%
Bpifrance Investissement	1,051,491	15,37%	1,864,227	19,26%
CDC	**1,117,223**	**16,33%**	**1,929,959**	**19,94%**

Ce franchissement de seuil résulte d'une cession d'actions Adocia sur le marché.

(1) Jointly controlled at the highest level to 50% by Caisse des Dépôts et Consignations and 50% by EPIC Bpi Group . BPI Group SA holds 100% of Bpifrance Participations SA and the latter holds 100% of Bpifrance Investment Bpi

(2) On the basis of a capital composed, on that date, of 6,842,163 shares representing 9,679,516 voting rights, pursuant to the second paragraph of Article 223-11 of the General Regulation

Crossing the threshold Bpifrance Investment Company

In a letter received August 7, 2015, the EPIC Bpi Groupe (27-37 avenue du Général Leclerc, 94710 Maisons Alfort Cedex), said having crossed downwards, August 5, 2015, indirectly through Bpifrance Investissement (1) acting on behalf of funds Bioam 1a Innobio compartment II and Innobio which it manages, the 15% threshold of the voting rights and hold, on that date, for the behalf of said funds, ADOCIA 1,021,177 shares representing 1,833,913 voting rights, ie 14.92% of capital and 18.95% of the voting rights distributed as follows:

	Shares	%	Voting rights	% voting rights
Innobio	777,348	11.36%	1,477,368	15.26%
Bioam 1bis Compartiment II	243,829	3.56%	356,545	3.68%
Total	**1,021,177**	**14.92%**	**1,833,913**	**18.95%**

Ce franchissement de seuil résulte d'une cession d'actions Adocia sur le marché.

(1) Jointly controlled at the highest level to 50% by Caisse des Dépôts et Consignations and 50% by EPIC Bpi Group . BPI Group SA holds 100% of Bpifrance Participations SA and the latter holds 100% of Bpifrance Investment Bpi
(2) On the basis of a capital composed, on that date, of 6,842,163 shares representing 9,679,516 voting rights, pursuant to the second paragraph of Article 223-11 of the General Regulation

Crossing the threshold Bpifrance Investment Company

In a letter received September 8, 2015, the Caisse des Depots et Consignations (CDC) (56 rue de Lille, 75356 Paris) said , by way of adjustment, having crossed downwards, July 28, 2015, indirectly through Bpifrance Participations SA, which it controls through the company Bpifrance Group SA (1), and CDC Entreprises Valeurs moyennes the 15% threshold of the voting rights of Adocia company and indirectly held 997,507 Adocia shares representing 1,810,243 rights voting or 14.57% of the capital and 18.74% of voting rights in this company (3), as follows:

	Shares	%	Voting rights	% voting rights
CDC	0	0	0	0
Bpifrance Participations SA	0	0	0	0
CDC Entreprises Valeurs moyennes	65,732	0.96%	65,732	0.68%
Bpifrance Investissement	931,775	13.61%	1,744,511	18.06%
Total CDC	**997,507**	**14.57%**	**1,810,243**	**18.74%**

This threshold crossing results from a sale of Adocia's shares on the market.

The declarant said hold on September 8, 2015, 969,001 Adocia shares representing 1,707,640 voting rights, ie 14.16% of the capital and 17.80% of voting rights in this company (4), as follows:

	Shares	%	Voting rights	% voting rights
CDC	0	0	0	0
Bpifrance Participations SA	0	0	0	0
CDC Entreprises Valeurs moyennes	65,732	0.96%	65,732	0.68%
Bpifrance Investissement	903,269	13.20%	1,641,908	17.11%
Total CDC	**969,001**	**14.16%**	**1,707,640**	**17.80%**

(1) Acting as management company of FCPI Innobio and FCPI Bioam 1bis C2 (cf. including D&I 215C1207 August 7, 2015).
(2) *Jointly controlled at the highest level to 50% by Caisse des Dépôts et Consignations and 50% by EPIC Bpi Group . BPI Group SA holds 100% of Bpifrance Participations SA and the latter holds 100% of Bpifrance Investment Bpi*
(3) *On the basis of a capital composed, on that date, of 6,844,963 shares representing 9,660,533 voting rights, pursuant to the second paragraph of Article 223-11 of the General Regulation*
(4) *On the basis of a capital composed, on that date, of 6,844,963 shares representing 9,595,649 voting rights, pursuant to the second paragraph of Article 223-11 of the General Regulation*

18.2 Distribution of capital and voting rights as of December 31, 2015 on a fully diluted basis

	Situation at December 31, 2015 on an undiluted basis			Situation at December 31, 2015 on a fully diluted basis (1)		
	Nombre d'actions	% du capital	% des droits de vote	Nombre d'actions	% du capital	% des droits de vote
Soula Family	**1 525 933**	**22,3%**	**31,8%**	**1 673 933**	**23,4%**	**32,3%**
Gérard Soula	898 463	13,1%	18,8%	958 463	13,4%	18,8%
Olivier Soula	307 490	4,5%	6,32%	357 490	5,0%	6,6%
Rémi Soula	302 490	4,4%	6,32%	340 490	4,8%	6,5%
Laure Soula	17 490	0,3%	0,4%	17 490	0,2%	0,4%
Financial investors	**1 166 639**	**17,0%**	**24,4%**	**1 166 639**	**16,3%**	**23,6%**
Innobio *(Bpifrance Investissement)*	625 923	9,1%	13,1%	625 923	8,8%	12,7%
Fonds BioAM *(Bpifrance Investissement)*	112 716	1,6%	2,4%	112 716	1,6%	2,3%
Subtotal BPIfrance investissement	*738 639*	*10,79%*	*15,43%*	*738 639*	*10,3%*	*15,0%*
Fonds Viveris	67 439	1,0%	1,4%	67 439	0,9%	1,4%
Oréo Finance	40 561	0,6%	0,8%	40 561	0,6%	0,8%
Famille Deleage	0	0,0%	0,0%	0	0,0%	0,0%
SHAM (*)	320 000	4,67%	6,7%	320 000	4,48%	6,5%
Key employees	**40 270**	**0,6%**	**0,76%**	**174 720**	**2,4%**	**2,1%**
Scientific committees (stock warrants)	700	0,0%	0,0%	**2 100**	**0,0%**	**0,0%**
administrator (stock warrants)	0	0,0%	0,0%	**20 000**	**0,3%**	**0,2%**
Treasury shares	**4 185**	**0,1%**	0,0%	**4 185**	**0,1%**	0,0%
other shareholders (2)	**4 108 636**	**60,0%**	**43,1%**	**4 108 636**	**57,5%**	**41,8%**
Total	**6 846 363**	**100,0%**	**100,0%**	**7 150 213**	**100,0%**	**100,0%**

(*) *SHAM : Société Hospitalière d'Assurance Mutuelles*

(1) *At the date of this reference document, the dilutive instruments issued by the Company consist of (i) 61,750 shares (after taking into account the division by 10 of the par value of shares decided by the General Meeting on October 24, 2011) freely allocated by the Company to key employees are in vesting period as more fully described in paragraph 21.1.7 of this Reference Document and (ii) 1,400 warrants entitling subscription of shares in the subscription of 1,400 shares (after taking into account the division by 10 of the par value of shares decided by the General Meeting on October 24, 2011) and (iii) 20,000 share subscription warrants entitling to the subscription of 20,000 shares granted to independent directors (iv) 196,700 entrepreneur share warrants entitling to subscribe for 196,700 shares and (v) 24,000 stock options entitling to the subscription of 24,000 shares.*

(2) *Including any shares held in bearer form by the company's long-standing financial investors*

18.3 Major shareholders not represented on the board of directors

The Innobio and Bioam Funds and significant shareholders of the Company amounting to 10.79% of the capital and 15.43% of voting rights at December 31, 2015 are represented on the board by Bpifrance Investments.

The company Société Hospitalière d'Assurance Mutuelles (SHAM) shareholder of the Company in the amount of 4.67% and firm KKR & Co.LP, shareholder of the Company amounting to 5.68% of capital and 3.93% of rights voting (according to threshold crossing declarations dated March 30, 2015 - see section 18.1 of this registration document) are not represented on the board.

18.4 Voting rights of major shareholders

A voting right double that which is conferred on other shares, based on the portion of share capital they represent, is assigned to all fully paid-up shares (regardless of their class) registered in the name of the same shareholder for at least two years, it being stipulated that the conversion of preferred shares into ordinary shares has no impact on the calculation of the holding period.

This right is also conferred at the time of issue, in case of a capital increase by capitalization of reserves, earnings or issue premiums, to registered shares granted free of charge to a shareholder in exchange for old shares for which this right is already enjoyed.

18.5 Control of the company

As of the filing date of this reference document, no single shareholder owned a percentage likely to raise a presumption of control of the company within the meaning of Article L. 233-3 of the French Commercial Code (*Code de commerce*).

The company has therefore not been required to take measures to ensure that such control is not improperly exercised.

No pact between shareholders is in force at the date of this reference document, with the exception of the collective commitment of conservation of the securities of the Company, said the pact "Dutreil," concluded Gérard Soula, Olivier Soula, Remi Soula Soula and Laure under the provisions of Article 787 B of the General Tax Code.

The Company's shareholder Soula the family group, which currently includes Gérard Soula (CEO), Olivier Soula (Deputy CEO), Remi Soula, Laure and Sylvie Soula Soula. Gérard Soula and Olivier Soula serve on the Company's Board of Directors, respectively as Chairman and Director, along with four other directors (Olivier Martinez, Laurent Arthaud representing Bpifrance Investment, Dominique Takizawa and Ekaterina Smirnyagina). The family group Soula conducts consolidated statements (see paragraph 18.1 of this Reference Document) filed and obtained a waiver from the obligation to launch a public offer as a result of exceeding the 30% threshold by familly group Soula..

18.6 Agreements that can lead to a change in control

No specific element of the issuer's instrument of incorporation, bylaws, charter or regulations could have the effect of delaying, deferring or preventing a change in its control.

18.7 Pledges of the company's shares

None.

19 RELATED-PARTY TRANSACTIONS

The regulated agreements that exist to date are mentioned in the special reports of the statutory auditors presented below.

19.1 Intra-group agreement

None

An annual contract for services ("Services Agreement") was entered into between Adocia and Adocia Inc. from March 2015. That contract provides for the re-invoicing of costs incurred by the Company as part of its business, plus a 10% commission to cover the running costs of the US subsidiary.

The impact linked to the creation of this new company on the financial statements at December 31, 2015 is limited, the subsidiary having 9 months old. Expenses amounting to 0.9 million euro correspond to the staff costs of 2 employees and their travel and representation costs.

19.2 Related-party transactions

None

19.3 Statutory auditors' report on regulated agreements made for the fiscal year ended December 31, 2015

Adocia

Shareholders' meeting held to approve the financial statements for the fiscal year ended December 31, 2015

Statutory Auditors' Special Report on Regulated Agreements

ODICEO
115, boulevard de Stalingrad
B.P. 52038
69616 Villeurbanne Cedex
Limited liability company with €275,000 in share capital

Statutory Auditor
Member of the Compagnie
Régionale de Lyon

ERNST & YOUNG et Autres
Tour Oxygène
10-12, boulevard Marius Vivier Merle
69393 Lyon Cedex 03
Simplified joint stock company with variable capital

Statutory Auditor
Member of the Compagnie
Régionale de Versailles

Adocia

Shareholders' meeting held to approve the financial statements for the fiscal year ended December 31, 2015

Statutory Auditors' Special Report on Regulated Agreements

Dear Shareholders,

In our capacity as your company's statutory auditors, we present to you our report on regulated agreements and commitments.

It is our responsibility to inform you, based on the information provided to us, of the characteristics and essential terms and conditions of the agreements and commitments brought to our attention or about which we may have learned during the course of our audit, without our being required to comment on their usefulness and relevance or to determine the existence of other agreements and commitments. It is your responsibility, pursuant to Article R. 225-31 of the Commercial Code, to assess the advantage of entering into these agreements and commitments with a view to their approval.

It is also our responsibility, where applicable, to provide you with the information referred to in Article R. 225-31 of the Commercial Code regarding the performance, during the previous fiscal year, of the agreements and commitments already approved by the shareholders' meeting.

We have conducted the work that we deemed necessary in accordance with the accounting standards of the *Compagnie nationale des commissaires aux comptes* that apply to this audit.

Agreements subject to the approval of the shareholders' meeting

We inform you that we have not been advised of any agreement or commitment authorized during the previous fiscal year which is subject to the approval of the shareholders' meeting pursuant to Article L. 225-38 of the Commercial Code.

Agreements already approved by the shareholders' meeting

We inform you that we have not been advised of any agreement or commitment already approved by the shareholders' meeting which remained in force during the previous fiscal year.

Villeurbanne and Lyon, April 7, 2016

The statutory auditors

ODICEO

Sylvain Boccon-Gibod

ERNST & YOUNG et Autres

Sylvain Lauria

20 FINANCIAL INFORMATION CONCERNING THE COMPANY'S ASSETS, FINANCIAL POSITION AND EARNINGS

20.1 Consolidated financial statements prepared under IFRS for the years ended December 31, 2014 and 2015

IFRS balance sheet

STATEMENT OF FINANCIAL POSITION ASSETS - (in € thousands)	Notes	12/31/2015	12/31/2014
Intangible assets	3.1	-	2
Laboratory equipment	3.2	812	557
Other property, plant and equipment	3.2	1 118	418
Holdings in affiliates		0	0
Financial assets	3.3	182	808
NON-CURRENT ASSETS		**2 112**	**1 786**
Inventories	3.5	23	35
Trade and similar receivables	3.6	5 150	158
Other current assets	3.7	8 747	765
Cash and cash equivalents	3.8	72 062	49 800
CURRENT ASSETS		**85 983**	**50 758**
**** GRAND TOTAL ****		**88 095**	**52 544**

STATEMENT OF FINANCIAL POSITION LIABILITIES - (in € thousands)	Notes	12/31/2015	12/31/2014
Share capital		685	622
Share premium		78 670	49 097
Group translation gains and losses		2	0
Group reserves		(44 858)	(26 499)
Group net profit/loss		12 553	(20 715)
NON-CONTROLLING INTERESTS			
EQUITY	3.9	**47 052**	**2 505**
Long-term financial debt	3.10	702	728
Long-term provisions	3.11	1 095	396
Deferred tax liabilities		0	0
Other non-current liabilities	3.12	18 839	29 568
NON-CURRENT LIABILITIES		**20 636**	**30 692**
Short-term financial debt	3.14	89	1 573
Other current financial liabilities	3.14	46	111
Trade and similar payables	3.13	5 461	2 649
Other current liabilities	3.13	14 811	15 014
CURRENT LIABILITIES		**20 407**	**19 347**
**** GRAND TOTAL ****		**88 095**	**52 544**

IFRS Income Statement

STATEMENT OF COMPREHENSIVE INCOME (in € thousands)	Notes	12/31/2015	12/31/2014
Revenue	3.16	36 936	704
Other income	3.17	7 818	3 459
Total income		**44 753**	**4 163**
Operating expenses excluding additions and reversals	3.15	(34 182)	(20 928)
Additions to and reversals of depreciation, amortization and	3.20	(468)	(397)
PROFIT/LOSS FROM ORDINARY OPERATING ACTIVITIES		**10 103**	**(17 161)**
Financial income		2 548	608
Financial expense		(430)	(84)
FINANCIAL INCOME/EXPENSE	3.21	**2 118**	**524**
PROFIT/LOSS BEFORE TAX		**12 220**	**(16 637)**
Tax expense	3.22	333	(4 078)
NET PROFIT/LOSS		**12 553**	**(20 715)**
Non-controlling interests			
GROUP NET PROFIT/LOSS		**12 553**	**(20 715)**
Base earnings per share (€)	3.23	1,9	(3,3)
Diluted earnings per share (€)		1,8	(3,3)
GROUP NET PROFIT/LOSS		**12 553**	**(20 715)**
Actuarial adjustments on defined pension liabilities		*(629)*	*(73)*
Deferred taxes		*0*	*24*
Unclassified elements in the Group net profit/loss		*(629)*	*(49)*
TOTAL PROFIT/LOSS FOR THE YEAR		***11 924***	***(20 764)***

IFRS Cash Flow Statement

STATEMENT OF CASH FLOWS (in € thousands)	**12/31/2015**	**12/31/2014**
Net profit/loss	**12 553**	**(20 715)**
Net depreciation, amortization & provisions (excl. current assets)	507	347
Capital gains and losses on non-current assets	-	(25)
Calculated income and expenses	3 027	3 537
loan writte-off	(1 050)	0
Cash flow from operations after cost of net financial debt and tax	**15 037**	**(16 856)**
Cost of net financial debt	-	-
Tax expense (including deferred taxes)	-	-
Cash flow from operations before cost of net financial debt and tax	**15 037**	**(16 856)**
Taxes paid	(544)	0
Change in deferred revenues	**(10 749)**	40 380
Change in working capital requirement (including employee benefits)	**(9 959)**	**7 037**
NET CASH FLOW GENERATED BY OPERATING ACTIVITIES	**(6 216)**	**30 561**
Acquisitions of property, plant and equipment & intangible assets	(1 284)	(401)
Disposals of property, plant and equipment & intangible assets	-	25
Acquisitions of non-current financial assets	(20)	(1)
Disposals of non-current financial assets	-	202
Other cash flows related to investing activities	500	0
NET CASH FLOW RELATED TO INVESTING ACTIVITIES	**(804)**	**(174)**
Capital increase	29 782	-
New loans and reimbursable advances	-	-
Repayments of loans and reimbursable advances	(500)	-
Net financial interest paid	-	-
Other cash flows related to financing activities	-	-
NET CASH FLOW RELATED TO FINANCING ACTIVITIES	**29 282**	**0**
CHANGE IN NET CASH AND CASH EQUIVALENTS	**22 262**	**30 386**
Opening cash	49 800	19 415
Closing cash	72 062	49 800

Detailed analysis of changes in working capital requirement (WCR):

WORKING CAPITAL REQUIREMENT (in € thousands)	Change 2015/2014
Inventories	12
Trade and similar receivables	(4 992)
Other receivables and advances	(7 594)
Pre-paid expenses / other receivables	(388)
Provision - employee benefits	-
Trade and similar payables	(2 617)
Other debt	(386)
Change in working capital requirement	**(9 959)**

Components of net cash and cash equivalents analyzed by type and reconciliation with the balance sheet:

NET CASH AND CASH EQUIVALENTS (in € thousands)	12/31/2015	12/31/2014
Short-term investment securities (due in < 3 months)	10 108	6 304
Cash on hand	61 954	43 495
Net cash and cash equivalents	**72 062**	**49 800**

Statement of Changes in Equity, IFRS

(in € thousands)	Share capital: Number of shares	Share capital: Amount	Paid-in capital	Reserve	Net profit / (loss)	Other comprehensive income (OCI)	Total equity
Balance at 12/31/2013	**6 211 876**	**621**	**48 810**	**-26 136**	**-4 293**	**128**	**19 130**
Profit for the year 2014					-20 715		-20 715
gain (losses) on actuarial adjustments on defined pension liabilities						-69	-69
translation adjustment							0
Comprehensive income for the period					**-20 715**	**-69**	**-20 783**
allocation of profit for the year 2013				-4 293	4 293		0
increase in capital							0
costs of capital increases							0
Exercise of equity instruments (warrants)	4 200	0	0			12	12
Share-based payment				3 328			3 328
Liquidity Contract - Elimination of treasury shares			288	531			819
Total shareholder relations	**4 200**	**0**	**287**	**-435**	**4 293**	**12**	**4 158**
Balance at 12/31/2014	**6 216 076**	**622**	**49 097**	**-26 571**	**-20 715**	**71**	**2 505**
Profit for the year 2015					12 553		12 553
gain (losses) on actuarial adjustments on defined pension liabilities						-629	-629
translation adjustment							0
Comprehensive income for the period					**12 553**	**-629**	**11 924**
allocation of profit for the year 2014				-20 715	20 715		0
increase in capital	621 887	62	31 903				31 965
costs of capital increases			-2 152				-2 152
Exercise of equity instruments (warrants)	8 400	1	33				34
Share-based payment				2 903			2 903
Liquidity Contract - Elimination of treasury shares			-211	84			-127
Total shareholder relations	**630 287**	**63**	**29 573**	**-17 728**	**20 715**	**0**	**32 623**
Balance at 12/31/2015	**6 846 363**	**685**	**78 670**	**-44 299**	**12 553**	**-558**	**47 052**

NOTES TO THE FINANCIAL STATEMENTS PREPARED UNDER IFRS

1. Presentation of business activity and major events

1.1. Information about the company and its activity

Adocia is a limited company (société anonyme) under French law created on December 22, 2005.
It specializes in the development of best-in-class medicines from already approved therapeutic protein and anti-cancer molecules.
The Company holds a 100% subsidiary (Adocia Inc.) established in March 2015 which aims to represent the company in the US.

The consolidated financial statements under IFRS for the year ended 31 December 2015 were approved by the Board of Directors of 15 March 2016 and authorized for publication. They are presented on a consolidated basis for Adocia and its subsidiary (Adocia Inc), the whole being called "the Company".

1.2. Major events of the fiscal year ended December 31, 2015

The year 2014 had ended with the signing of a major license agreement with Eli Lilly for the development of ultra-fast insulin analog formulation with the technology BioChaperone.

The year 2015 was marked by intense activity in the framework of partnership, with, from 20 January to launch a clinical trial of the effect of ultrafast insulin Lispro BioChaperone after the meal. After the publication of the positive results of this trial end in June 2015, three trials were then launched in the second half:

- Two Phase 1b studies of repeated administration of ultrafast insulin, one conducted in patients with type 1 and one conducted in patients with type 2,
- A Phase 1b study of type 1 diabetes using an insulin pump

The results of these three studies are expected during the first half of 2016.
As provided in the license agreement and collaboration, Lilly supports all internal and external expenses incurred by Adocia.

In parallel to these trials U100 formulation, a formulation twice concentrated U200 has been tested during a pilot bioequivalence study compared the formulation U100. The positive results of this test, published in December, allowed Adocia receive a milestone payment of $ 10 million. This is the first milestone payment received under the license agreement that provides for a potential $ 520 million if the product reaches certain milestones in clinical, regulatory and certain sales targets.

The year 2015 was also dense for projects developed on equity by Adocia:

- BioChaperone Combo, the unique combination of slow insulin glargine and insulin lispro, with the two clinical trials in 2015: one of 28 type 1 diabetic patients comparing BioChaperone Combo with Humalog Mix 75/25 and the other in 24 type 2 diabetic patients in comparison with Humalog Mix 75/25 and the double injection of Lantus and Humalog.

  In the 2 tests, the results have shown a significantly higher share early prandial and metabolic effect of prolonged BioChaperone Combo versus HumalogMix 75/25. The study on type 2 patients has also established the proof of concept that the product developed by Adocia had an effect similar to that of the double injection of Lantus and Humalog

  The results of these studies to fully validate the continued clinical development in 2016

- BioChaperone ® human insulin (HinsBet): the results of the Phase II clinical study published in February 2015 showed that the action of HinsBet was significantly faster than Humulin® and

comparable to that of Humalog in the first hour (critical for blood sugar control). With its results, the Company continued development and future studies which prepared for launch early 2016.

- BioChaperone PDGF-BB: clinical phase 3 trial continued throughout 2015 with the recruitment and treatment of 252 patients. Results are expected for the first half 2016.

In addition, the Company continued to work with great actors of the pharmacy undertaking feasibility studies of innovative formulations of monoclonal antibodies.

Financially, 2015 was marked by the completion of a private placement of almost 30 million euros to institutional investors, including American. This fundraiser of nearly 10% of capital has strengthened the Adocia cash position and to increase its visibility within the financial community and with players in the pharmaceutical world

In terms of organization, Adocia has entered a new phase in its development. It first created a subsidiary in the United States and hired a general manager and a chief medical officer.It also strengthened its teams in France to recruit nearly 25 people to support the development of its projects. It has extended its premises and fitted nearly 700 m² of additional laboratory and office space.

Finally, in December 2015, the Company celebrated its 10th anniversary during a day gathering employees, individuals and companies that have contributed to its success.

1.3. Events subsequent to year end

On 18 January 2016, the Company signed a sale agreement with the Metropolis of Lyon for the acquisition of the building where are located its offices 115 Avenue Lacassagne, 69003 Lyon. The promise of sale is the building called "Pépinière Lacassagne" with a total area of 7.120 m², the land on which the building is located and 43 parking spaces.

The Company has the immediate use and enjoyment of the property, and that, upon signature of the sale agreement.

The signing of the deed of sale is expected during the month of April 2016.

2. Accounting methods and principles used to draw up the financial statements

2.1. Principles used to draw up the company's financial statements

Declaration of compliance

In accordance with EU regulation 1606/2002 of July 19, 2002 on international standards, the company's year-end financial statements 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, available on the website of the European Commission (http://ec.europa.eu/internal_market/accounting/ias_fr.htm), include the international accounting standards (IAS and IFRS) and the interpretations of the Standing Interpretations Committee (SIC) and the International Financial Interpretations Committee (IFRIC).

Principles used to prepare the financial statements

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.

Going concern

The going concern assumption was used given the company's financial ability (available cash assets) to meet its financing requirements over the next 12 months.

Accounting principles and methods

The accounting principles and methods used by the company for the year-end financial statements are the same as those used in the financial statements for the year ended December 31, 2013.

The income recognized at December 31, 2015 and Decmber 31, 2014 (respectively 70.6 and 73 thousand euros) following the introduction of the tax credit for competitiveness and employment (CICE) is recorded in the financial statements in accordance with IAS 19 as a deduction from payroll expense.

In addition, the new mandatory texts applicable to fiscal years beginning on January 1, 2015 are as follows:

Normes, amendements de normes et interprétations applicables depuis le 1er janvier 2015 :

- IFRIC 21 - Duties and taxes (applicable at the latest for fiscal years beginning after June 17, 2014)
- Recognition of a liability of a right or a required fee.
- Amendment to IFRS 13 – valuation at fair value;

Other Amendments:

- Amendment to IFRS 1 – First application of IFRS;
- Amendment to IFRS 3 – business combination;
- Amendment to IAS 40 –investment property

These new standards are not subject to developments in the context of financial information to the extent that they are not applicable to the Company

New standards, amendments and interpretations applicable at a later date and adopted by the European Union:

- Amendment to IAS 19 – contribution to staff ;
- Amendment to IFRS 2 – share based payment ;
- Amendment to IFRS 8 – operational areas ;
- Amendment des bases de conclusion d'IFRS 13 ;
- Amendment to IAS 16 and IAS 38 – tangible and intangible assets ;
- Amendement to IAS 24 – information on related parties

The company has not applied these interpretations in advance. None is expected to have a material impact on the financial statements.

Consolidation methods

The consolidated financial statements include by full consolidation, the accounts of all subsidiaries whose Adocia holds directly or indirectly control. Control is determined in accordance with IFRS10 on the basis of three criteria: the power, exposure to variable returns and the relationship between power and those returns.

In March 2015, the Company created a subsidiary called Adocia Inc. 100% owned and consolidated at the end of December 2015 by global integration.

The entrance to the subsidiary Adocia Inc. in the scope of consolidation is 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 subsidiary Adocia Inc. and the Company and internal results in the consolidated group are eliminated.

Translation of foreign subsidiay accounts

The financial statements of the Company are prepared in euro, which is the presentation currency.

The method used by the Company is that of the closing rate. This method is thus is to convert the balance sheet at the closing rate and income items at the average rate for the year; the translation differences, both on the opening balance sheet items on the income statement are included in equity under "Translation differences".

2.2. Use of judgments and estimates

To prepare the financial statements in accordance with IFRS, certain estimates, judgments and assumptions have been made by the company's management, which may have affected the amounts shown for the assets, liabilities and contingent liabilities as of the date of preparation of the financial statements, and the amounts shown for income and expenses during the year.

These estimates are based on the going concern assumption and are based 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 year-end 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, 2014. These assumptions include fall of IFRS 2 ("Share-based Payment") and IFRS 15 ("Revenue from contracts with customers") and are explained in the following paragraphs resp. §2.15 and §2.21.

2.3. Functional presentation currency

The company's financial statements are prepared in euros, which is the presentation currency and functional currency of the parent company and its subsidiary.

2.4. Current/non-current distinction

The balance sheet presentation used by the company makes a distinction between current and non-current assets and liabilities.

This distinction is made based on the following rules:

- assets and liabilities that fall within the scope of the company's operating working capital requirement are classified as "current";
- assets and liabilities that are not part of the company's normal operations are presented as "current" or "non-current" based on whether their due date is more than or less than one year.

2.5. 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:

- (a) technical feasibility needed to complete the development project is established,
- (b) the company intends to complete the project,
- (c) the company is able to use the intangible asset,
- (d) the company is able to demonstrate the probability that the asset will generate future economic benefits,
- (e) the company has the technical, financial and other resources to complete the project, and (f) the development costs are measured reliably.

Patents:

The costs incurred prior to filing and obtaining patents are capitalized by the company based on the same provisions as those used to capitalize development costs.

Other intangible assets:

Intangible assets acquired separately by the company are recognized at cost and those acquired through a business combination are recognized at fair value.
Concessions, licenses and software are amortized over the expected useful life (two to five years depending on the type of software).

2.6. 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, with the exception of acquisitions of parking lots, which the company has chosen not to depreciate.

Depreciation is calculated on a straight-line basis according to the estimated useful life of the assets and, if applicable, the residual values:

	Life
Fixtures and facilities	1 to 6 years
Laboratory equipment	3 to 5 years
Furniture, office equipment	5 years

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.

2.7. Leasing (including lease financing)

Where applicable, an asset held under a finance lease (which substantially transfers all the risks and rewards of ownership of the asset to the company) is recorded as an asset and a liability (in the same amount) on the balance sheet at the lower of the fair value of the asset and the sum of the discounted payments.
These assets are depreciated according to the same methods and rules described above in note 2.6. The corresponding liabilities are recorded on the balance sheet and repaid in an amount equal to the theoretical amortization of loans whose characteristics are comparable to those of the lease agreements.

Operating lease agreements are recorded as expenses on a straight-line basis over the term of the agreement until its expiration.

2.8. 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.

2.9. 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 of the last cash flow of the test to infinity.

As of December 31, 2015, there is no internal or external impairment indicator for any non-current assets.

2.10. Basis of measurement of inventories

Inventories are recognized at the lower of cost and net realizable value. They may be depreciated if they have expired or /and if the project which is relates has been dropped by the Company and has been declared as failure. The cost of inventories is determined using the first-in first-out method.

2.11. Financial assets

Financial assets are classified into four categories based on their type and the intention to hold the:

- 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 agreemen :

The cash reserve related to the liquidity agreement for the buyback of the company's own shares is recorded as non-current financial assets.

2.12. 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 changes in value. They are measured at fair value and changes in value are recorded in financial profit or loss.

For the purposes of the statement of cash flows, 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.

2.13. Reimbursable advances

The company receives a certain amount of government assistance in the form of reimbursable advances. Government grants are recognized as assets when there is reasonable assurance that:

- the company will comply with the conditions attached to the grants; and
- the grants will be received.

Reimbursable 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 20. Since they are financial advances granted at below-market interest rates, they are measured according to IAS 39 if the impacts are material. .

2.14. 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.

2.15. Share-based payments

In accordance with IFRS 2, benefits granted to certain employees in the form of share-based payments are measured at the fair value of the instruments granted.

This payment can take the form of equity-settled instruments or cash-settled instruments.

The company has introduced several equity-settled payment plans.

For example, stock options are granted to senior managers, certain company employees and other private individuals.

The company uses the Black-Sholes 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.

2.16. 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.

2.17. Corporate commitments

In accordance with IAS 19R, retirement plans, similar payments and other employee benefits that are considered defined benefit plans (plan in which the company agrees to guarantee a defined amount or benefit level) are recorded in the balance sheet based on an actuarial assessment of the obligations on the closing date, reduced by the fair value of the plan assets. These calculations mainly include:

- an assumption related to the benefit payment date;
- a financial discount rate;
- an inflation rate;
- assumptions related to salary increases, employee turnover rate and mortality rate.

The main actuarial assumptions made at December 31, 2015 are described in note 3.11.

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.

2.18. 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.

2.19. 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.

2.20. 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 liability method of tax allocation 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, as well as for tax loss carryforwards.
A deferred tax asset, generated by tax losses, is recognized when there is persuasive evidence that a sufficient taxable profit will be available.

2.21. 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 is generally 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, an initial payment (up-front fee) may be stipulated in the agreement. If the company has fulfilled all its obligations at closing, the amount has been definitively received and the company is not obligated to provide additional services over the term of the agreement, this initial payment is recognized immediately in the income statement for the fiscal year. Adocia considers the circumstances and facts to determine whether such payments received should be spread out over the entire payment period of the agreement or recognized immediately.
To date, the company's revenue corresponds primarily to revenue generated for research and development services which are assessed based either on the attainment of technical milestones or on

the accrued cost method. Where appropriate, impairment may be recorded when the collectibility of the invoiced amounts is uncertain.

2.22. Other income

Grants :

Due to its innovative nature, since its creation the company has received a certain amount of assistance and grants from the French government and public authorities to help finance its operation or recruit specific individuals.

These grants are recognized as income over the fiscal year in which the corresponding costs or expenses are recorded.

Research tax credit:

The French government grants research tax credits to companies to encourage them to conduct technical and scientific research. Companies that can substantiate expenditures meeting the required criteria (research costs in France or, since January 1, 2005, within the European Community or in another State that is part of the Agreement on the European Economic Area and has signed a tax treaty with France containing an administrative assistance clause) are eligible for a tax credit that can be used to pay the corporation tax due for the fiscal year in which the expenses are incurred and the following three fiscal years or, where appropriate, be reimbursed for the excess share of such tax.

2.23. 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.

2.24. Presentation of the income statement

The company presents its income statement by nature.
The purpose of the expenses is provided in note 3.15.

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 reimbursable advances
- Income related to interest received.

Foreign-exchange gains and losses are also recognized in financial income/expense.

Tax expenses:

Income tax : This item includes tax recorded for the year on a prospective recipient taxable income (French GAAP).
Deferred taxes are recognized for all temporary differences arising from the difference between the tax and accounting bases of assets and liabilities in the financial statements. The main temporary differences relate to tax loss carryforwards. The statutory tax rate to 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 losses carried forward. Given the stage of development that does not establish the result of projections considered sufficiently reliable, the Company did not recognize the asset balance of deferred tax for loss carryforwards.

2.25. 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.

2.26. Fair value of financial instruments

Fair value measurements are detailed by level according to the following fair value hierarchy:

- the instrument is quoted in an active market (level 1);
- measurement uses valuation techniques based on observable inputs, either directly (price) or indirectly (price derivatives) (level 2);
- at least one material component of fair value is based on unobservable inputs (level 3).

Fair value of financial instruments traded in active markets is based on quoted prices on the balance sheet date. A market is considered active if quoted prices are easily and regularly available from an exchange, trading officers, brokers, an appraiser or a regulatory agency and such prices are based on regular trades. These instruments are classified as level 1.

Fair value of financial instruments that are not quoted in an active market (for example, over-the-counter derivatives) is determined based on valuation techniques. These methods maximize the use of observable market inputs, if available, and, for the most part, are not based on the company's own estimates. If all the elements required to calculate the fair value of the instrument are observable, this instrument is classified as level 2.

If one or more of the main calculation elements are not based on observable market inputs, the instrument is classified as level 3.

3. Additional information regarding certain balance sheet and income statement items

3.1. Intangible assets

INTANGIBLE ASSETS (in € thousands)	GROSS AMOUNT	AMORTIZATION AND IMPAIRMENT	NET AMOUNT
Value at December 31, 2014	**75**	**73**	**2**
Acquisitions/(Additions) (Disposals)/reversals		2	(2)
Value at December 31, 2015	**75**	**75**	**0**

Intangible assets consist of software.

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.

The amounts recognized as expenses are provided in note 3.15.

3.2. Immobilisations corporelles

GROSS AMOUNT (in € thousands)	Laboratory equipment	Fixtures and facilities	Furniture, office equipment	Total
Total value at December 31, 2014	**1 841**	**677**	**681**	**3 198**
Acquisitions	489	734	212	1 434
Disposals	(1)	0	(73)	(74)
Total value at December 31, 2015	**2 329**	**1 410**	**819**	**4 559**

DEPRECIATION AND IMPAIRMENT (in € thousands)	Laboratory equipment	Fixtures and facilities	Furniture, office equipment	Total
Total value at December 31, 2014	**1 283**	**416**	**523**	**2 223**
Additions	235	148	96	480
Reversals/Disposals	(1)	0	(73)	(74)
Total value at December 31, 2015	**1 518**	**564**	**546**	**2 629**

NET AMOUNT (in € thousands)	Laboratory equipment	Fixtures and facilities	Furniture, office equipment	Total
Total value at December 31, 2014	**557**	**261**	**157**	**976**
Total value at December 31, 2015	**811**	**846**	**273**	**1 930**

The company owns several assets financed through leasing. It holds two agreements. The first is a property the acquisition value of 72 thousand euro funded over 3 years and the second relates to equipment with a total acquisition value of 85 thousand euro financed over 4 years. These 2 contracts end uin 2016 and 2017.

3.3. Non-current financial assets

The company's non-current financial assets are as follows:

NON-CURRENT INVESTMENTS (in € thousands)	GROSS AMOUNT	AMORTIZATION AND IMPAIRMENT	NET AMOUNT
Value at December 31, 2014	**809**		**809**
Acquisitions/(Additions)	20	0	20
(Disposals)/reversals	(646)	0	(646)
Value at December 31, 2015	**183**		**183**

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 paragraph entitled "Capital management" in note 3.09.).

3.4. Additional information regarding deferred taxes

The company cannot determine with sufficient reliability when it will be able to absorb its accumulated losses. Therefore, the company has not recognized deferred tax assets related to these losses.

The amount of deferred tax assets not recognized for prior carry-over losses was €37.1 million at December 31, 2014 and €41 million at December 31, 2015.

3.5. Inventories

Net value of inventories is €35 thousand at 31/12/2014 and €23 thousand at 31/12/2015.

Depreciation relates to inventories related to projects for which the Company recognized that it has failed.

INVENTORIES (in € thousands)	31/12/2015	31/12/2014
Raw materials	**23**	**35**
Semi-finished products		
Finished products		
Total net value	**23**	**35**

3.6. Receivables

TRADE RECEIVABLES (in € thousands)	12/31/2015	12/31/2014
Gross amount	**5 150**	**158**
Impairment	0	0
Total net value	**5 150**	**158**

Some receivables are not yet due. They relate to collaboration contracts.

3.7. Other current assets

OTHER CURRENT ASSETS (in € thousands)	12/31/2015	12/31/2014
Research tax credit	6 768	
VAT claims	637	356
Receivables from suppliers	330	109
Pre-paid expenses	676	288
Carryback	333	
Miscellaneous	4	12
Total other current assets	**8 747**	**765**

All other current assets remains with a maturity of less than one year.

Since its inception, the company has been entitled to a research tax credit. It thus recognized as the end of each period a receivable calculated on the eligible expenses of the year. However, since the Company recorded deficits up to 2013, the Company could not charge this credit against its tax and therefore requested reimbursement that has been obtained the following year.

For the fiscal 2014 period, the fiscal income was positive, leading to the recognization of corporate tax. The Company has charged the 2014 Reseach Tax Credit (CIR) against this tax.

In 2015, due to the fiscal net loss, the CIR has been recognized in current assets for € 6.8 million.

Pre-paid expenses relate to current expenses.

In addition to social security claims and other sundry creditors, the miscellaneous item includes grants receivable.

3.8. Classification and fair value of financial assets

FINANCIAL ASSETS (in € thousands)	2015	Valeur au bilan selon IAS 39				2015
	Value on the balance sheet	Assets at fair value through profit or loss	Held-to-maturity investments	Loans and receivables	Available-for-sale financial assets	Fair value
Non-current financial assets						
Trade receivables	5 150			5 150		5 150
Other current financial assets	8 747			8 747		8 747
Cash on hand	61 954	61 954				61 954
Cash equivalents (UCITS)	10 108	10 108				10 108
Total assets	**85 960**	**72 062**		**13 898**		**85 960**

FINANCIAL ASSETS (in € thousands)	2014	Value on the balance sheet under IAS 39				2014
	Value on the balance sheet	Assets at fair value through profit or loss	Held-to-maturity investments	Loans and receivables	Available-for-sale financial assets	Fair value
Non-current financial assets						
Trade receivables	158			158		158
Other current financial assets	765			765		765
Cash on hand	43 495	43 495				43 495
Cash equivalents (UCITS)	6 304	6 304				6 304
Total assets	**50 724**	**49 800**		**924**		**50 724**

The only financial assets measured at fair value are cash and cash equivalents, which include money market mutual funds in euros, time accounts quoted in an active market and interest-bearing accounts. They therefore constitute level 1 financial assets at fair value.

3.9. Equity

For easier cross-reference between the two periods, the number of shares in fiscal year 2011 has been restated to reflect the decision by the shareholders' meeting on October 24, 2011 to approve a 10-for-1 stock split and to grant 10 shares, each with a par value of €0.10, for a previously held share with a par value of €1.

Share capital

The company was created on December 22, 2005. All the shares issued are fully paid-up.
The company owns treasury shares under its liquidity agreement.
Following the initial public offering, preferred shares were converted into ordinary shares and the Ratchet stock warrants became null and void.

	Number of shares (*)	Ordinary shares	Preferred shares - category A	Preferred shares - category B	Nominal amount (euros)
At January 1, 2007	**140 000**			**140 000**	**1 400 000**
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
	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
12/13/2013 - Grant of bonus shares	1 400	1 400			140
15/12/2014 - Grant of bonus shares	1 400	1 400			140
02/12/2015 - Grant of BSA	700	700			70
03/03/2015 - Grant of BSPCE	700	700			70
03/27/2015 - Grant of BSPCE	1 400	1 400			140
03/31/2015 - Issue of IPO Shares by private placeme	621 887	621 887			62 189
03/31/2015 - Grant of Bonus shares	1 400	1 400			140
2015/07/28 - Grant of BSPCE	2 800	2 800			280
2015/12/16 - Grant of bonus shares	1 400	1 400			140
At December 31, 2015	**6 846 363**	**6 846 363**	**0**	**0**	**684 636**

Stock warrants

Stock options were granted (i) to certain employees in the form of start-up warrant of company stock ("BSPCE") (ii) to two independent directors on the board of directors in the form of warrants of shares ("BSA") and (iii) to scientific consultants in the form of warrants of shares (“BSA”).

The main characteristics of the warrants of shares and the principal assumptions used to measure the fair value of the options based on the Black-Sholes model are as follows:

situation at 12/31/2015	BSPCE$_{12\text{-}2013}$ Plan No. 1	BSPCE$_{12\text{-}2013}$ Plan No. 2	BSA$_{12\text{-}2013}$	BSPCE 2014 Plan No. 1	BSPCE 2014 Plan No. 2	BSPCE 2014 Executives
Recipients	employees	employees	independent directors	employees	employees	employees and executives
Number of warrants issued	28 000	22 400	20 000	14 000	5 600	100 000
Number of warrants granted	28 000	22 400	20 000	14 000	5 600	100 000
Number of warrants subscribed	28 000	22 400	20 000	14 000	5 600	100 000
Date of shareholders' meeting	06/18/2013			06/24/2014		
Date of Board of Directors' meeting	12/13/2013			09/25/2014		
Issue price	free		0,588 €	free		
Strike price	5,76 €		5,88 €	34,99 €		
Deadline to exercise warrants	12/13/2023			09/25/2024		
Start date to exercise options	1/4: Jan. 1, 2014 1/4: Jan. 1, 2015 1/4: Jan. 1, 2016 1/4: Jan. 1, 2017	1/4: Jan. 1, 2015 1/4: Jan. 1, 2016 1/4: Jan. 1, 2017 1/4: Jan. 1, 2018	13,333: Jan. 1, 2014 3,333: Jan. 1, 2015 3,333: Jan. 1, 2016	1/4: Jan. 1, 2015 1/4: Jan. 1, 2016 1/4: Jan. 1, 2016 1/4: Jan. 1, 2018	1/4: Jan. 1, 2016 1/4: Jan. 1, 2017 1/4: Jan. 1, 2018 1/4: Jan. 1, 2019	Immediate vesting on 1 Jan 2015, following the fulfillment of conditions set out in Plan
Parity	One warrant for one share			One warrant for one share		
Dividend yield	none			none		
Volatility	67%			97%		
Risk-free rate of return	2% (iBoxx Sovereign AA 7-10)			0,9% (iBoxx Sovereign AA 7-10)		

situation at 12/31/2015	SO 2015 Plan N°1	SO 2015 Plan N°2	BSPCE Plan N°1
Recipients	employees	employees	excecutives
Number of warrants issued	10 000	4 000	40 000
Number of warrants granted	10 000	4 000	40 000
Number of warrants subscribed	10 000	4 000	40 000
Date of shareholders' meeting	06/24/2014	11/12/2015	11/12/2015
Date of Board of Directors' meeting	03/31/2015	12/16/2015	12/16/2015
Issue price	free	free	free
Strike price	55,64 €	71,12 €	74,60 €
Deadline to exercise warrants	03/31/2025	12/16/2025	12/16/2025
Start date to exercise options	1/4 : Jan 1, 2016 1/4 : Jan 1, 2017 1/4 : Jan 1, 2018 1/4 : Jan 1, 2019	1/4 : Jan 1, 2017 1/4 : Jan 1, 2018 1/4 : Jan 1, 2019 1/4 : Jan 1, 2020	immediate vesting to 16 December 2015, following the completion of conditions in Plan
Parity	One warrant for one share	One warrant for one share	One warrant for one share
Dividend yield	none	none	none
Volatility	74%	74%	74%
Risk-free rate of return	1% (iBoxx Sovereign AA 7-10)	1% (iBoxx Sovereign AA 7-10)	1% (iBoxx Sovereign AA 7-10)

The cost of services rendered is recognized as a payroll expense and external charge over the vesting period. The total expense was €2.6 million as of December 31, 2015.

Bonus shares

Bonus shares have been granted to certain employees of the company since 2008.

Movements in bonus shares are as follows:

Date d'attribution	01/23/2008	06/06/2008	12/15/2009	03/05/2010	12/07/2010	12/10/2015	12/16/2015	TOTAL
Number of free shares awarded (1)	42 000	5 600	5 600	5 600	5 600	39 150	22 600	**126 150**
Number of free shares canceled	2 100	-		-	-	-	-	**2 100**
Number of bonus shares sold	11 600		410	200				**12 210**
acquired shares, available or under conservation	28 300	5 600	5 190	5 400	5 600	-	-	**50 090**
Shares granted but not yet vested	-	-	-	-	-	39 150	22 600	**61 750**

BONUS SHARES - Date of ESM decision	12/20/2007				12/20/2007				12/20/2007				12/20/2007				12/20/2007			
Date of grant by the Board of Directors	01/23/2008				06/06/2008				12/15/2009				03/05/2010				12/07/2010			
Number of vesting years	2	3	4	5	2	3	4	5	2	3	4	5	2	3	4	5	2	3	4	5
Performance condition	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
Total number of bonus shares granted	10 500	10 500	10 500	10 500	1 400	1 400	1 400	1 400	1 400	1 400	1 400	1 400	1 400	1 400	1 400	1 400	1 400	1 400	1 400	1 400
Share value on grant date (euros)	8,57	8,57	8,57	8,57	8,57	8,57	8,57	8,57	8,57	8,57	8,57	8,57	8,57	8,57	8,57	8,57	8,57	8,57	8,57	8,57
Fair value of a bonus share (euros)	8,57	8,57	8,57	8,57	8,57	8,57	8,57	8,57	8,57	8,57	8,57	8,57	8,57	8,57	8,57	8,57	8,57	8,57	8,57	8,57
Initial valuation (€ thousands)	90	90	90	90	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
Number of bonus shares to be issued at 12/31/2014																**1 400**				**1 400**
Number of bonus shares granted																				
Number of bonus shares canceled																				
Number of bonus shares definitively granted																-1400				
Number of bonus shares to be issued at 12/31/2015																				**1 400**
December 2014 accounting expenses (€ thousands)		0				0				2				3				5		
December 2015 accounting expenses (€ thousands)														0,4				2		

BONUS SHARES - Date of ESM decision	11/12/2015				11/12/2015				11/12/2015				11/12/2015				Total
Date of grant by the Board of Directors	12/16/2015				12/16/2015				12/16/2015				12/10/2015				
Number of vesting years	1				1				1	2	3	4	1	2	3	4	
Performance condition	No				No				No	No	No	No	No				
Total number of bonus shares granted	5 000				5 000				3 150	3 150	3 150	3 150	39 150				126 150
Share value on grant date (euros)	76,74				76,74				76,74	76,74	76,74	76,74	70,80				
Fair value of a bonus share (euros)	76,74				76,74				76,74	76,74	76,74	76,74	70,80				
Initial valuation (€ thousands)	384				384				242	242	242	242	2 772				5 058
Number of bonus shares to be issued at 12/31/2014																	**2 800**
Number of bonus shares granted	5 000				5 000				3 150	3 150	3 150	3 150	39 150				
Number of bonus shares canceled																	0
Number of bonus shares definitively granted																	-1 400
Number of bonus shares to be issued at 12/31/2015	**5 000**				**5 000**				**3 150**	**3 150**	**3 150**	**3 150**	**39 150**				**63 150**
December 2014 accounting expenses (€ thousands)																	10,4
December 2015 accounting expenses (€ thousands)		15				15				19				76			127

The cost of services rendered is recognized as a payroll expense over the vesting period. The expense amounted to €10.4 thousand at 31 December 2014 and €127 thousand at December 31, 2015.

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.

In late December 2014, 2,323 Adocia's shares and 778,747.18 euros in cash included in the contract of the account between the Company and Kepler Capital Markets.

Under the terms of the liquidity contract, the Company has decided February 10, 2015 to proceed with a partial recovery of the resources allocated to this contract up to an amount of €700,000 euro. September 10, 2015, the resources made available under the liquidity contract at Kepler Capital Markets S.A. were increased by €200,000.

During fiscal 2015, the share buyback program was used exclusively in the context of the liquidity agreement with the objective of animation and liquidity of securities of the Company. At 31 December 2015, the Company held as part of this contract 4,185 shares and €132,740 in cash.

3.10. Long-term financial debt

As of December 31, 2014 and 2015, reimbursable advances accounted for most of the long-term financial debt. Details about these advances and repayment terms are available in note 3.1 to the individual financial statements prepared under French GAAP for the fiscal years ended December 31, 2014 and 2015 provided in Chapter 20.3 of this reference document.

At the end of 2015, the classification as current and non-current was as follows:

FINANCIAL DEBT (in € thousands)	Current	Non-current	Total	Bank overdrafts
Reimbursable advances	89	702	791	0
Other financial debt	46	0	46	0
Total financial debt	**135**	**702**	**839**	

Details about advances granted and repayment in fiscal year 2015:

REIMBURSABLE ADVANCES		(in € thousands)	Historical cost	
Value at December 31, 2014		**2 301**	**2 441**	(A)
	Long-term portion	*728*		
	Short-term portion	*1 573*		
Grant during the year				
Repayment during the year		(500)	(500)	
forgiveness of debt		(1 044)	(1 050)	
Discount on grant during the year				
Financial expenses		*35*		
Value at December 31, 2015		**792**	**891**	(B)
	Long-term portion	*702*		
	Short-term portion	*89*		

(A) in € thousands	12/31/2014	Less than 1 year	1 to 5 years	More than 5 years
Osteoporosis advance	1 550	1 550		
Insulin advance (2012)	800		280	520
Coface advance (2013)	91		91	

(B) in € thousands	12/31/2015	Less than 1 year	1 to 5 years	More than 5 years
Osteoporosis advance				
Insulin advance (2012)	800		800	
Coface advance (2013)	91		91	

3.11. Provisions

PROVISIONS (in € thousands)	Employee benefits	Other long-term provisions	Provisions for risks and charges - less than one year	Total
Value at December 31, 2014	**396**			**396**
Additions	698			698
Reversal of used provisions				
Reversal of unused provisions				
Value at December 31, 2015	**1 095**			**1 095**

Retirement indemnities:

The provision for retirement indemnities was measured 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:

Retirement indemnities (in € thousands)	**12/31/2015**	**12/31/2014**
Economic assumptions		
Discount rate	2%	1,5%
Rate of annual salary increase	5 to 6%	2% to 4%
Demographic assumptions		
Retirement age	67	67
Type of retirement	Initiated by employee	Initiated by employee
Mortality table	INSEE 08-10	INSEE 07-09
Rate of tax and social security charges	44,5%	46%
Annual mobility	Average or High depending on category	Average or High depending on category
Provision		
Present value of obligations	1 095	396
Payments to a fund		
Provision recorded on the balance sheet	**1 095**	**396**
Past service costs for the period	63	63
Financial expense	7	7
Actuarial gains and losses	-629	-73
Annual expense	**70**	**70**

3.12. Other non-current liabilities

Other non current liabilities include the long term part of the initial up-front payment received from Eli Lilly for a total of $50 million (€40.7 million). Under IFRS rules, this amount is recognized in revenues linearly over the duration of the development plan as anticipated at the time of the signature of the agreement. A part of these €40.7 million has been recognized in revenue in 2014 for €0.4 million given the contract signing date to December 18, 2014 and in 2015 for €10.7 million. The balance was accounted for in other current liabilities (portion of less than 1 year: €10.8 million cf note 3.13) and other non-current liabilities (portion for more than 1 year: €18.8 million).

3.13. Trade payables and other current liabilities

The company's current liabilities are as follows:

(in € thousands)	12/31/2015	12/31/2014
Subsidiary accounts	2 303	1 369
Notes payable		
Invoices pending	3 158	1 280
Trade payables	**5 461**	**2 649**
Customer credit balances		
Tax and social security liabilities	3 950	4 185
Other debt	13	17
Unearned income	10 848	10 812
Other current liabilities	**14 811**	**15 014**
TOTAL CURRENT OPERATING LIABILITIES	**20 272**	**17 663**

All trade payables and other current liabilities a have a maturity of less than one year.

Tax and social security liabilities are as follows:

TAX AND SOCIAL SECURITY LIABILITIES (in € thousands)	31/12/2015	12/31/2014
Compensation owed	1 986	1 818
Debt owed to social welfare agencies	1 489	1 207
Value added tax		
Other tax and social security liabilities	475	1 159
Tax and social security liabilities	**3 950**	**4 184**

Compensation payable and debts due to social security agencies at the end of year 2015 include bonus granted for the fiscal year 2015 and paid in fiscal year 2016. In 2014, this line also included the statutory employee profit sharing and the related social security charges.

Other tax and social security liabilities to the December 31, 2015 include the employer contribution plans granting free shares to employees. In 2014, they integrated the corporate income tax under the profit tax result and the CVAE.

3.14. Financial liabilities

	12/31/2015			
(in € thousands)	Value on the	Fair value	Breakdown by instrument category	
			Fair value through profit or loss	Debt at amortized cost
Reimbursable advances	702	702		702
Financial debt				
Other non current liabilities	18 839	18 839		18 839
Total non-current financial liabilities	**19 541**	**19 541**		**19 541**
Short-term reimbursable advances	89	89		89
Short-term financial debt	46	46		46
Trade and similar payables	5 461	5 461		5 461
Other debt	3 963	3 963		3 963
Unearned income	10 848	10 848		10 848
Total current financial liabilities	**20 407**	**20 407**		**20 407**
TOTAL FINANCIAL LIABILITIES	**39 949**	**39 949**		**39 949**

(in € thousands)	Value on the balance sheet	12/31/2014 Fair value	Breakdown by instrument category	
			Fair value through profit or loss	Debt at amortized cost
Reimbursable advances	728	728		728
Financial debt				
Other non current liabilities	29 568	29 568		29 568
Total non-current financial liabilities	**30 296**	**30 296**		**30 296**
Short-term reimbursable advances	1 573	1 573		1 573
Short-term financial debt	111	111		111
Trade and similar payables	2 649	2 649		2 649
Other debt	4 202	4 202		4 202
Unearned income	10 812	10 812		10 812
Total current financial liabilities	**19 347**	**19 347**		**19 347**
TOTAL FINANCIAL LIABILITIES	**49 643**	**49 643**		**49 643**

3.15. Operating profit/loss

INCOME STATEMENT (in € thousands)	Notes	12/31/2015	12/31/2014
Research agreements and license revenue	3.16	36 936	704
Grants, public financing and research tax credit	3.17	7 818	3 459
Income		**44 753**	**4 163**
Cost of goods sold		(1 133)	(961)
Payroll expense	3.19	(12 690)	(11 025)
External charges	3.18	(20 119)	(8 319)
Taxes		(240)	(622)
Depreciation, amortization & provisions	3.20	(468)	(397)
Other current operating income and expenses		0	(0)
Operating expenses		**(34 651)**	**(21 324)**
PROFIT/LOSS FROM ORDINARY OPERATING		**10 103**	**(17 161)**
Non-recurring operating income and expenses			
PROFIT/LOSS FROM OPERATING ACTIVITIES		**10 103**	**(17 161)**

Breakdown of expenses by function:

EXPENSES BY FUNCTION (in € thousands)	12/31/2015	12/31/2014
Research and development costs	(28 625)	(17 006)
Administrative costs	(6 025)	(4 319)
Operating expenses	**(34 651)**	**(21 324)**

Research and development costs are as follows:

RESEARCH AND DEVELOPMENT COSTS (in € thousands)	12/31/2015	12/31/2014
Cost of goods sold	(1 133)	(953)
Payroll expense	(8 312)	(7 390)
External charges	(18 588)	(7 802)
Taxes	(187)	(510)
Depreciation, amortization & provisions	(405)	(350)
Total research and development costs	**(28 625)**	**(17 006)**

3.16. Revenue

REVENUE (in € thousands)	12/31/2015	12/31/2014
Research agreements	17 048	321
License revenue	19 888	383
Other		
Total	**36 936**	**704**

Revenue consists of:

- Under research agreements: revenue amounting for 2015 to € 16.8 million, mainly reflecting the assumption by Lilly of all internal and external expenses incurred by Adocia in the development of licensed project. Last year in the same period, revenues of EUR 0.3 million were made up only of feasibility contracts for the development of monoclonal antibodies. During 2015, these contracts have continued and have generated €0.2 million,
- Under licences: the generated revenues totaled €19.9 million and include:
  - 1) accounting depreciation totaling €10.7 million of the initial payment (up-front payment) of $50 million received from Lilly end of December 2014. Under IFRS, this payment is recognized in license revenue linearly over the duration of the development plan as defined in the contract. Last year, due to the execution of the contract on December 18, 2014, this amortization had a slight impact impact on revenue (€0.4 million).
  - 2) The milestone payment of $ 10 million, or 9.2 million, received from Lilly following positive results of a pilot bioequivalence study. This is the first milestone paid pursuant to the contract which includes a potential $ 520 million in development and commercial milestones

3.17. Other income

OTHER INCOME (in € thousands)	12/31/2015	12/31/2014
Project financing	1 050	0
Research tax credit	6 768	3 461
Other		(2)
Total	**7 818**	**3 459**

The reimbursable advance of an initial amount of €2.25 million received from Bpifrance Financing for the bone reconstruction project (osteoporosis) was cleared out during 2015. Consequent to the decision of a partial failure of the program in 2015, an amount of €1.050 million was forgiven and recognized as a

grant. The remaining amount which was not yet reimbursed (€ 0.5 million) was paid by Adocia September 30, 2015.

3.18. Other purchases and external charges

These are mainly in-vivo studies, clinical trials, lease payments and all operating expenses of the Company.

3.19. Payroll expense

Payroll expense is as follows:

PAYROLL EXPENSE (in € thousands)	12/31/2015	12/31/2014
Wages and salaries	6 966	8 769
Social contributions	5 724	2 256
Total payroll expense	**12 690**	**11 025**

STAFF	12/31/2015	12/31/2014
Technicians	51	37
Management personnel	58	43
Total employees	**109**	**80**

At December 31, 2015, the company had 40 postdoctoral.

Over 80% of employees are directly dedicated to research and development activities.

The number of training hours acquired at the end of December 2014 under employees' individual right to training (DIF) was 5,476. This system was abolished on January 1st, 2015 and replaced by the personal training account. Account management is no longer done by the company but by the Caisse des Dépôts et Consignations.

3.20. Depreciation, amortization and impairment losses

Net depreciation, amortization and provisions are as follows:

DEPRECIATION, AMORTIZATION AND IMPAIRMENT (in € thousands)	12/31/2015	12/31/2014
Depreciation of property, plant and equipment	424	351
Amortization of intangible assets		
Depreciation of leased assets	45	45
Depreciation, amortization and provisions for fixed assets	**468**	**397**
Provisions for risks and charges (additions)		
Provisions for current assets (additions)		
Reversals		
Additions to/Reversals of Depreciation, Amortization and Provisions	**468**	**397**

3.21. Financial income/expense

The cost of net financial debt is as follows:

FINANCIAL INCOME/EXPENSE (in € thousands)	31/12/2015	31/12/2014
Cash and cash equivalents income	2 548	608
Interest on conditional advances	(37)	(71)
Cost of net financial debt	**2 511**	**537**
Foreign exchange gains and losses		
Other financial income and expenses	(393)	(13)
FINANCIAL INCOME/EXPENSE	**2 118**	**524**

3.22. Corporation tax

Last year, with €41 million net sales recognized according to French Gaap, the Company had a net profit before tax of €24.8 million. The deferred tax losses that could be carried forward on this profit were limited to €12.9 million. As a consequence, the taxable profit for 2014 amounted to €11.9 and led to the recognition of a total amount of tax of €4 million with an exceptionnal contribution of €0.1 million. In 2015, with a tax loss of nearly 5 million, no tax expense was recognized. The company attributed part of its fiscal deficit on the income of the previous year, generating a tax receivable (carryback) of 333 thousand euro.

The remaing deferred losses to be carried forward , after imputation made in 2015, amounts to €41 million. This loss is not limited in time. The Company can not determine with sufficient reliability, how horizon it will reduce its accumulated deficit, it does not recognize deferred tax asset relating to this deficit.

In 2015, with a tax loss of nearly 5 million, no tax expense was recorded.

The difference between pre-tax profit/loss and the actual tax expense is shown below:

(in € thousands)	12/31/2015	12/31/2014
Profit/loss before tax	12 220	(16 637)
Notional tax of 34.43%	(4 207)	5 728
Permanent differences	(2 227)	(34)
Uncapitalized tax loss adjusted for deferred tax	(1 981)	(9 772)
Actual tax expense	**0**	**(4 078)**
Actual tax rate	*0%*	*25%*

No tax asset was recognized since the company cannot determine with sufficient reliability when it will be able to absorb its losses.

3.23. Earnings per share

	12/31/2015	12/31/2014
Consolidated net profit/loss (in € thousands)	**12 553**	**(20 715)**
Average number of shares	6 689 199	6 213 077
Net earnings per share (in euros)	**1,9**	**(3,3)**
Net earnings per share (in euros) - fully diluted	**1,8**	**(3,3)**

Equity instruments outstanding are not included in the calculation of earnings per share since they are considered anti-dilutive given the company's losses over previous fiscal years.

4. 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 are described in the table below.

(in € thousands)	12/31/2015	12/31/2014
short-term benefits	1 107	965
posterior employment benefits	82	51
Other long term benefits	0	0
Termination benefits employment contract	0	0
Share-based payment	2 240	2 015
TOTAL	**3 429**	**3 031**

5. 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.

Up to date, the company had little exposure to changes in the euro/US dollar exchange rate. As a result of the licensing and collaboration agreement signed with the American Eli Lilly pharmaceutical group at the end of 2014, the company may have to carry out euro/US dollar foreign currency hedging transactions and forward sale transactions.

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.

Credit risk

The debt related to the government grants and research tax credit poses 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 customer’s ability to pay, the Company believes that it is not very exposed to a credit risk because of the its customer‘s profile with whom partnership agreements have been signed (world’s leading pharmaceutical companies). Furthermore, policies have been implemented and thus ensuring the Company 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

The company has no debt with financial institutions and therefore no interest rate risk.

Equity risk

The company has no non-consolidated holdings or investment securities tradable on a regulated market.

6. Off-balance sheet commitments

None

20.2 Statutory auditors' reports on the consolidated financial statements prepared under IFRS for the fiscal year ended December 31, 2015

Adocia

Fiscal year ended December 31, 2015

Statutory auditors' audit report on the year-end consolidated financial statements

ODICEO
115, boulevard Stalingrad
B.P. 52038
69616 Villeurbanne Cedex
Corporation with €275,000 in share capital

Statutory Auditor
Member of the Compagnie
Régionale de Lyon

ERNST & YOUNG et Autres
Tour Oxygène
10-12, boulevard Marius Vivier Merle
69393 Lyon Cedex 03
Simplified joint stock company with variable capital

Statutory Auditor
Member of the Compagnie
Régionale de Versailles

Adocia

Fiscal year ended December 31, 2015

Statutory auditors' audit report on the year-end consolidated financial statements

To the shareholders

In compliance with the assignment entrusted to us by your general meetings, we hereby present our report for the year ended 31 December 2015 on

- the audit of consolidated financial statements of Adocia company, as attached to this report
- the justification of our assessments
- the specific verification required by law

The consolidated financial statements were approved by the Board of Directors. It is our responsibility, based on our audit, to express an opinion on these accounts.

I. Opinion on the consolidated financial statements

We conducted our audit in accordance with professional standards applicable in France; These standards require the implementation of procedures to obtain reasonable assurance whether the financial statements are free of material misstatement. An audit includes examining, on a test basis or using other selection methods, evidence supporting the amounts and disclosures in the consolidated accounts. An audit also includes assessing the accounting principles used and significant estimates made and the overall financial statement presentation. We believe that the evidence we have obtained is sufficient and appropriate basis for our opinion.

We certify that the consolidated financial statements, prepared in accordance with IFRS as adopted in the European Union, regular and sincere and give a fair view of the assets, financial situation and results of the group consisting of entities included in the consolidation

II. Basis of opinion

Pursuant to Article L. 823-9 of the Commercial Code relating to the justification of our assessments, we bring to your attention the following matters:

The note "2.21 Turnover" of the consolidated financial statements sets out the rules and accounting policies for revenue recognition. As part of our assessment of accounting rules and principles followed by your company, we have verified the appropriateness of accounting policies and disclosures in the consolidated accounts and we ensured their correct application.

The assessments were made in the context of our audit of the consolidated financial statements taken as a whole, and therefore contributed to the formation of our opinion expressed in the first part of this report

III. specific verification

We have also verified in accordance with professional standards applicable in France, the specific verification required by law information on the group given in the management report.

We have no comment to make on the fairness and consistency with the consolidated financial statements.

Villeurbanne and Lyon, April 7, 2016

The Statutory Auditors

ODICEO — ERNST & YOUNG et Autres

Sylvain Boccon-Gibod — Sylvain Lauria

20.3 Individual financial statements prepared under French GAAP for the fiscal years ended December 31, 2014 and 2015

Balance sheet (French GAAP)

ASSETS - (in € thousands)	12/31/2015			12/31/2014
	Gross Amount	*Depr./Amort. and Prov.*	*Net Amount*	*Net Amount*
Intangible assets				
* Start-up costs	11	11	0	0
* Concessions, patents and similar rights	75	75	0	2
TOTAL Intangible assets	**86**	**86**	**0**	**2**
Tangible fixed assets				
* Land	127		127	127
* Fixtures & fittings, industrial equipment	2 245	1 474	771	495
* Other tangible fixed assets	1 775	998	777	242
* Construction work in progress	155		155	
* Advances and payments on account	33		33	
TOTAL Tangible fixed assets	**4 334**	**2 472**	**1 862**	**863**
Financial assets:				
* Other financial assets	491		491	886
TOTAL Financial assets	**491**	**0**	**491**	**886**
LONG-TERM ASSETS	**4 911**	**2 558**	**2 353**	**1 751**
Inventory and work in progress	**85**	**62**	**23**	**35**
Receivables				
* Advance payments made on orders	330		330	109
* Trade and similar receivables	5 150		5 150	158
* Other receivables	7 824		7 824	368
* Subscribed capital called but not paid				
TOTAL Receivables	**13 304**		**13 304**	**636**
Cash assets and Misc.				
* Short-term investment securities	40 182		40 182	2 036
* Cash assets	31 720		31 720	47 762
* Pre-paid expenses	344		344	288
TOTAL Cash assets and Misc.	**72 247**		**72 247**	**50 086**
CURRENT ASSETS	**85 636**	**62**	**85 574**	**50 757**
Translation losses	16		16	2
TOTAL ASSETS	**90 562**	**2 620**	**87 943**	**52 510**

LIABILITIES - (in € thousands)	12/31/2015	12/31/2014
	Net Amount	***Net Amount***
Net position		
Paid-up capital	685	622
Additional paid-in capital	79 587	49 803
Balance brought forward	(7 272)	(31 006)
Profit/loss for the year	4 478	23 734
TOTAL Net position	77 477	43 152
EQUITY	**77 477**	**43 152**
Conditional advances	891	2 441
OTHER EQUITY	**891**	**2 441**
Provisions for risks	16	3
Provisions for charges		
PROVISIONS FOR RISKS AND CHARGES	**16**	**3**
Financial debt		
Convertible bonds		
Other bond issues		
Loans and debt with credit institutions		
Misc. loans and financial debt	163	
TOTAL Financial debt	163	
Advance payments received on pending orders		
Misc. debt		
Trade and similar payables	5 443	2 649
Tax and social security liabilities	3 843	4 190
Debt on fixed assets and similar accounts		
Other debt	11	12
TOTAL Misc. debt	9 297	6 851
Unearned income	99	63
DEBT	**9 558**	**6 913**
Translation gains	0	1
TOTAL LIABILITIES	**87 943**	**52 510**

Income statement (French GAAP)

INCOME STATEMENT - (in € thousands)	12/31/2015			12/31/2014
	France	*Export*	*Net Amount*	*Montant Net*
Sales of goods				
Sales of services	4	26 185	26 189	41 043
TOTAL Net revenue	4	26 185	26 189	41 043
Operating subsidies			1 050	(2)
Reversals of depr./amort. and prov., transfers of charges			159	67
Other income			0	
OPERATING INCOME	**4**	**26 185**	**27 397**	**41 107**
External charges				
Purchases of raw materials and other supplies			1 109	946
Change in inventory of raw mat. and supplies			25	15
Other purchases and external charges			20 899	8 363
TOTAL External charges			22 033	9 324
Taxes and similar payments			255	622
Wages and salaries			6 410	4 982
Social contributions			3 024	2 256
TOTAL Payroll expense			9 434	7 238
TOTAL Operating allowances			491	352
Other operating expenses			42	41
OPERATING EXPENSES			**32 254**	**17 576**
OPERATING PROFIT/LOSS			**(4 857)**	**23 531**
Financial income on investments				
Income from other securities and receivables on long-term assets			584	80
Other interest and similar income				
Reversals of provisions and transfers of charges			22	151
Foreign exchange gains			1 937	528
Net income on sales of short-term investment securities				
TOTAL Financial income			2 543	758
Depreciation allowance and provisions				22
Interest and similar expenses			16	
Foreign exchange losses			374	5
TOTAL Financial expenses			390	27
FINANCIAL INCOME/EXPENSE			**2 153**	**732**
PROFIT/LOSS FROM ORDINARY ACTIVITIES BEFORE TAX			**(2 704)**	**24 263**
Extraordinary income				
Extraordinary income from management operations			16	6
Extraordinary income from capital transactions			120	503
Reversals of provisions and transfers of charges				
TOTAL Extraordinary income			136	510
Extraordinary expenses on capital transactions			55	1
TOTAL Extraordinary expenses			55	1
EXTRAORDINARY PROFIT/LOSS			**81**	**509**
Employee profit-sharing				(421)
Income tax			7 101	(617)
PROFIT OR LOSS			**4 478**	**23 734**

Assets (French GAAP)

ASSETS - (in € thousands)	Period from 01/01/2015 to 12/31/2015			Period from 01/01/2015 to 12/31/2015			
	Gross amount at start of fiscal year	*Increases by revaluation*	*Acquisitions, contributions, creation, transfers*	*Decreases by transfer*	*Decreases by disposals and removals from service*	*Gross amount at end of fiscal year*	*Statutory revaluations*
Start-up and development costs	11					11	
Other intangible assets	75					75	
TOTAL Intangible assets	**86**		**0**		**0**	**86**	
Constructions	127					127	
Fixtures & fittings and industrial equipment	1 756		489		(1)	2 245	
General facilities, fixtures and misc.	550		546			1 096	
Office, computer equipment and furniture	540		212		(73)	679	
Tangible fixed assets in progress	0		155			155	
TOTAL Tangible fixed assets	**2 974**		**1 434**		**(74)**	**4 334**	
Loans and other financial assets	905	85	200		(700)	491	
Total Financial assets	**905**	**85**	**200**		**(700)**	**491**	
GRAND TOTAL	**3 965**	**85**	**1 634**		**(774)**	**4 911**	

ASSETS - (in € thousands)	Period from 01/01/2014 to 12/31/2014			Period from 01/01/2014 to 12/31/2014			
	Gross amount at start of fiscal year	*Increases by revaluation*	*Acquisitions, contributions, creation, transfers*	*Decreases by transfer*	*Decreases by disposals and removals from service*	*Gross amount at end of fiscal year*	*Statutory revaluations*
Start-up and development costs	11					11	
Other intangible assets	73		1			75	
TOTAL Intangible assets	**84**		**1**		**0**	**86**	
Constructions sur sol propre	127					127	
Fixtures & fittings and industrial equipment	1 531		225			1 756	
General facilities, fixtures and misc.	544		7			550	
Office, computer equipment and furniture	490		50			540	
Tangible fixed assets in progress	8			(8)		(0)	
TOTAL Tangible fixed assets	**2 699**		**282**		**0**	**2 973**	
Loans and other financial assets	628	876	300		(900)	905	
Total Financial assets	**628**		**300**		**(900)**	**905**	
GRAND TOTAL	**3 412**		**583**		**(900)**	**3 963**	

Depreciation and amortization (French GAAP)

DEPRECIATION/AMORTIZATION - (in € thousands)	Period from 01/01/2015 to 12/31/2015						
POSITION AND MOVEMENTS DURING THE FISCAL YEAR DEPRECIABLE/AMORTIZABLE ASSETS	*Amount at start of fiscal year*	*Increases additions*	*Decreases reversals*	*Amount at end of fiscal year*	*Straight-line depr./amort.*	*Straight-line depr./amort.*	*Extraordinary depr./amort.*
Intangible assets							
Start-up and development costs	11			11	11		
Other intangible assets	73	2		75	75		
TOTAL Intangible assets	**84**	**2**	-	**86**	**86**	-	-
Buildings on own land							
Fixtures & fittings and industrial equipment	1 262	213	1	1 474	1 474		
General facilities, fixtures and misc.	416	149		565	565		
Office, computer equipment and furniture	433	73	73	433	433		
TOTAL Tangible fixed assets	**2 111**	**435**	**74**	**2 472**	**2 472**	-	-
Expenses for purchases of equity interests							
GRAND TOTAL	**2 195**	**437**	**74**	**2 558**	**2 558**	-	-

DEPRECIATION/AMORTIZATION - (in € thousands)	Period from 01/01/2014 to 12/31/2014						
POSITION AND MOVEMENTS DURING THE FISCAL YEAR DEPRECIABLE/AMORTIZABLE ASSETS	*Amount at start of fiscal year*	*Increases additions*	*Decreases reversals*	*Amount at end of fiscal year*	*Straight-line depr./amort.*	*Straight-line depr./amort.*	*Extraordinary depr./amort.*
Tangible fixed assets							
Start-up and development costs	11			11	11		
Other intangible assets	70	3	- 0	73	73		
TOTAL Intangible assets	**81**	**3**	**- 0**	**84**	**84**	**-**	**-**
Buildings on own land							
Fixtures & fittings and industrial equipment	1 094	168		1 262	1 262		
General facilities, fixtures and misc.	368	48		416	416		
Office, computer equipment and furniture	376	57		433	433		
TOTAL Tangible fixed assets	**1 837**	**273**	**-**	**2 110**	**2 110**	**-**	**-**
Expenses for purchases of equity interests							
GRAND TOTAL	**1 918**	**276**	**- 0**	**2 195**	**2 195**	**-**	**-**

Provisions recorded on the balance sheet (French GAAP)

PROVISIONS RECORDED ON THE BALANCE SHEET - (in € thousands)	Period from 01/01/2015 to 12/31/2015			Period from 01/01/2014 to 12/31/2014		
	Increases additions	*Decreases reversals*	*Amount at end of fiscal year*	*Increases additions*	*Decreases reversals*	*Amount at end of fiscal year*
REGULATORY PROVISIONS	**-**	**-**	**-**	**-**	**-**	**-**
Provisions for foreign exchange losses	13,2		15,7	2,5		3
PROVISION FOR RISKS AND CHARGES	**13,2**	**-**	**15,7**	**2,5**	**-**	**3**
PROVISIONS FOR IMPAIRMENT		**-**	**-**			**3**
GRAND TOTAL	**13,2**	**-**	**15,7**	**2,5**	**-**	**3**

Due dates of receivables and debts (French GAAP)

	Period from 01/01/2015 to 12/31/2015							
RECEIVABLES - (in € thousands)	*Gross amount*	*Up to 1 year*	*1 year or more*	**DEBTS - (in € thousands)**	*Gross amount*	*Up to 1 year*	*1 to 5 years*	*1 to 5 years*
Other financial assets	491		491	* up to 1 year at origin				
TOTAL Long-term assets	491		491	* more than 1 year at origin				
Current assets				Loans and misc. financial debt				
Bad and doubtful debts				Trade and similar payables	5 443	5 443		
Other trade receivables	5 150	5 150		Staff and similar accounts	1 805	1 805		
Receivables represent. securities lent or used as collateral				Social security and other agencies	1 489	1 489		
Staff and similar accounts				Income tax				
Social security and other social agencies	16	16		Value added tax	0	0		
Government - Income tax	7 101	6 768	333	Guaranteed bonds				
Government - Value added tax	637	637		Other taxes and similar	549	549		
Government - Other taxes and similar payments	71	71		Debt on fixed assets and similar accounts				
Government - Misc.				Group and partners	163	163		
Group and partners				Other debt	11	11		
Misc. debtors	330	330		Debt representing borrowed securities				
TOTAL Current assets	13 304	12 971	**333**					
Pre-paid expenses	344	344		Unearned income	99	99		
GRAND TOTAL	**14 139**	**13 315**	**824**		**9 558**	**9 558**		

	Period from 01/01/2014 to 12/31/2014							
RECEIVABLES - (in € thousands)	*Gross amount*	*Up to 1 year*	*1 year or more*	DEBTS - (in € thousands)	*Gross amount*	*Up to 1 year*	*1 to 5 years*	*1 to 5 years*
Other financial assets	905		905	* up to 1 year at origin				
TOTAL Long-term assets	905		905	* more than 1 year at origin				
Current assets				Loans and misc. financial debt				
Bad and doubtful debts				Trade and similar payables	2 649	2 649		
Other trade receivables	158			Staff and similar accounts	1 823	1 823		
Receivables represent. securities lent or used as collateral				Social security and other agencies	1 207	1 207		
Staff and similar accounts				Income tax	544			
Social security and other social agencies	12	12		Value added tax	1	1		
Government - Income tax	0	0		Guaranteed bonds				
Government - Value added tax	356	356		Other taxes and similar	615	615		
Government - Other taxes and similar payments				Debt on fixed assets and similar accounts				
Government - Misc.				Group and partners				
Group and partners				Other debt	13			
Misc. debtors	109	109		Debt representing borrowed securities				
TOTAL Current assets	635	476	**0**					
Pre-paid expenses	288	288		Unearned income	63			
GRAND TOTAL	**1 828**	**765**	**905**		**6 913**	**6 913**		

Accrued expenses (French GAAP)

ACCRUED EXPENSES INCLUDED IN THE FOLLOWING BALANCE SHEET ITEMS – (in € thousands)	Period from 01/01/2015 to 12/31/2015
Trade and similar payables	3 158
Tax and social security liabilities	3 002
TOTAL	**6 160**

Period from 01/01/2014 to 12/31/2014	Period from 01/01/2013 to 12/31/2013
Trade and similar payables	1 280
Tax and social security liabilities	3 160
TOTAL	**4 440**

Revenue accruals (French GAAP)

REVENUE ACCRUALS INCLUDED IN THE FOLLOWING BALANCE SHEET ITEMS – (in € thousands)	Period from 01/01/2015 to 12/31/2015
Financial assets	
Receivables	
Trade and similar receivables	5 065
Social agencies	0
Government	71
Misc. revenue accruals	
Other receivables	330
Cash assets	102
TOTAL	**5 568**

REVENUE ACCRUALS INCLUDED IN THE FOLLOWING BALANCE SHEET ITEMS – (in € thousands)	Period from 01/01/2014 to 12/31/2014
Financial assets	
Receivables	
Trade and similar receivables	158
Social agencies	12
Government	356
Misc. revenue accruals	
Other receivables	109
Cash assets	16
TOTAL	**651**

Pre-paid expenses and unearned income (French GAAP)

PRE-PAID EXPENSES AND UNEARNED INCOME (in € thousands)	Period from 01/01/2015 to 12/31/2015
Operating income or expense Financial income or expense Extraordinary income or expense	246
TOTAL	**246**

PRE-PAID EXPENSES AND UNEARNED INCOME (in € thousands)	Period from 01/01/2014 to 12/31/2014
Operating income or expense Financial income or expense Extraordinary income or expense	226
TOTAL	**226**

Share capital structure (French GAAP)

SECURITIES CATEGORIES - Period from 01/01/2015 to 12/31/2015	*Number*	*Nominal value*
1- Stocks or partnership shares composing the share capital at start of fiscal year	*6 216 076*	*62 108*
2- Stocks or partnership shares issued during fiscal year	*630 287*	*63 029*
3- Stocks or partnership shares redeemed during fiscal year		
4- Stocks or partnership shares composing the share capital at end of fiscal year	6 846 363	684 636,3

SECURITIES CATEGORIES - Period from 01/01/2014 to 12/31/2014	*Number*	*Nominal value*
1- Stocks or partnership shares composing the share capital at start of fiscal year	*6 211 876*	*621 188*
2- Stocks or partnership shares issued during fiscal year	*4 200*	*420*
3- Stocks or partnership shares redeemed during fiscal year		
4- Stocks or partnership shares composing the share capital at end of fiscal year	6 216 076	621 607,6

Workforce

STAFF	12/31/2015	12/31/2014
Technicians	51	37
Management personnel	58	43
Total employees	**109**	**80**

NOTES TO THE FINANCIAL STATEMENTS PREPARED UNDER FRENCH GAAP

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, 2015 was €87943 million.
The net accounting profit was €4.748 million.

The following notes and tables form an integral part of the year-end financial statements.

These year-end financial statements were approved by the board of directors on March 15, 2016.

The financial statements were prepared in accordance with:

- the 1999 General Chart of Accounts approved by the ministerial order of June 22, 1999
- law 83 353 of April 30, 1983
- decree 83 1020 of November 29, 1983:
  - 2000-06 and 2003-07 on liabilities
  - 2002-10 on depreciation, amortization and impairment of assets
  - 2004-06 on the definition, recognition and valuation of assets

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 year-end financial statements.

The basic method used to determine the value of the items accounted for is the historical cost method.

1.1. Intangible assets

Start-up costs were capitalized and amortized over a three-year period.
Research and development costs are not capitalized. They are recognized as expenses incurred by the company.

1.2. Immobilisations corporelles

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:

- Software: 1 year
- Fixtures & fittings: 3-5 years (used – new)
- Misc. fixtures and facilities: 1-6 years
- Office and computer equipment: 3-5 years
- Office furniture: 5 years

Other purchases of tangible fixed assets correspond to the acquisition of parking lots, for which no impairment was recorded.

Moreover, in accordance with the General Chart of Accounts and under the lease signed with the greater Lyon area, the company revised in 2014 the depreciation schedule for "Facilities and fixtures", extending the end of the depreciation period to October 12, 2017 (expiration date of the lease).

1.3. Equity holdings and other long-term investments

At the accounts settlement date, the Company created a subsidiary in US which name is Adocia In and which employs 2 persons: a chief medical officer and a marketing directeor. The company's share capital amounts to $1 and is composed of 100 shares, of which 100% own by Adocia.

1.4. 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 2015, the unrealized capital gain on these investments was €26.4 thousand.

1.5. Inventories

Inventories are measured using the "first-in first-out" method. There are impaired if the date of expiry date has already gone by, or/and if the concerned project has been stopped by the Company because of statement of failure.

1.6. Revenue

Revenues amounted to €26.2 million in 2015, against €41.1 million for 2014.
It corresponds to revenues from research and collaboration contracts totalling €17 million, which primarily reflects the assumption by Lilly of all internal and external expenses incurred by Adocia under development of the licenced project. Last year, over the same period, the income of 0.3 million euro was only due to feasibility contracts for the formulation of monoclonal antibodies. Over 2015, these contracts continued and generated €0.2 million.
Revenues from licenses in 2015 of € 9.2 million include a milestone payment of €10 million received from Lilly following positive results of a pilot bioequivalence clinical study. This is the first milestone paid pursuant to the contract which includes a potential total amount of $520 million in development milestones and commercial milestones.
In 2014, the revenus is mainly driven by the upfront payment received from Lilly at the sigature of the contract. This amount of $50 million (€41 million) is fully recognized in 2014: the payment is not refundable and the Company received the cash on December 31, 2014.

1.7. Changes in methods

None

2. Highlights of the fiscal year

The year 2014 had ended with the signing of a major license agreement with Eli Lilly for the development of ultra-fast insulin analog formulation with BioChaperone® technology.

The year 2015 was marked by intense activity in the framework of partnership, with, from 20 January to launch a clinical trial of the effect of ultrafast insulin Lispro BioChaperone after the meal. After the publication of the positive results of this trial end in June 2015, three trials were then launched in the second half:

- Two Phase 1b studies of repeated administration of ultrafast insulin, one conducted in patients with type 1 and one conducted in patients with type 2
- A Phase 1b study of type 1 diabetes using an insulin pump.

The results of these three studies are expected during the first half of 2016.
As provided in the license agreement and collaboration, Lilly supports all internal and external expenses incurred by Adocia.

In parallel to these trials U100 formulation, a formulation twice concentrated U200 has been tested during a pilot bioequivalence study compared the formulation U100. The positive results of this test, published in December, allowed Adocia receive a milestone payment of $10 million. This is the first milestone payment received under the license agreement that provides for a potential $520 million if the product reaches certain milestones in clinical, regulatory and certain sales targets.

The year 2015 was also dense for projects developed on equity by Adocia:

- BioChaperone Combo, the unique combination of slow insulin glargine and insulin Lispro, with the two clinical trials in 2015: one of 28 type 1 diabetic patients comparing BioChaperone Combo with Humalog Mix 75/25 and the other in 24 type 2 diabetic patients in comparison with Humalog Mix 75/25 and the double injection of Lantus and Humalog.
  In two trials, the results have shown a significantly higher share early prandial and metabolic effect of prolonged BioChaperone Combo versus HumalogMix 75/25. The study on type 2 patients has also established the proof of concept that the product developed by Adocia had an effect similar to that of the double injection of Lantus and Humalog.
  The results of these studies to fully validate the continued clinical development in 2016.
- BioChaperone ® human insulin (HinsBet): the results of the Phase II clinical study published in February 2015 showed that the action of HinsBet was significantly faster than Humulin® and comparable to that of Humalog in the first hour (critical for blood sugar control). With its results, the Company continued development and has prepared the next studies that will be launched early 2016.
- BioChaperone PDGF-BB: clinical phase 3 trial continued throughout 2015 with the recruitment and treatment of 252 patients. Results are expected for the first half 2016.

In addition, the Company continued to work with great actors pharmacy by conducting feasibility studies of innovative formulations of monoclonal antibodies.

Financially, 2015 was marked by the completion of a private placement of almost 30 million euro from institutional investors, especially Americans. This fundraiser nearly 10% of capital has strengthened the Adocia cash position and to increase its visibility within the financial community and with players in the pharmaceutical world.

In terms of organization, Adocia has entered a new phase in its development. It first created a subsidiary in the United States and hired a general manager and chief medical officer. It also strengthened its teams in France by hiring about 25 people to support the development of its projects. It has extended its premises and fitted nearly 700 m² of additional laboratory and office.

Finally, in December 2015, the company celebrated its 10th anniversary during a day uniting all employees, individuals and companies that have contributed to its success.

3. Additional notes to certain items in the financial statements

3.1. Reimbursable advances and Bpifrance grants

3.1.1. Bpifrance Financement (ex-OSEO Innovation) agreement of March 12, 2007

As part of the Osteoporosis project, the company signed an agreement with Bpifrance Financement on March 12, 2007 under which it received a reimbursable advance totaling €2.25 million for the development of a new system for local controlled release of growth factors for bone regeneration. After fulfilling all the technical and financial conditions, the company received the full amount of this reimbursable advance in four payments made between March 15, 2007 and February 15, 2010.

Under the terms of the agreement, €0.7 million was repayable by March 31, 2013 regardless of the outcome of the program, which is unknown as of the date of this reference document. The company repaid the first €0.3 million installment in 2012 and a second payment of €0.4 million was made on April 1, 2013.
The balance of the advance (i.e. €1.55 million) will be repayable only if OSEO recognizes the technical and/or commercial success of the financed project.

A technical file of settlement failure has been recorded on March 25, 2014 and has given rise to a financial and technical audit. At the date of the submission of the reference document request, the Company doesn't have more information about the follow up of this file.

The repayable advance of an initial amount of 2.25 million euros received from Bpifrance Financing on the bone reconstruction project (osteoporosis) was cleared out during 2015. Consequent to the decision of a partial failure program in 2015, an amount of €1.050 million was forgiven and recognized as a grant. The remaining amount of the advance which was not yet reimbursed (€0.5 million) was paid by Adocia on September 30, 2015.

3.1.2 Bpifrance Financement (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 the company received a reimbursable 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 reimbursable assistance on April 30, 2012.

3.1.3 Coface-International business development insurance agreement of October 1, 2012

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

Under the terms of the agreement, Coface guarantees the reimbursement of 75% of the expenses incurred during the four-year guarantee period, which runs from October 1, 2012 to September 30, 2016. For the expenses incurred during the first insured period, i.e. from October 1, 2012 to September 30, 2013, the company received the sum of €91 thousand on December 17, 2013.

During the period between October 1, 2013 and September 30, 2014, the Company has not committed exploration expenditures on target markets and the contract has been cancelled. Consequently the Company entered into a période of amortization of received amounts until now (91 thousand of euros) as provided by the contract in the above.
As no turnover has been achieved in 2015, the balance of the advance received has not changed

3.2. Income statement

The revenue of the company of €26.2 million mainly derived from the contract signed with Lilly in 2014.

Operating expenses totaled €32.3 million, compared to €17.6 million in 2014.
Expenses include the following items (in € thousands):

- Costs of materials: 1.133
- Payroll costs : 9.434
- External expenses : 20.899
- Taxes: 255
- Depreciation and amortization, operating provisions : 491
- Other expenses: 42

Operating income was a loss of € 4.9 million against a profit of 23.5 million euros for the previous year.

Financial income and expenses totaled €2.543 thousand and €390 thousand resulting in a net financial income of €2.153 thousand, compared with net financial income of €732 thousand the previous year. The increase by €1.421 thousand mainly comes from the foreign exchange gain realized with the receipt of the intital payment of $50 million from Lilly.

As a result, income before tax results in a loss of €2.7 million, compared to a profit of €24.3 million for the previous year.

A extraordinary result has been recorded for € 0.1 million during 2015 compared to €0.5 in 2014.

With a Research Tax Credit amount of €6.8 million and a €0.3 million tax debt resulting from the carry back of the 2015 deficit for a maximum amount or €1 million (ie €1 million * 0.33%) on the 2014 result, the 2015 year was a net result after tax of €4.5 million euros, compared to a net profit of 23.7 million euros in 2014.

3.3. Balance sheet

3.3.1 Assets

Tangible fixed assets amounted to net €1.9 million at 31 December 2015, against €0.9 million 2014. This increase is mainly explained by the renovation and expansion of laboratories, and the acquisition of research and hardware equipment consequent to the sustained growth of the workforce over the period.

The "financial assets" stood at 31 December 2015 to EUR 0.5 million, net of provision, compared to €0.9 million in 2014. The decrease is mainly due to the variation of the allocated means given to Kepler to ensure the liquidity of the share. Indeed, under the terms of the liquidity contract, the Company has decided February 10, 2015 to proceed with a partial recovery of the resources allocated to this contract up to an amount of 700,000 euros. September 10, 2015, the resources made available under the liquidity contract at Kepler Capital Markets S.A. was increased by €200,000.

During fiscal 2015, the share buyback program was exclusively used in the context of the liquidity agreement meets the objective of animation and liquidity of securities of the Company. At December 31, 2015, the Company held as part of this contract 4.185 shares with a total book value of €308.4 thousand assessed at purchase shares.

Current assets amounted to the net sum of 85.57 million euros, of which € 71.90 million of availability.

Receivables rose sharply from €0.6 million at December 31, 2014 to €13.3 million at December 31, 2015. The balance of trade receivables essentially consists of the receivable from Eli Lilly, arising from the quarterly invoicing of expenses pursuant to the licencing agreement signed in December 2014. The balance of other receivables includes receivables from the state, including the research tax credit (CIR) for €6.8 million, the carryback claim for €0.3 million, the VAT debt and the competitive employment tax credit (CICE). In 2014, the debt of CIR was charged against the corporate tax liability (IS).

At 31 December 2015, cash and cash equivalents amounted to € 72 million compared to € 49.8 million at December 31, 2014. This increase in cash of €22.3 million is particularly related to the capital increase of nearly 30 million euros (net of fees) conducted in March 2015 with specialized healthcare investors. The year-end cash position also included the receipt of a $10 million (€ 9.2 million) milestone payment received from Eli Lilly following positive results from a pilot bioequivalence study comparing BioChaperone Lispro U200 to U100 BioChaperone.
For the full year 2015, net cash required to finance operations totaled 15.4 million euros, compared to 10.6 million for the same period last year.

The prepaid expenses amounted to 0.3 million euros, in line with 2014.

3.3.2 Liabilities

The share capital amounted to the sum of €684,636.30 at December 31, 2015, against €621,607.60 at the end of last year. The issue and merger premiums amounted to the total sum of €79.5 million against €49.8 million at year-end 2014. This increase of €29.7 million is explained by the private placement of €30 million made at beginning of year 2015.

Retained losses amouted to €7.3 million compared to €31 million last year, the variation corresponding to the allocation of earnings recorded in 2014 for €23.7 millions.

The reimbursable advances decreased to €2.4 million at December 31, 2014 to €0.9 million at December 31, 2015 (see note 3.1 on refundable advances).

3.3.3 The company's debt position based on business volume and complexity

Debts amount to of €9.6 million against €6.9 million last year, and mainly include:

- trade and similar payables: €5.4 million
- tax and social security liabilities: €3.8 million

The increase in liabilities is mainly related to trade payables, and reflects the strong increase in activity during the year, including the cooperation agreement signed Eli Lilly end of 2014.

Pursuant to Article L. 441-6-1 of the French commercial code (Code de commerce), trade payables, which totaled €5.7 million, compared with €2.6 million the previous year, by due date were as follows:

Supplier category (in € thousands)	Fiscal Year 2015	Fiscal Year 2014
Cash payment	1 126	541
Payment in 30 days	1 026	663
Payment in 45 days	271	143
Payment in 60 days	39	11
Litigation	93	13
Suppliers, incoices pending	3 158	1 280

5. Proposed allocation of losses for fiscal year 2015

A proposal is made to allocate the profit for the fiscal year ended December 31, 2015 totaling €4.5 million to retained losses.

As a reminder, the company has not paid out dividends over the last three years.

6. Non-tax-deductible expenses

In accordance with Article 223 (4) of the French General Tax Code (Code Général des Impôts), the amount of luxury and non-deductible expenses referred to in Article 39-4 of this code totaled €15,553 for the fiscal year ended December 31, 2015.

7. Off-balance sheet commitments

7.1. 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 €1.1 million thousand at December 31, 2015 compared to €0.4 million last year..
(See note 3.11 to the consolidated financial statements prepared under IFRS provided in Chapter 20.1 of this reference document).

7.2. Lease signed with the greater Lyon area

The company's registered office is located at 115, avenue Lacassagne, 69003 in Lyon. It occupies approximately 2,709 square meters on two floors of a building that houses innovative biotech companies.
The company also signed a lease agreement for a covered parking garage, which took effect on October 13, 2011.
(See Chapter 8.1 of this reference document regarding leases signed)

The lease expense (excluding building occupancy expenses) was €378 thousand and the building occupancy expenses totaled €139 thousand for the fiscal year ended December 31, 2015.

7.3. . Signing of two financial leases

As of Decembre 31, 2015, the company owns several assets financed through leasing. It holds two agreements. The first concerns an asset with an acquisition cost of €72 thousand financed for three years and the second concerns equipment with a total acquisition cost of €85 thousand financed over four years.

8. Other Information

8.1. Bonus shares

Followind General Assembly meeting dated December 20, 2007, the Board decided to grant Free Shares as followed:

	Dates of the Boards decided to award				
	01/23/2008	06/06/2008	12/15/2009	03/05/2010	12/07/2010
Number of shares granted	42 000	5 600	5 600	5 600	5 600
Shares cancelled	2 100	0	0	0	0
Acquired and available shares	39 900	5 600	4 200	2 800	2 800
Exercised stock	11 600		410	200	0
Acquired and remaining available shares	28 300	5 600	3 790	2 600	2 800
Shares acquired under conservation	0	0	1 400	2 800	2 800
Actions attribuées mais non encore acquises	0	0	0	0	0
End of acquisition period	*completed*	*completed*	*completed*	*completed*	*completed*
End of retention period	*completed*	*completed*	1 400 stock : dec. 2016	1 400 stock : march 2016 1 400 stock : march 2017	1 400 stock : dec 2016 1 400 stock : dec 2017

Following the delegation received from the EGM of November 12, 2015, several awards were held in 2015:

- A first plan, decided by the Board on 10 December 2015, within the 10 years Adocia, involved all staff with an individual amount of actions depending on the status and seniority of the employee. This plan covers 39,150 shares. The shares will vest upon the expiration of a 2 years period, December 10, 2017, provided that the beneficiary is still an employee of the group Adocia that date. There is no retention period.
- A second plan, decided by the Board of 16 December 2015, was granted the benefit of three employees, including Olivier Soula, Deputy CEO, for a total of 10,000 shares on the basis of the performance year 2015. The shares will vest at the expiration of a period of one year, ie December 16, 2016, provided that the beneficiary is still in the group at that date Adocia. The retention period is set at one year from December 16, 2016.
- A third plan decided by the Board as of December 16, 2015 for a total 12 600 shares established for employees under one of the following categories: Directors, Manager, Senior Project Leader and / or expert and senior researcher / expert. A quarter of the shares granted will vest at the end of each previous year as of December 16, 2015, with a first quarter December 16, 2016. The vesting of shares is conditional on the presence of the beneficiary within the Adocia group until the end of each vesting period considered. The retention period has been set at one year starting to run from the expiration of each vesting period.

The table below summarizes the number of shares granted:

	Date of the Boards decided to award			TOTAL
	12/10/2015	12/16/2015	12/16/2015	
Number of shares granted	39 150	5 000	12 600	**121 150**
Shares cancelled	0	0	0	**2 100**
Acquired and available shares	0	0	0	**55 300**
Exercised stock	0	0	0	**12 210**
Acquired and remaining available shares	0	0	0	**43 090**
Shares acquired under conservation	0	0	0	**7 000**
Actions attribuées mais non encore acquises	39 150	5 000	12 600	**56 750**
End of acquisition period	39 150 stock : dec 2017	5 000 stock : dec 2016	3 150 stock : dec 2016 3 150 stock : dec 2017 3 150 stock : dec 2018 3 150 stock : dec 2019	
End of retention period	No retention period considering the vesting period of 2 years	5 000 stock : dec 2017	3 150 stock : dec 2017 3 150 stock : dec 2018 3 150 stock : dec 2019 3 150 stock : dec 2020	

8.2. Stock warrants

Following the delegation received from the Ordinary General Meeting of 20 December 2007, the Board of Directors proceeded to issue 210 warrants autonomous actions (BSA), issued free at benefit consultants performing functions science in society.

Making use of the authorization granted at the Annual General Meeting of 18 June 2013, the Board of Directors dated December 13, 2013 decided to issue 20,000 warrants for the benefit of independent directors.

As of March 31, 2015, pursuant to the authorization granted by the Ordinary and Extraordinary General Meeting of the Company dated 18 June 2013, the Board of Directors decided to grant stock options to two employees of Adocia Inc. A total of 20,000 common shares of stock options was thus granted, each employee receives 10,000 common share options.

For each beneficiary, the stock options may be exercised at a price of 55.64 euros, per quarter, each year on January 1st, with the first installment exercisable as of January 1, 2016. The options may be exercised at the expiration of a period of ten years commencing on the day of grant, or before March 31, 2025. At the end of the period of ten years following the issuance of stock options, the options not yet exercised will lapse and will no longer entitle to subscribe for shares.

On December 16, 2015, pursuant to the authorization granted by the Extraordinary General Meeting of the Company dated 12 November 2015 the Board of Directors decided to grant stock options to two employees of Adocia Inc. A total of 4,000 shares of stock options was thus agreed.

For each beneficiary, the stock options may be exercised at a price of 71.12 euros, per quarter, each year on January 1st, with the first installment exercisable as of January 1, 2017. The options may be exercised at the expiration of a period of ten years commencing on the day of grant, or before December 16, 2025. At the end of the period of ten years following the issuance of stock options, the options not yet exercised will lapse and will no longer entitle to subscribe for shares.

700 warrants had been subscribed during the year 2015.

8.3. Start-up company stock purchase warrants ("BSPCE")

In accordance with the authorization granted by the company's ordinary and extraordinary shareholders' meeting on June 18, 2013, at its meeting on December 13, 2013 the board of directors decided to issue, free of charge, a total of 50,400 BSPCE to certain company employees which give a right to subscribe for 50,400 new shares, each with a par value of €0.10.

In accordance with the authorization granted by the company's ordinary and extraordinary shareholders' meeting on June 18, 2014, at its meeting on December 25, 2014 the board of directors decided to issue, free of charge, a total of 119,600 BSPCE to certain company employees and executives which give a right to subscribe for 119,600 new shares, each with a par value of €0.10.

Making use of the authorization granted at the Annual General Meeting of November 12, 2015 the board of directors of December 16, 2015 decided to issue 40,000 "BSPCE 2015 Officers" for the benefit of Gérard Soula, CEO, entitling to subscribe for 40,000 new shares with a nominal value of €0.10

5,600 BSPCE have been exercised during 2015.

8.4. Individual right to training

The individual right to training allows all employees to acquire credit for training hours which they can use at their own discretion, with the employer's agreement as to the choice of training.
Employees have a right to 20 hours of training per year, which can be accumulated over six years up to a maximum of 120 hours.
The number of accumulated training hours corresponding to the rights acquired by the company's employees and not used as of December 31, 2014 was 5,476.

Two trainings linked to the individual right in the training (DIF) were undertaken during year 2014 for a total volume of 68 hours and one employee left for individual training vacation (CIF) from September 1rst 2014 to end of may 2015.
From January 1st, 2015, the system of the DIF is suppressed. The unused hours of DIF on December 31st, 2014 could be transferred, on demand received from the employee, to his new personal account of training.

8.5. Events subsequent to year end

On 18 January 2016, the Company signed a preliminary sale agreement with the “Metropole of Lyon” for the acquisition of the building where are located its offices 115 Avenue Lacassagne, 69003 Lyon. The promise of sale is the building called "Pépinière Lacassagne" with a total area of 7.120 m², the land on which the building is located and 43 parking spaces. The purchase price of the whole was set at 5 million euros, excluding VAT and costs of records. The Company plans to finance this acquisition through bank loans (suspensive condition of promise.

The Company has immediate use and enjoyment of the property, and that, upon signature of the preliminary sale agreement.

The signing of the deed of sale is expected during the month of April 2016.

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20.4 Statutory auditors' report on the individual financial statements prepared for the fiscal year ended December 31, 2015

ODICEO | ERNST & YOUNG et Autres

Adocia
Fiscal year ended December 31, 2015

Statutory auditors' report
on the year-end financial statements

ODICEO
115, boulevard de Stalingrad
B.P. 52038
69616 Villeurbanne Cedex
Corporation with €275,000 in share capital

Statutory Auditor
Member of the Compagnie
Régionale de Lyon

ERNST & YOUNG et Autres
Tour Oxygène
10-12, boulevard Marius Vivier Merle
69393 Lyon Cedex 03
Simplified joint stock company with variable capital

Statutory Auditor
Member of the Compagnie
Régionale de Versailles

Adocia

Fiscal year ended December 31, 2015

Statutory auditors' report on the year-end financial statements

Dear Shareholders:

Pursuant to the mission entrusted to us by your shareholders' meetings, we present to you our report for the fiscal year ended December 31, 2015 on:

- the audit of the year-end financial statements of Adocia, as attached to this report;
- the basis for our assessments;
- the specific verifications and information required by law.

The year-end financial statements were approved by the board of directors. It is our task, on the basis of our audit, to express an opinion on these financial statements.

I. Opinion on the year-end financial statements

We have conducted our audit in accordance with the accounting standards applicable in France. These standards require the use of due diligence to provide reasonable assurance that the year-end financial statements do not contain any significant misstatements. An audit entails verifying, on a test basis or through other selection methods, evidence supporting the amounts and information contained in the year-end financial statements. It also entails assessing the accounting principles applied, the significant estimates used and the overall presentation of the financial statements. We believe that the information we have collected is sufficient and appropriate to provide a basis for our opinion.

We certify that the year-end financial statements, in accordance with French accounting rules and principles, are true and in good order and fairly present the company's net profit/loss from operations during the previous year, as well as its financial position and assets at the end of said year.

II. Basis for the assessments

Pursuant to the provisions of Article L. 823-9 of the French Commercial Code (*Code de commerce*) related to the basis for our assessments, we wish to bring the following points to your attention:

Note "1.6 Revenue"" of the year-end financial statements describes accounting rules and methods relating to the revenue recognition, in particular the payment received from Eli Lilly following the signature of the licensing agreement. As part of our assessment of the accounting rules and principles applied by your company, we have verified the appropriateness of the accounting methods and information provided in the notes to the year-end financial statements, and have ensured their proper application.

The assessments thus made are an integral part of our audit of the year-end financial statements as a whole, and therefore helped us from our opinion, as expressed in the first part of this report.

III. Specific verifications and information

In accordance with the accounting standards applicable in France, we also conducted the specific verifications required by law.

We have no observation to make as to the fairness and consistency with the year-end financial statements of the information provided in the board of directors' management report and in the documents sent to the shareholders regarding the financial position and year-end financial statements.

Concerning the information provided pursuant to the provisions of Article L. 225-102-1 of the French Commercial Code (*Code de commerce*) on compensation and benefits paid to corporate officers and commitments made to them, we have verified its consistency with the financial statements or with the data used to prepare these financial statements and, where appropriate, with the information collected by your company from the companies that control it or are controlled by it. Based on this work, we certify the accuracy and fairness of this information.

As required by law, we have ensured that the information related to the identity of holders of capital and voting rights was provided to you in the management report.

Villeurbanne and Lyon, April 7, 2016

The Statutory Auditors

ODICEO	ERNST & YOUNG et Autres
Sylvain Boccon-Gibod	Sylvain Lauria

20.5 Income for the last five years (in € thousands)

	2015	2014	2013	2012	2011
CAPITAL DURING THE FISCAL YEAR					
Share capital	684 636	621 608	621 188	619 788	445 871
Number of existing ordinary shares	6 846 363	6 216 076	6 211 876	6 197 876	4 458 710
Number of existing ordinary shares cum dividend	6 846 363	6 216 076	6 211 876	6 197 876	4 458 710
Maximum number of future shares to be created					
- by bond conversion					
- by exercise of subscription rights	61 750	2 800	7 000	23 100	41 300
TRANSACTIONS AND RESULTS FOR THE FISCAL YEAR (in € thousands)					
Pre-tax revenue	26 189	41 043	(26)	2 013	9 169
Profit/loss before tax, employee profit-sharing, depreciation, amortization and provisions	(2 131)	24 994	(12 540)	(10 732)	(4 292)
Income tax	(7 101)	617	(3 218)	(3 069)	1 855
Employee profit-sharing owed for the year		421	-	-	-
Profit/loss after tax, employee profit-sharing, depreciation, amortization and provisions	4 478	23 733	(9 689)	(8 029)	1 355
Distributed profit	-	-	-	-	-
EARNINGS PER SHARE (in euros per share)					
Profit/loss after tax and employee profit-sharing, but before depreciation, amortization and provisions	0,66	3,85	(1,50)	(1,24)	(0,55)
Profit/loss after tax, employee profit-sharing, depreciation, amortization and provisions	0,65	3,82	(1,56)	(1,30)	0,30
Dividend per share	-	-	-	-	-
STAFF (in € thousands)					
Average number of employees during the year	95	77	72	64	53
Total payroll for the year	6 410	4 982	3 745	3 531	2 806
Total employee benefits paid for the year (social security, social agencies, etc.)	2 953	2 329	1 669	1 380	1 150

20.6 Dividend payout policy

20.6.1 Dividends paid over the last three years

None

20.6.2 Dividend payout policy

Given its positioning as a growth company, as of the filing date of this reference document, the company does not intend to implement a regular dividend payout policy.

20.7 Legal and arbitration proceedings

During the 12 months preceding the filing date of this reference document, the company was not involved in any administrative, criminal, legal or arbitration proceedings that could have a significant negative impact not reflected in its financial statements on the company, its business, its financial position, its earnings or its development nor, to its knowledge, is the company subject to the threat of such proceedings as of the filing date of this reference document.

20.8 Significant change in the financial or trading position

None

21 ADDITIONAL INFORMATION

21.1 Share capital

21.1.1 Amount of share capital

As of the filing date of this reference document, the Company's capital was €684,636.30 divided into 6,846,363 fully paid common shares, each with a par value of €0.10.

21.1.2 Shares not representing capital

None.

21.1.3 Company shares pledged as collateral, guarantees or security

None.

21.1.4 Acquisition by the company of its own shares

The combined shareholders' meeting of the company held on May 27, 2015 authorized the board of directors, for an 18-month period from the date of the meeting, to implement a share buyback program under Article L. 225-209 of the French commercial code (Code de commerce) and in accordance with the General Regulation of the Autorité des marchés financiers (AMF) under the conditions detailed below:

Maximum number of shares that may be purchased: 10% of the share capital on the share buyback date. When the shares are acquired for the purpose of making a 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.

The objectives of the share buyback are to :

- ensure the liquidity of the company's share under a liquidity agreement to be entered into with an investment services provider, in accordance with the code of conduct recognized by the Autorité des marchés financiers;
- honor obligations associated with stock option, bonus share or employee savings plans or other allocations of shares to employees and managers of the company or affiliated companies;
- deliver shares upon the exercise of rights attached to marketable securities giving access to the capital;
- purchase shares for the purpose of holding them for subsequent delivery as a means of exchange or payment for a potential acquisition; or
- cancel any or all of the repurchased shares, provided resolution eight below is adopted and, if so, under the conditions specified therein,

Maximum purchase price: €200 per share. This purchase price will be adjusted, if necessary, to reflect transactions involving the capital (including capitalization of reserves and bonus issues, share splits or reverse splits) that may have occurred during the authorization period;
The number of shares acquired by the company for the purpose of holding them for subsequent delivery as a means of payment or exchange in a merger, spin-off or split-up transaction may not exceed 5% of the company's capital.

Maximum amount of funds that may be used for share buybacks: €5,000,000

The repurchased shares may be canceled.

On May 5, 2014, the Company announced that it was ending, dated 30 April 2014, the liquidity contract dated March 14, 2012 told DSF MARKETS (formerly BIL Finance). The ressources that were then in the liquidity account on that date consisted of 15,026 Adocia treasury shares and 502,312.46 euros in cash.

On 19 May 2014, the Company signed a new liquidity contract with Kepler Capital Markets SA by allocating the following resources: 15,026 treasury shares and € 0.3 million in cash.

As of December 31, 2014, under this agreement, Kepler Capital Markets SA held 2,323 shares and 778,747.18 euro in cash.
Under the terms of the liquidity contract, on 10 February 2015, the Company reduced resources allocated to this contract by € 700,000 euro.

September 10, 2015, the resources made available under the liquidity contract at Kepler Capital Markets S.A. was increased by 200,000 euros.

Over the fiscal year 2015, the share buyback program was therefore 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. At December 31, 2015, the company held 4,185 shares (representing 0.06% of the capital), **each** with a par value of €0.10, under this agreement, for a book value of €308,419.40 measured at the purchase price of the shares. These shares were purchased at an average price of €73.70. Over the course of fiscal year 2014, 26,955 shares were purchased and 24,593 shares were sold under this agreement. The average purchase price was €74.23 and the average sale price was €73.14. Trading costs in 2014 were €22.500. The company did not purchase any treasury shares outside of the liquidity agreement.

As of December 31, 2015, under this agreement, Kepler Capital Markets SA held 4,185 shares and 132,740 euro in cash.

21.1.5 Potential capital

As of the filing date of this reference document, there were three different types of shares giving access to the capital. Details are provided below :

21.1.6 Stock warrants plan (bons de souscription d'actions – BSA)

Stock warrant plan (bons de souscription d'actions — BSA)

	$BSA_{06\text{-}2011}$	**$BSA_{09\text{-}2011}$**	**$BSA_{12\text{-}2013}$**
Date of shareholders' meeting	June 17, 2011	June 17, 2011	June 18, 2013
Date of chairman's decision	**By the shareholders' meeting**	**September 27, 2011**	**December 13, 2013**
Number of BSAs authorized	140	70	30,000
Number of BSAs issued	140	70	20,000

Total number of shares that may be subscribed (1)	1,400	700	20,000
Of which the number that may be subscribed by corporate officers	0	0	20,000
Name of non-corporate officer beneficiaries	J.M Lehn	B. Cabane	Dominique Takizawa Ekaterina Smirnyagina
Earliest BSA exercise date	June 17, 2011	September 27, 2011	January 1, 2014 for 13,333 BSAs January 1, 2015 for 3,333 BSAs January 1, 2016 for 3,333 BSAs
BSA expiration date	June 17, 2021	September 27, 2021	December 13, 2023
BSA issue price	free	free	0.588
BSA exercise price	€85.71 (or €8.571 per share) (1)	€85.71 (or €8.571 per share) (1)	€5.88
Exercise conditions	(2)	(2)	(3)
Number of shares subscribed as of the filing date of the reference document	0	700	0
Aggregate number of lapsed or canceled BSAs as of the filing date of the reference document	0	0	0
BSAs remaining as of the filing date of the reference document	140	70	20,000
Total number of shares that may be subscribed as of the filing date of the reference document	1,400 (1)	0 (1)	20,000

(1) The exercise conditions for the BSAs have been adjusted to reflect the 10-for-1 stock split approved by the shareholders' meeting of October 24, 2011. The phrase "Total number of shares that could originally be subscribed" corresponds to quantified information after accounting for this split.
(2) The BSAs may in principle be exercised over a 10-year period from their allocation date, provided the holder of the BSAs has served continuously, until the BSAs are exercised, as an external scientific advisor to the company.
(3) The BSA$_{12\text{-}2013}$ are exercisable (i) regarding Mrs. Dominique Takizawa, in whole at any time on or after December 13, 2013 for a period of 10 years and (ii) regarding Ms Ekaterina Smirnyagina, up to a third as of December 13, 2013, then an additional third parties as of 13 December 2014 and in full effective December 13, 2013.

As of the filing date of the reference document, the full exercise of all the BSAs allocated could lead to the creation of 21,400 shares with a par value of €0.10 (after accounting for the 10-for-1 stock split approved by the shareholders' meeting of October 24, 2011).

21.1.7 Free shares (Actions gratuites - AGA)

Date d'attribution	01/23/2008	06/06/2008	12/15/2009	03/05/2010	12/07/2010	12/10/2015	12/16/2015	TOTAL
Number of free shares awarded [1]	42 000	5 600	5 600	5 600	5 600	39 150	22 600	**126 150**
Number of free shares canceled	2 100	-		-	-	-	-	**2 100**
Number of bonus shares sold	11 600		410	200				**12 210**
acquired shares, available or under conservation	28 300	5 600	5 190	5 400	5 600	-	-	**50 090**
Shares granted but not yet vested	-	-	-	-	-	39 150	22 600	**61 750**

[1] For the plans 2008, 2009 & 2010, shares are issued only to employees (who are not corporate officers). This issue vests at the end of each vesting period indicated below (*the "vesting period"*) in the following proportions:

- 25% after a two-year period following the share issue date,
- 25% after a three-year period following the share issue date,
- 25% after a four-year period following the share issue date, and
- 25% after a five-year perio following he share issue date,

provided the beneficiaries meet the conditions and criteria for the issue established by the board of directors. Beneficiaries are required to hold the shares for at least two years after the applicable vesting period (*the "holding period"*). Beneficiaries must be categorized as "executives" whose "CCN" (*national collective bargaining agreement for the pharmaceutical industry*) coefficient is greater than or equal to 9A or as Project Managers, based on criteria such as the importance of the project, its degree of innovation and its complexity, as well as the management dimension of the Project Manager. They must have retained their status as employee for the entire vesting period.

In 2015, several awards were held.

- A first plan, decided by the Board on 10 December 2015, within the 10 years Adocia, involved all staff with an individual amount of actions depending on the status and seniority of the employee. This plan covers 39,150 shares. The shares will vest upon the expiration of a 2 years period, December 10, 2017, provided that the beneficiary is still an employee of the group Adocia that date. There is no retention period.
- A second plan, decided by the Board of 16 December 2015, granted to the benefit of three employees, including Olivier Soula, Deputy CEO, for a total of 10,000 shares on the basis of the performance year 2015. The shares will vest at the expiration of a period of one year, ie December 16, 2016, provided that the beneficiary is still in the group at that date Adocia. The retention period is set at one year from December 16, 2016.
- A third plan decided by the Board as of December 16, 2015 for a total 12 600 shares established for employees under one of the following categories: Directors, Manager, Senior Project Leader and / or expert and senior researcher / expert. A quarter of the shares granted will vest at the end of each previous year as of December 16, 2015, with a first quarter December 16, 2016. The vesting of shares is conditional on the presence of the beneficiary within the Adocia group until the end of each vesting period considered. The retention period has been set at one year starting to run from the expiration of each vesting period.

21.1.8 Busines founders' stock warrants (BSPCE)

Date d'attribution	13/12/2013 *Plan 2013 n°1*	13/12/2013 *Plan 2013 n°2*	25/09/2014 *Plan 2014 n°1*	25/09/2014 *Plan 2014 n°2*	25/09/2014 *Plan 2014 Executives*	16/12/2015 *Plan 2015 Executives*	TOTAL
Number of BSPCE issued [2]	28 000	22 400	14 000	5 600	100 000	40 000	**210 000**
Number of BSPCE canceled	-	-	2 800	5 600	-	-	**8 400**
Number of BSPCE subscribed remaining	28 000	22 400	11 200	0	100 000	40 000	**201 600**
Number of BSPCE exercised	4 200	700	-	-	-	-	**4 900**
Number of BSPCE remaing to exercise	23 800	21 700	11 200	0	100 000	40 000	**196 700**

[2] The exercise BSPCE plans schedule is detailed in section 9.2

At the registration date of this reference document, 196,700 BSPCE awarded under the 2013, 2014 and 2015 plans are exercisable and the exercise in full of these BSPCE could lead to the creation of 196,700 shares of 0.10 par value.

21.1.9 Stock options

	Stock options	
Date d'assemblée	June 18, 2013	November 12, 2015
Board of director granting the options	March 31, 2015	December 16, 2015
Total number of options granted	20,000	4,000
The number that may be subscribed by certain emplyees [1]	20,000	4,000
The number that may be subscribed by directors and officiers	0	0
Point de départ d'exercice des options	January 1, 2016	January 1, 2017
Option expiration Date	31 mars 2025	December 16, 2025
Prix d'exercice	€55.64	€71.12
Conditions of exercise	¼ exercisable between 1 January 2016 and each additional quarter to the end of each previous year as of January 2016 du1er.	¼ exercisable between 1 January 2017 and each additional quarter to the end of each previous year as of January 2017 du1er.
Number of shares subscribed as of the regristration date of this reference document	0	0
Total number of options outstanding at the date of this reference document	20,000	4.000
Total number of shares may be subscribed at the registration date of this document	0	0

(1) The options were granted for the benefit of both employees Adocia Inc.

21.2 Authorized capital

Resolutions concerning issuances approved by the extraordinary shareholders' meeting of November 12, 2015 and May 27, 2015 are summarized:

	Period of validity/ Expiration	Ceiling (par value)	Procedures for setting the price	Date and conditions of use by the board of directors
General Meeting of Shareholders November 12, 2015				
Authorisation to the Board to grant options to subscribe or purchase shares of the Company	38 months / January 12, 2019	200,000 shares (1)	Refer to (2)	The Board exercised this authorization by allocating 4,000 stock options 16 December 2015
Authorization for the Board to proceed with the free allocation of existing shares or issue	38 months / January 12, 2019	200,000 shares and a maximum of 10% of the share capital at the time of grant (1)	N/A	The Board used this authorization by allocating free shares 39 150 December 10, 2015 and 22,600 free shares December 16, 2015
Authorization granted to the Board of Directors to issue and allot free of charge for entrepreneurs share warrants to employees and officers of the Company	May 10, 2017 or (ii) the date on which the conditions laid down in Article 163 bis G of the General Tax Code would cease to be met	135,000 shares (1)	Refer to (3)	The Board made use of this authorization by giving 40,000 business creator equity warrants December 16, 2015
Authorization granted to the Board of Directors to issue warrants of shares to (i) of the Board of Directors of the Company in office at the date of grant of the good not having the quality of employees or officers of the Company or one of its subsidiaries, (ii) persons bound by a contract for services or consultant to the Company, or (iii) members, who are not quality employees or officers of the Company or one of its subsidiaries, any other committee that the board has or would set up	18 months / May 12, 2017	40,000 warrants entitling to 40,000 shares (1)	Refer to (4)	The Board has not used this delegation during the year
General Meeting of Shareholders May 27, 2015				
Authorization granted to the Board of Directors to proceed with the issue, with preferential subscription rights, shares and / or securities giving immediate and / or future capital of the Company	26 months / July 27, 2017	€210,000 (5)		The Board has not exercised this authorization
Authorization granted to the Board of Directors to proceed with the issue without preferential subscription rights, by a public offering, shares and / or securities giving immediate and / or future capital of the Company and option to grant a priority right	26 months / July 27, 2017	€135,000 (5)	Refer to (6)	The Board has not exercised this authorization
Delegation granted to the Board of Directors to proceed with the capital increase immediately or over time by issuing ordinary shares or any securities convertible into shares, within the limit of 20% of share capital per year with cancellation of preferential subscription rights of shareholders, by offering to qualified investors or a restricted circle of investors as defined in paragraph II of	26 months / July 27, 2017	€135,000 (5) and a maximum of 20% of existing share capital on the date of the transaction and per year	Refer to (6)	The Board has not exercised this authorization during the year

Article L. 411-2 of the French monetary and financial code (private placement)				
Delegation granted to the Board of Directors to proceed with the capital increase by issuing ordinary shares or any securities convertible into shares without preferential subscription rights for the benefit of a category of persons in the part of a financing line in equity,	18 months / Novenber 27, 2016	€65,000 (5)	Refer to (7)	The Board has not exercised this authorization during the year
Authorisation to the Board in the event of issuance of shares or any securities convertible into shares without preferential subscription rights for shareholders, to set the issue price within the limit of 10% of share capital and the limits set by the general meeting	26 months / July 27, 2017	within the limit of 10% of share capital per year	Refer to (8)	The Board has not exercised this authorization during the year
Delegation of authority to the Board to increase the number of shares to be issued in case of capital increase with or without preferential subscription rights	26 months / July 27, 2017	15% if the initial issue (5) (9)	Same price than the initial issuance	The Board has not exercised this authorization during the year
Delegation of authority to the Board to proceed with the issuance of common shares or securities giving access to capital to remunerate contributions of securities in a public offer with an exchange component initiated by the Society.	26 months / July 27, 2017	€68,000 (5)		The Board has not exercised this authorization during the year
Delegation of authority to the Board to increase the share capital within the limits of 10% of capital to remunerate contributions in kind of equity securities or securities giving access to third-party capital outside a exchange offer	26 months / July 27, 2017	€68,000 and within the limit of 10% of share capital per year (5)		The Board has not exercised this authorization
Delegation of authority to the Board to increase the share capital by incorporation of premiums, reserves, earnings or other	26 months / July 27, 2017	€100,000		The Board has not exercised this authorization

(1) The sum of (i) shares may be issued or acquired on exercise of options granted, (ii) the shares to be allocated for free, (iii) shares to be issued upon exercise of business founders' stock warrants and (iv) shares may be issued on exercise of stock warrants may not exceed 250,000 shares, it being specified that this ceiling will be added to the additional amount of shares to be issued, in accordance with contractual stipulations, the rights of holders of securities and other rights giving access to shares.

(2) The purchase price or share subscription will be set by the Board of Directors the day the option is granted within the limits provided by law and this resolution may not be less than eighty-five percent (95 %) of the average share price over the twenty trading days preceding the date of the Board's decision to award the options rounded to the lower euro, nor, in the case of stock options, 80% the average purchase price of treasury shares by the Company rounded to the euro lower

(3) The subscription price will be determined by the Board of Directors at the time of allocation of BSPCE and must be at least equal to the greater of three values, as follows:

- *The selling price of a share at the close on the regulated market on the day preceding the decision of the Board to assign BSPCE ;*
- *Ninety-five percent (95%) of the average share price over the twenty trading days preceding the date of the Board's decision to award the BSPCE ;*
- *If one or more capital increases forestay (are) carried (s) less than six months before the decision of the Board to assign BSPCE concerned, the subscription price of a common share of the Company held in the latest frame of said capital increase valued at the grant date of each BSPCE ;*

(4) the common share subscription price of the Company on exercise of warrants will be determined by the Board of Directors at the time of allocation of the BSA and must be at least equal to the higher of two values :

- *The selling price of a share at the close on the regulated market on the day preceding the Board's decision to award the BSA; and*
- *The weighted average share price over the twenty trading days preceding the date of the Board's decision to award the BSA;*

(5) These amounts are not an aggregate. The maximum aggregate ceiling authorized by the shareholders' meeting for capital increases in par value terms is set at €210,000. The total par value of issues of debt securities of the company giving access to the company's capital may not exceed €30,000,000;

(6) The issue price of the shares shall be at least equal to the weighted average of the price over the last three trading days prior to the date on which it is set, less, if applicable, the discount authorized by law (i.e., currently 5%) and corrected for any difference in the ex-date. The issue price of marketable securities giving access to the capital shall be such that the amount the company receives immediately plus, if applicable, the amount it is subsequently likely to receive (i.e., for each share issued as a result of the issue of these marketable securities) is at least equal to the issue price defined above;

(7) the issue price of shares issued will be determined by the Board of Directors and will be at least equal to the average of the average weighted by the volumes of the last 3 trading days preceding the pricing of the possibly reduced emission of a discount of 20%, taking into account applicable from their date of entitlement; it being specified that (i) in the case of the issue of securities convertible into shares, the issue price of the shares that may result from their exercise, conversion or exchange them can be optionally set, at the discretion of the Board by reference to a formula defined by it and applicable after the issue said securities (eg, upon exercise, conversion or exchange) which case the maximum discount may abovementioned be appreciated, if the Board sees fit, on the date of application of the formula (and not the date of fixing of the issue price), and (ii) the issue price of securities giving access to capital if any issued under this resolution shall be such that the amount if any received immediately by the Company plus the amount likely to be received by it upon the exercise or conversion of such securities, either for each share issued as a result of the issuance of these securities, at least equal to the minimum amount abovementioned.

(8) Up to a limit of 10% of the company's capital (as at the transaction date) per 12-month period, the board may disregard the price-setting conditions specified in the above resolutions and set the issue price of issued common shares and/or marketable securities giving immediate or future access to the capital as follows:

- the issue price of common shares shall be at least equal to the weighted average of the price over the last three trading days prior to the date on which it is set, possibly less a maximum discount of 20%; in any case, it may not be less than the par value of a company share on the issue date of the relevant shares, being specified that in the event of the issue of securities convertible into shares, the issue price of the shares that may result from their exercise, conversion or exchange their will if necessary be fixed at the discretion Board by reference to a formula defined by it and applicable after the issue said securities (eg, upon exercise, conversion or exchange) in which case the aforementioned maximum discount may be appreciated, if the Board deems appropriate, on the date of application of the formula (and not the date of fixing of the issue price), and
- the issue price of marketable securities giving access to the capital shall be such that the amount the company receives immediately plus, if applicable, the amount it is subsequently likely to receive (i.e., for each share issued as a result of the issue of these marketable securities) is at least equal to the issue price defined in the above paragraph

(9) 15% or any other percentage that may have been set by decree;

21.2.1 Information about the capital of the company which is under option or agreed conditionally or unconditionally to be put under option

To the best knowledge of the Company, there is no call or put options or other commitments to company shareholders or granted by company shareholders on company shares.

21.2.2 Historical changes

21.2.2.1 Historical evolution:

The table below presents the changes in the company's capital since its creation. These historical data do not reflect the 10-for-1 stock split decided by the shareholders' meeting from October 24, 2011 to November 15, 2011. From that date, the data reflect this 10-for-1 stock split.

Issue date	Type of transaction	Capital	Issue premium	Number of shares issued	Number of shares constituting the capital	Par value	Share capital	Issue price per share before 10-for-1 stock split
12/30/2005	Incorporation (i)	€4,000,000	-	400,000	400,000	10	€4,000,000	€10
05/05/2006	Capital reduction (ii)	-€3,000,000	-	-300,000	100,000	10	€1,000,000	N/A
07/01/2006	Capital reduction (iii)	-€200,000	-	-20,000	80,000	10	€800,000	N/A
07/31/2006	Issue of shares (iv)	€600,000	-	60,000	140,000	10	€1,400,000	€10
10/19/2007	Conversion of common shares into class B preferred shares	-	-	-	140,000	10	€1,400,000	N/A
10/19/2007	Issue for cash of Class A preferred shares with ratchet BSAs attached	€933,390	€7,066,695.69	93,339	233,339	10	€2,333,390	€85.71
12/20/2007	Issue for cash of Class A preferred shares with ratchet BSAs attached	€466,680	€3,533,234.28	46,668	280,007	10	€2,800,070	€85.71
10/22/2009	Capital reduction (v)	-€2,520,063	-	-	280,007	1	€280,007	N/A
10/22/2009	Issue for cash of Class A preferred shares with Tranche 2 BSAs and ratchet BSAs attached	€43,056	€3,647,273.76	43,056	323,063	1	€323,063	€85.71
11/02/2009	Exercise of Tranche 2 BSAs	€3,616	€306,311.36	3,616	326,679	1	€326,679	€85.71
12/01/2009	Issue for cash of Class A preferred shares with Tranche 4 BSAs and ratchet BSAs attached	€15,556	€1,317,748.76	15,556	342,235	1	€342,235	€85.71
12/14/2009	Exercise of Tranche 2 BSAs	€2,333	€197,628.43	2,333	344,568	1	€344,568	€85.71
12/14/2009	Exercise of Tranche 4 BSAs	€7,778	€658,874.38	7,778	352,346	1	€352,346	€85.71
12/23/2009	Issue for cash of Class A preferred shares with Tranche 4 BSAs and ratchet BSAs attached	€46,668	€3,953,246.28	46,668	399,014	1	€399,014	€85.71
03/05/2010	Vesting of bonus shares	€1,050	-	1,050	400,064	1	€400,064	N/A
04/06/2010	Exercise of Oreo BSAs	€5,424	-	5,424	405,488	1	€405,488	€85.71
06/01/2010	Vesting of bonus shares	€140	-	140	405,628	1	€405,628	N/A
06/18/2010	Exercise of Tranche 2 BSAs	€852	€72,172.92	852	406,480	1	€406,480	€85.71
06/18/2010	Exercise of Tranche 2 BSAs	€431	€36,510.01	431	406,911	1	€406,911	€85.71
12/10/2010	Exercise of Tranche 2 BSAs	€14,296	€1,211,014.16	14,296	421,207	1	€421,207	€85.71

Issue date	Type of transaction	Capital	Issue premium	Number of shares issued	Number of shares constituting the capital	Par value	Share capital	Issue price per share before 10-for-1 stock split
12/10/2010	Exercise of Tranche 4 BSAs	€23,334	€1,976,623.14	23,334	444,541	1	€444,541	€85.71
03/04/2011	Vesting of bonus shares	€1,050	-	1,050	445,591	1	€445,591	N/A
06/20/2011	Vesting of bonus shares	€140	-	140	445,731	1	€445,731	N/A
12/15/2011	Vesting of bonus shares	€140	-	1,400	4,458,710	0.10	€445,871	N/A
02/14/2012	Issue of shares – public offering	€159,279.80	€25,134,352.44	1,592,798	6,051,508	0.10	€605,150.80	€15.88
03/07/2012	Vesting of bonus shares	€1,050	-	10,500	6,062,008	0.10	€606,200.80	N/A
03/14/2012	Issue of shares – public offering (overallotment clause)	€13,026.80	€2,055,629.04	130,268	6,192,276	0.10	€619,227.60	€15.88
06/15/2012	Vesting of bonus shares	€280		2,800	6,195,076	0.10	€619,507.60	N/A
12/19/2012	Vesting of bonus shares	€280	-	2,800	6,197,876	0.10	€619,787.60	N/A
03/26/2013	Vesting of bonus shares	€840	-	8,400	6,206,276	0.10	€620,627.60	N/A
06/18/2013	Vesting of bonus shares	€280		2,800	6,209,076	0.10	€620,907.60	N/A
12/13/2013	Vesting of bonus shares	€280	-	2,800	6,211,876	0.10	€621,187.60	N/A
02/04/2014	vesting of free shares	€140	-	1,400	6,213,276	0.10	€621,327.60	N/A
16/12/2014	vesting of free shares	€280	-	2,800	6,216,076	0.10	€621,607.60	N/A
26/03/2015	Exercise of warrants and BSPCE	€280	11 815	2,800	6,218, 876	0.10	€621,887.60	N/A
26/03/2015	Private placement	€62,188.70	31,902,803.10	621,887	6,840,763	0.10	€684,076.30	N/A
2105/03/31	Vesting of free shares	€140		1,400	6,842,163	0.10	684,216.30€	N/A
2015/07/28	Exercise of BSPCE	€280	€15,848	2,800	6,844,963	0.10	684,496.30€	N/A
2015/12/16	Vesting of free shares	€140		1,400	6 846 363	0.10	684,636.30€	N/A

(i) One-fifth of the 400,000 shares constituting the share capital were paid up on December 16, 2005, with the balance paid up on December 20, 2005.

(ii) Capital reduction through the outright cancellation of 300,000 shares.

(iii) Capital reduction to offset losses.

(iv) 60,000 new shares were paid up at one-quarter of their par value on subscription, with the balance paid up on November 15, 2006.

(v) Capital reduction due to losses.

21.2.2.2 Change in the company's shareholder structure since December 31, 2013

	Situation at December 31, 2015			Situation at December 31, 2014			Situation at December 31, 2013		
	Number of shares	% of capital	% of voting rights	Number of shares	% of capital	% of voting rights	Number of shares	% of capital	% of voting rights
Soula Family	**1 525 933**	**22,3%**	**31,8%**	**1 540 933**	**24,8%**	**32,0%**	**1 550 933**	**25,0%**	**29,7%**
Gérard Soula	898 463	13,1%	18,8%	898 463	14,5%	18,6%	898 463	14,5%	16,9%
Olivier Soula	307 490	4,49%	6,32%	317 490	5,11%	6,60%	317 490	5,1%	6,2%
Rémi Soula	302 490	4,42%	6,32%	307 490	4,95%	6,40%	317 490	5,1%	6,2%
Laure Soula	17 490	0,3%	0,4%	17 490	0,3%	0,4%	17 490	0,3%	0,3%
Financial investors	**1 166 639**	**17,0%**	**24,4%**	**1 831 650**	**29,5%**	**38,1%**	**2 916 042**	**46,9%**	**53,5%**
Innobio *(Bpifrance Investissement)*	625 923	9,1%	13,1%	700 020	11,3%	14,6%	700 020	11,3%	13,6%
Fonds BioAM *(Bpifrance Investissement)*	112 716	1,6%	2,4%	286 256	4,6%	6,0%	341 820	5,5%	6,7%
Subtotal BPIfrance investissement	*738 639*	*10,8%*	*15,4%*	*986 276*	*15,9%*	*20,5%*	*1 041 840*	*16,8%*	*20,3%*
Fonds IdInvest	0,00	0,00	0,00	0,00	0,00	0,00	683 710	11,0%	13,3%
Fonds Amundi	0,00	0,00	0,00	0,00	0,00	0,00	179 890	2,9%	3,5%
Fonds Viveris	67 439	1,0%	1,4%	364 754	5,9%	7,6%	364 754	5,9%	6,9%
Oréo Finance	40 561	0,6%	0,8%	81 561	1,3%	1,7%	191 343	3,1%	2,2%
Famille Deléage	0	0,0%	0,0%	17 090	0,3%	0,4%	68 360	1,1%	1,3%
SHAM (1)	320 000	4,7%	6,7%	381 969	6,1%	7,9%	386 145	6,2%	6,0%
Key employees	**40 270**	**0,65%**	**0,76%**	**50 090**	**0,8%**	**0,9%**	**49 000**	**0,8%**	**0,7%**
Scientific committees (stock warrants)	700	0,0%	0,0%	0	0,0%	0,0%	0	0,0%	0,0%
administrator (stock warrants)	0	0,0%	0,0%	0	0,0%	0,0%	0	0,0%	0,0%
Treasury shares	**4 185**	**0,06%**	**0,0%**	**2 323**	**0,0%**	**0,0%**	**40 326**	**0,6%**	**0,0%**
other shareholders *	**4 108 636**	**60,0%**	**43,1%**	**2 791 080**	**44,9%**	**29,1%**	**1 655 575**	**26,7%**	**16,2%**
Total	**6 846 363**	**100,0%**	**100,0%**	**6 216 076**	**100,0%**	**100,0%**	**6 211 876**	**100,0%**	**100,0%**

(*) SHAM : Société Hospitalière d'Assurance Mutuelles

(1) On the date of this reference document, the dilutive instruments issued by the company consisted of (i) 2,800 shares (after accounting for the 10-for-1 stock split decided by the shareholders' meeting of October 24, 2011) issued as bonus shares by the company to key employees, of which 9,800 shares are in the vesting period as described in detail in section 21.1.5 herein; (ii) 2,100 stock warrants (BSAs) entitling holders to subscribe 2,100 shares (after accounting for the 10-for-1 stock split decided by the shareholders' meeting of October 24, 2011); (iii) 20,000 stock warrants (BSAs) entitling holders to subscribe 20,000 shares granted to independent directors; and (iv) 167,900 business founders' stock warrants (BSPCEs) entitling to subscribe for 167,900 shares and (v) 20,000 stock options granted in March 2015.

(2) Including any bearer shares held by the company's long-standing financial investors, and Investors who participated in the private placement in March 2015

21.2.2.3 Share price performance – Risk of price fluctuations

The shares have been traded on the Euronext regulated market in Paris since February 18, 2012 at €15.88 at the time of its IPO.

During 2014, the share traded at a low of €5.93 on January 3, 2014 and a high of €48.25 on December 31,2014.

During 2015, the share traded at a low of €51.01 on March 27, 2015 and a high of €93.65 on July 20,2015. In late December 2015, the price was 73.22 euros, leading to a market capitalization of € 501 million

In the first months of the 2016 fiscal year, the share moved from €70.89 at January 1, 2016 to €62.42 to 6 April 2016, thus leading the market capitalization of the Company to an amount of €427 million.

21.3 Articles of incorporation and bylaws

21.3.1 Corporate purpose

The company's purpose, directly or indirectly, in France and abroad, is:

- 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 purpose;
- the design, development, manufacture, distribution, import, export and use, by any means, of medicines, proprietary drugs and other healthcare goods;
- the creation, acquisition, rental, and lease management of all businesses, the leasing, establishment, and operation of all entities, businesses, plants and workshops relating to any of the specified activities;
- the company's direct or indirect participation in all financial, real-estate or personal transactions and in any civil, commercial or industrial companies that may fall within the scope of the corporate purpose or any similar, related or complementary purpose.

21.3.2 Management and supervisory bodies

21.3.2.1 Board of directors

21.3.2.1.1 *Composition of the board of directors (Articles 11.1 and 11.2 of the bylaws)*

The company shall be administered by a board composed of natural persons or legal entities whose number shall be determined by the ordinary shareholders' meeting within the limits of the law.

Any legal entity may, upon appointment, designate a natural person as permanent representative to the board of directors. The permanent representative's term of office shall be the same as that of the legal-entity director that he or she represents. If the legal entity dismisses its permanent representative, it shall immediately appoint a replacement. The same provisions shall apply in the event of the death or resignation of the permanent representative.

Directors are appointed for a three-year term, which shall expire at the close of the ordinary shareholders' meeting called to approve the financial statements for the previous fiscal year and held in the year in which the term of said director expires.

Directors may be reappointed; they may be dismissed at any time by decision of the shareholders' meeting.

Should one or more directorships become vacant due to death or resignation, the board of directors may make provisional appointments between two shareholders' meetings.

Appointments made by the board pursuant to the above paragraph shall be subject to approval by the next ordinary shareholders' meeting.

The absence of such approval shall not affect the validity of the board's prior resolutions and acts.

When the number of directors falls below the legal minimum, the remaining directors shall immediately call an ordinary shareholders' meeting so as to fill the vacant positions on the board.

An employee of the company may be named director. His or her employment contract must, however, correspond to actual employment. In that case, he or she shall not lose the benefit of his or her employment contract.

The number of directors bound to the company by an employment contract may not exceed one-third of directors in office.

The number of directors over the age of 70 may not exceed one-third of directors in office. When this limit is exceeded during a term of office, the oldest director shall be considered to have automatically resigned at the close of the next shareholders' meeting..

21.3.2.1.2 *Board observers (Article 15 of the bylaws Censeurs)*

The ordinary shareholders' meeting may, on the proposal of the board of directors, appoint board observers (censeurs). The board of directors may also appoint them directly, subject to approval by the next shareholders' meeting.

The board observers, who may not number more than five, shall form a board. They shall be selected freely for their expertise.

They shall be appointed for a three-year term expiring at the close of the ordinary shareholders' meeting called to approve the financial statements for the previous fiscal year.

This advisory board shall consider matters submitted by the board of directors or its chairman for its opinion. Board observers shall attend meetings of the board of directors and take part in deliberations only in an advisory capacity; their absence shall not, however, affect the validity of the deliberations.

They shall be called to meetings of the board under the same conditions as directors.

The board of directors may pay board observers compensation out of the amount of directors' fees allocated to directors by the shareholders' meeting..

21.3.2.1.3 *Meetings of the board of directors (Article 12 of the bylaws)*

The board of directors shall meet as often as the interests of the company so require.

The chairman shall call directors to meetings of the board. This may be done by any means, whether in writing or verbally.

The chief executive officer may also ask the chairman to call a meeting of the board of directors to consider a specific agenda.

Additionally, directors representing at least one-third of the members of the board may validly call a board meeting. In that case, they must specify the meeting agenda.

When a works council has been formed, the representatives of this council, appointed in accordance with the provisions of the French labor code (Code du travail), shall be called to all meetings of the board of directors.

Meetings of the board shall be held either at the registered office or at any other location in France or abroad.

Decisions of the board shall be valid only if the number of members in attendance is at least equal to half the members.

Decisions of the board of directors shall be made by a majority of votes; in the event of a tie, the chairman of the meeting shall cast the deciding vote.

The board of directors may adopt its own rules of procedure which may specify, in particular, that directors attending the meeting by means of videoconferencing or other telecommunications equipment in accordance with existing regulations shall be deemed present for the purposes of calculating a quorum

and a majority. This provision shall not apply to the adoption of the decisions referred to in Articles L. 232-1 and L. 233-16 of the French commercial code.

Directors shall receive the information required to fulfill their duties and mandates and may request all documents they deem necessary.

Any director may authorize, by letter, telegram, telex, fax, email or any other means of remote transmission, another director to represent him or her at a board meeting, but each director may only hold one proxy during a meeting.

Copies or extracts of the deliberations of the board of directors shall be duly certified by the chairman of the board of directors, the chief executive officer, the director temporarily delegated to perform the duties of chairman or a duly authorized proxy holder.

21.3.2.1.4 *Powers of the board of directors (Article 13 of the bylaws)*

The board of directors shall set the company's business strategy and oversee its implementation. Subject to the powers expressly granted to shareholders' meetings and within the limit of the corporate purpose, it shall consider all issues relating to the company's operations and make decisions on matters affecting the company.

In its relations with third parties, the company shall be bound even by acts done by the board of directors that are not within the corporate purpose, unless it can prove that the third party knew that the act was outside this purpose or could not in view of the circumstances have been unaware of it; disclosure of the bylaws shall not of itself be sufficient proof thereof.

The board of directors shall perform the audits and verifications it deems appropriate.

Furthermore, the board of directors shall exercise the special powers granted to it by law.

21.3.2.2 Executive management (Article 14 of the bylaws)

The chairman of the board of directors, or another natural person appointed by the board of directors and holding the position of chief executive officer, shall oversee the executive management of the company, which is under his or her responsibility.

The chief executive officer shall have extensive powers to act in all circumstances on behalf of the company. He or she shall exercise his or her powers within the limit of the corporate purpose and subject to those expressly granted by law to shareholders' meetings and the board of directors.

He or she shall represent the company in its relations with third parties. The company shall be bound even by acts done by the chief executive officer that are not within the corporate purpose, unless it can prove that the third party knew that the act was outside this purpose or could not in view of the circumstances have been unaware of it; disclosure of the bylaws shall not of itself be sufficient proof thereof.

The chief executive officer may not be more than 75 years old. If the chief executive officer reaches that age, he or she shall be considered to have automatically resigned. His or her term of office may be extended, however, to the next meeting of the board of directors, during which a new chief executive officer shall be appointed.

When the chief executive officer is a director, his or her term of office may not exceed his or her term as director.

The board of directors may dismiss him or her at any time. If the decision to dismiss is made without just cause, it may give rise to damages, except when the chief executive officer assumes the duties of chairman of the board of directors.

By simple decision made by a majority of votes of directors present or represented, the board of directors shall choose between the two methods of executive management referred to in the first subparagraph of the paragraph.

Shareholders and third parties shall be informed of this decision in accordance with legal and regulatory conditions.

The decision so made by the board of directors shall remain in effect until the board decides otherwise or, at its discretion, for the term of office of the chief executive officer.

When the chairman of the board of directors is responsible for the executive management of the company, the provisions applicable to the chief executive officer shall apply to him or her.

In accordance with Article 706-43 of the French code of criminal procedure, the chief executive officer may validly authorize any person of his or her choice to represent the company in criminal proceedings that may be brought against it.

On the proposal of the chief executive officer, the board of directors may empower one or more natural persons to assist the chief executive officer as vice-president.

In conjunction with the chief executive officer, the board of directors shall determine the scope and duration of the powers granted to the vice-president. The board of directors shall determine their compensation. When a vice-president is a director, his or her term of office may not exceed his or her term as director.

The vice-presidents shall have the same powers with respect to third parties as the chief executive officer; in particular, the vice-presidents may engage in legal proceedings.

There may not be more than five vice-presidents.

The vice-president(s) may be dismissed at any time by the board of directors, on the proposal of the chief executive officer. If the decision to dismiss is made without just cause, it may give rise to damages.

Vice-presidents may not be more than 65 years old. If a vice-president in office reaches that age, he or she shall be considered to have automatically resigned. His or her term of office may be extended, however, to the next meeting of the board of directors, during which a new vice-president may be appointed.

When the chief executive officer ceases to perform his or her duties or is prevented from doing so, the vice-president(s) shall continue to fulfill their roles and responsibilities, unless the board of directors decides otherwise, until a new chief executive officer is appointed.

21.3.3 Rights, privileges and restrictions attaching to shares of the company

21.3.3.1 Forms of securities (Article 7 of the bylaws Formes des titres)

Shareholders may choose to hold their fully paid-up shares in registered or bearer form, subject, however, to application of the legal provisions relating to the form of shares held by certain natural persons or legal entities. Shares that are not fully paid up must be held in registered form.

The shares shall be registered in an account under the terms and conditions specified in the applicable laws and regulations.

Ownership of shares delivered in registered form derives from their registration in a registered account.

21.3.3.2 Voting rights (excerpted from Article 9 of the bylaws)

Except where the law provides otherwise, and except in the case of double voting rights as set forth below, each shareholder shall have as many voting rights and may cast as many votes in shareholders' meetings as he or she owns fully paid-up shares. Each redeemable or redeemed share with the same par value, except in the case of double voting rights as set forth below, shall entitle the holder to one vote.

A voting right equivalent to twice that attributed to other shares, based on the proportion of the share capital they represent, may be attributed to all fully paid-up shares (regardless of their class) that can be proved to have been registered in the name of the same shareholder for at least two years; the conversion of preferred shares into common shares shall have no impact on the calculation of the holding period. This right shall also be attributed, in the event of a capital increase through capitalization of reserves, earnings or issue premiums, to newly issued registered shares granted as bonus shares to a shareholder for existing shares that already entitled him or her to this right.

21.3.3.3 Rights to dividends and profits (excerpted from Articles 9, 21 and 22 of the bylaws)

Each share shall entitle its holder to a share of ownership of the corporate assets, to a share of earnings and to the liquidation surplus in proportion to the number and par value of the existing shares.

Whenever it is necessary to own a certain number of shares, whether or not they are preferred shares, or marketable securities in order to exercise a particular right, shareholders or owners of marketable securities shall personally arrange to group the necessary number of shares or marketable securities.

At least five percent (5%) shall be deducted from earnings for the fiscal year, less any prior-year losses, to create a reserve fund known as the "legal reserve." This deduction shall no longer be required when the reserve fund reaches one-tenth of the share capital.

Distributable earnings shall consist of earnings for the fiscal year less prior-year losses and the deduction specified in the previous paragraph, plus earnings carried forward.

If the financial statements for the fiscal year, as approved by the shareholders' meeting, show that there are distributable earnings, the shareholders' meeting shall decide to allocate them to one or more reserve accounts whose allocation or use it controls, to carry them forward or to distribute them as dividends.

Having acknowledged the existence of reserves at its disposal, the shareholders' meeting may decide to distribute amounts from these reserves. In that case, the resolution shall expressly specify the reserve accounts from which these payments shall be drawn. However, dividends shall first be drawn from distributable earnings.

The shareholders' meeting or, alternatively, the board of directors shall set the conditions under which dividends are paid.

However, dividends must be paid no later than nine months after the close of the fiscal year.

The shareholders' meeting called to approve the financial statements for the fiscal year may give each shareholder, for all or part of the dividend paid, the choice between receiving the dividend in cash or in shares.

Similarly, the ordinary shareholders' meeting, acting in accordance with the conditions specified in Article L. 232-12 of the French commercial code, may grant each shareholder an interim dividend and, for all or part of said interim dividend, may give him or her the choice between receiving the interim dividend in cash or in shares. (…)

21.3.3.4 Preemptive rights

Shares in the company carry a preemptive right to subscribe to capital increases under the conditions specified in the commercial code.

21.3.3.5 Restrictions on voting rights

The bylaws contain no clause that restricts the voting rights attaching to the shares.

21.3.3.6 Identifiable bearer shares (Titres au porteur identifiables)

The company may, under applicable legal and regulatory conditions, at any time and at its own expense, ask any authorized body to provide it with the name or, in the case of a legal entity, the corporate name, nationality and address of holders of shares that grant an immediate or future voting right at its own shareholders' meetings, as well as the number of shares held by each of them and, if applicable, any restrictions on these shares.

21.3.3.7 Buyback by the company of its own shares

See section 21.1.4 "Acquisition by the company of its own shares."

21.3.4 Actions required to change the rights of shareholders

The rights of shareholders as stated in the company's bylaws may only be changed by an extraordinary meeting of the company's shareholders.

21.3.5 Shareholder's meetings

21.3.5.1 Holding of shareholder's meetings (Article 19 of the bylaws)

Shareholders' meetings shall be called and held under the conditions set by law.

When the company wishes to call a meeting by electronic means of communication rather than by mail, it must obtain the prior approval 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 shall be governed by applicable laws and regulations and shall be subject, among others, to registration of the securities in the name of the shareholder or registered intermediary by midnight, Paris time, on the third business day prior to the meeting, either in the registered securities accounts held by the company or in bearer share accounts held by the authorized intermediary.

If a shareholder is unable to attend the meeting in person, he or she may choose one of the following three options:

- appoint a proxy under the conditions permitted by law and by regulation,
- vote by mail, or
- send a proxy to the company without naming an agent,
- under the conditions specified by law and by regulation.

The board of directors may, under the conditions specified by the applicable laws and regulations, arrange for shareholders to attend the meetings and vote by videoconference or by means of telecommunications that permit them to be identified. If the board of directors decides to implement this option for a specific meeting, this decision by the board is stated in the notice of meeting and/or notification to attend. Shareholders attending meetings by videoconference or by any of the other means of telecommunications referred to above, at the board of directors' discretion, shall be deemed present for the purposes of calculating a quorum and a majority.

Meetings shall be chaired by the chairman of the board of directors or, in his or her absence, by the chief executive officer, a vice-president if he or she is also a director, or a director specially appointed for that purpose by the board. Otherwise, the meeting shall elect its own chairman.

The duties of teller (*scrutateur*) shall be performed by the two members of the meeting who are present, have agreed to perform these duties and have the most votes. The meeting officers (*bureau*) shall appoint the secretary, who need not be a shareholder.

An attendance sheet shall be drawn up under the conditions specified by law.

The proceedings of the ordinary shareholders' meeting, when first convened, shall only be valid if shareholders present or represented own at least one-fifth of shares with voting rights. The proceedings of the ordinary shareholders' meeting, when convened a second time, shall be valid regardless of the number of shareholders present or represented.

The resolutions of the ordinary shareholders' meeting shall be adopted by a majority of votes of shareholders present or represented.

The proceedings of the extraordinary shareholders' meeting, when first convened, shall only be valid if shareholders present or represented own at least one-quarter of shares with voting rights. The proceedings of the extraordinary shareholders' meeting, when convened a second time, shall be valid only if shareholders present or represented own at least one-fifth of shares with voting rights.

The resolutions of the extraordinary shareholders' meeting shall be adopted by a two-thirds majority of shareholders present or represented.

Copies or extracts of the minutes of the meeting shall be duly certified by the chairman of the board of directors, by a director performing the duties of the chief executive officer or by the meeting secretary.

21.3.5.2 Powers of the shareholders' meetings (Article 19 of the bylaws)

The ordinary and extraordinary shareholders' meetings shall exercise their respective powers under the conditions specified by law.

21.3.6 Provisions that may have the effect of delaying, deferring or preventing a change of control

The company's bylaws contain no provisions that may have the effect of delaying, deferring or preventing a change of control.

21.3.7 Specific provisions governing changes in the capital

The company's bylaws contain no specific provisions governing changes in its capital.

22 MAJOR AGREEMENTS

With the exception of the agreements described below, the company has not entered into any major agreements other than those signed in the normal course of business, it being understood that the company has signed several collaborative development agreements with large pharmaceutical groups for the development of new innovative formulations. However, at this stage of the company's development, none of these collaboration agreements is considered to be of major strategic importance given the insufficient technical progress made (see paragraphs 6.1 and 11.3 of this reference document).

22.1 OSEO Innovation agreement of March 12, 2007

As part of the Osteoporosis project, the company signed an agreement with OSEO on March 12, 2007 under which it received a reimbursable advance totaling €2.25 million for the development of a new system for local controlled release of growth factors for bone regeneration. After fulfilling all the technical and financial conditions, the company received the full amount of this reimbursable assistance in four payments made between March 15, 2007 and February 15, 2010.

Under the terms of the contract, an amount of €700,000 was reimbursed no later than March 31, 2013 under the technical achievements, and whatever the outcome of the program As such, the Company repaid the first deadline for €300,000 in 2012 and a second amount of €400,000 was repaid on April 1st, 2013.

In March 2014, the Company has made a demand for commercial and technical failure on this file. In June 2015, the Company obtained OSEO the finding of the partial failure of the project, leading to recognition of a grant of 1,050,000 euros, the balance of € 500,000 being paid on 30 September 2015. The advance is thus cleared out in late December 2015.

22.2 OSEO Innovation agreements of April 25, 2012

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

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

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

- €32,500 by March 31, 2017,
- €32,500 by June 30, 2017,
- €32,500 by September 30, 2017,
- €32,500 by December 31, 2017,
- €37,500 by March 31, 2018,
- €37,500 by June 30, 2018,
- €37,500 by September 30, 2018,
- €37,500 by December 31, 2018,

- €50,000 by March 31, 2019,
- €50,000 by June 30, 2019,
- €50,000 by September 30, 2019,
- €50,000 by December 31, 2019,
- €80,000 by March 31, 2020,
- €80,000 by June 30, 2020,
- €80,000 by September 30, 2020,
- €80,000 by December 31, 2020.

(iv) 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 technical or 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 according to the following terms:

- €32,500 by March 31, 2017,
- €32,500 by June 30, 2017,
- €32,500 by September 30, 2017,
- €32,500 by December 31, 2017,
- €37,500 by March 31, 2018,
- €37,500 by June 30, 2018,
- €37,500 by September 30, 2018,
- €37,500 by December 31, 2018.

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

22.3 Coface-International business development insurance agreement of October 1, 2012

As part of its business development in new markets (India and China), the company signed a business development agreement with Coface (French insurance company for foreign trade) on October 26, 2012 in return for the payment of a premium equivalent to 2% of the annual budget.
Under the terms of the agreement, Coface guarantees the reimbursement of 75% of the expenses incurred during the four-year guarantee period, which runs from October 1, 2012 to September 30, 2016.

The company agreed to repay the sums received from Coface according to the Terms and Conditions set out in the agreement during an amortization period that runs until September 30, 2012. The repayment terms are as follows:

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

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

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

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

During the period 1 October 2013 to 30 September 2014, the Company did not incur exploration expenditures on the targeted markets, the contract is terminated. Therefore, the Company entered into amortization period on amounts received previously, meaning 91 thousand euro and as provided in the contract and listed above.

22.4 Licensing and collaboration agreement with Eli Lilly

Refer to paragraph 11.3.2 of this reference document.

22.5 Acquisition of an exclusive licence for a nanotechnology (DriveIn®)

Refer to paragraph 11.3.3 of this reference document.

23 INFORMATION FROM THIRD PARTIES, EXPERTS' STATEMENTS AND DECLARATIONS OF INTERESTS

23.1 Designation of experts

None.

23.2 Designation of third parties

None.

24 DOCUMENTS AVAILABLE TO THE PUBLIC

Copies of this reference document are available free of charge at the company's registered office located at 115, avenue Lacassagne, 69003 Lyon. An electronic version is also available on the company's website (www.adocia.com) and on the website of the French financial markets authority (Autorité des marchés financiers - AMF) (www.amf-france.org).

The bylaws, minutes of shareholders' meetings and other corporate documents of the company, as well as historical financial information and any assessment or statement made by an expert at the company's request which must be made available to shareholders pursuant to the applicable legislation may be consulted free of charge at the company's registered office.

Regulatory information as provided by the General Regulations of the AMF is also available on the company's website (www.adocia.com).

25 INFORMATION REGARDING EQUITY INTERESTS

As of the filing date of this reference document, the company owns 100% of a subsidiary which name is Adocia Inc., located in the United States (please refer to chapter 7 of this reference document).

26 GLOSSARY

AFSSAPS	Agence Française de Sécurité Sanitaire et Produits de Santé/*French Agency for the Safety of Health Products*. 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.
Amphiphile	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.
Anionic group	Negatively charged group of ions (anions)
Ankylosis	Immobility of a joint caused by injury or disease.
Anticoagulation	Phenomenon reducing or preventing the transformation of liquid blood into a clot (a more viscous and more or less gelatinous form).
Arteriopathy	Any diseases of arteries.
Bedsore (eschar)	Skin lesion resulting from decreased blood flow following an ischemic process
Biosimilar	Generic form a drug whose patent has expired.
Chronic lesion	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.
Coacervation	The separation of certain macromolecular solutions into two phases.
Complex	Structure formed from several independent chemical entities.
Compliance	The extent to which a patient follows the treatment prescribed.
Crohn's disease	Chronic inflammatory disease of the digestive tract.
Deamidation of asparagine	Non-enzymatic and spontaneous process that converts asparagine, an amino acid of proteins, into aspartic acid.
Dermatitis	A skin reaction caused by exposure to substances that are allergens or irritants.
EMA	European Medicines Agency. This authority evaluates and supervises the development of new drugs for human and veterinary use in the European Union.
Endothelial barrier	Selective permeability barrier enabling and regulating exchanges of molecules of varying sizes (water, salts, proteins, etc.) between the blood and tissues

Enzymatic breakdown	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.
Epidermoid carcinoma	A form of skin cancer.
Erysipelas	Non-necrosing infection of the dermis or epidermis.
European Pharmacopoeia	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.
Excipient	Any substance in a drug product other than the drug substance(s).
FDA	Food and Drug Administration. American agency responsible for approving drugs and medical devices for marketing.
Glucose clamp technique	Reference method used in clinical research to measure sensitivity to insulin.
Glycoregulation	Regulation of the level of blood glucose, or glycemia, by the endocrine system.
Good Manufacturing Practices	Notion of quality assurance, established by the European Commission and applied to the manufacturing of drugs for human or veterinary use.
Graft	A chemical group bound to the molecule in question.
Granulation tissue	Temporary tissue covering a lesion during the healing process.
Growth factor	Protein required for the growth or regeneration of a tissue or organ.
Heparin	Anticoagulant substance present in the body.
ICH	International Conference of Harmonization. International body composed of American, European and Asian health authorities, as well as pharmaceutical companies.
Immunogenicity	Capacity of an antibody to cause an immune reaction.
Incidence	Number of new cases of a pathology found during a given period and for a given population.
Ischemia	Reduced blood flow to an extremity or an organ.
Islets of Langerhans	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.

IU	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.
kDa (kiloDalton)	Unit used to measure the molecular weight of molecules and atoms. The value of one Dalton is the atomic weight of the hydrogen atom.
Leukemia	Bone marrow cancer with anarchic proliferation of white blood cells.
Ligand	In chemistry, this is an atom, ion or molecule having the capacity to bind to one or several central atoms or ions.
Lymphoma	Malignant tumor of the lymphatic system.
Marketing Authorization (MA)	Approval of a medicine by health authorities prior to its commercialization.
Multiple sclerosis	Disease of the central nervous system, in particular the brain, optic nerves and spinal cord.
Muscular dystrophy	A progressive degenerative disease of the body's muscles.
Muscular hypoxia	Insufficient oxygenation of muscle tissues.
National Consultative Ethics Committee	Independent French advisory body whose principal mission is to provide opinions and reports dealing with ethics as pertaining to scientific progress.
Necrotizing fasciitis	Infection caused by group A *Streptococcus*.
Nerve fiber (axon)	Single extension emerging from the cell body of neurons whose function is to transport nerve impulses.
Neuropathy	Any disease of the nervous system.
Osteoarticular lesion	A lesion involving both bones and joints.
Pancreas	Gland in proximity to the stomach.
Pharmacodynamics	Study of the effects of a drug on the body, in particular the interaction between its cell receptor and the therapeutic substance.
Pharmacokinetics	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.
Polymer	Chemical compound formed by molecules whose feature is the repetition of one or several atoms or groups of atoms.
Polysaccharide	Complex sugar composed of several simple sugars of the same family of polymers.

Prevalence	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.
Primary dressing	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.
Proof of concept	Demonstration of the feasibility and efficacy of a therapeutic product.
Protein	Macromolecule composed of amino acids linked by peptide bonds and that ensure myriad functions in the body.
Regenerative medicine	The use of human cells to repair or improve the functions of a damaged organ.
Rheumatoid arthritis	Chronic, inflammatory, degenerative disease characterized by the inflammation of several joints.
Sanies	Fetid purulent matter mixed with blood.
Somatic cells	All cells except germ, or sex cells.
SOP	Standard Operating Procedure. A written detailed procedure to ensure the comparability and uniformity of studies of the performance of a given pharmaceutical product.
Sorbitol	A sugar-alcohol.
Stasis	Reduction or cessation of the circulation of a fluid.
Streptococcus	A genus of bacteria, certain species of which are pathogens, i.e. sources of infections.
Transgenesis	The set of techniques used to introduce a foreign gene in the genome of an organism to obtain a genetically modified organism.
Tryptophan	An amino acid forming proteins. It is called essential because it cannot be synthesized by the body and must be provided by the diet.
UDRP procedure	Uniform Dispute Resolution Policy. Principles of the Internet Corporation for Assigned Names and Numbers (ICANN) to resolve disputes involving domain names.
United States Pharmacopeia – National Formulary	Collection of quality control requirements of medicinal preparations, excipients and medical devices drafted by the United States Pharmacopeial Convention. The FDA is responsible for ensuring compliance with these requirements in the United States. These standards have been developed and used in more than 130 counties in the world.

ADOCIA

Corporation (société anonyme) with €684,636.30 in share capital
Registered office: 115 avenue Lacassagne - 69003 Lyon
487 647 737 Lyon trade and companies register

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REPORT OF THE CHAIRMAN OF THE BOARD OF DIRECTORS ON CORPORATE GOVERNANCE, INTERNAL CONTROL AND RISK MANAGEMENT

To the shareholders,

In accordance with Article L. 225-37 of the French commercial code, I am pleased to report to you, in my capacity as chairman of the board of directors, on the composition and conditions for the preparation and organization of the work of this board during fiscal year 2014 and on the internal control and risk management procedures implemented by the company.

This report, prepared by the company's administrative and finance department, was submitted to the audit committee and subsequently approved by the board of directors at its meeting of March 15, 2016.

1. Corporate governance

Until October 24, 2011, Adocia was incorporated as a simplified joint-stock company (société par actions simplifiée). At the time of its initial public offering, the company was converted, on October 24, 2011, into a corporation (société anonyme) 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 simplified joint-stock company.

The board of directors, at its meeting of October 24, 2011, adopted its own rules of procedure which specify, among others, 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 of their members. The board's rules of procedure can be accessed on the company's website (www.adocia.fr).

To structure its governance, the company has chosen to refer to the corporate governance code for small and midcaps as published in December 2009 by MiddleNext and approved as a reference code by the Autorité des marchés financiers (the "MiddleNext Code"). The board of directors, at its meeting of October 11, 2011, after reviewing the information presented in the "key issues" section of the MiddleNext Code, therefore decided to adopt this code as its corporate governance reference code.

1.1. Composition of the Board of Directors

In accordance with legal requirements and the bylaws, the board of directors is composed of at least three directors and at most 18, appointed by the shareholders' meeting for a three-year term. They may be reappointed when their term expires. In the event of a vacancy, directors may be coopted under the conditions specified in the applicable laws and regulations.

In accordance with its rules of procedure, the board of directors has at least two independent directors within the meaning of the MiddleNext Code. Members of the board are deemed independent if they have no relationship with the company, its group or its management that might adversely affect the exercise of their freedom of judgment.

The company has two independent directors within the meaning of the provisions of the MiddleNext Code, Ms. Dominique Takizawa and Ms. Ekaterina Smirnyagina.

The company intends to recruit one or more additional independent directors as part of its plan to improve its corporate governance.

The board reviews the independence of its members based on the following criteria set by the MiddleNext Code:

- the director is not an employee or corporate officer of the company, nor an employee or corporate officer of one of its subsidiaries, and has not been one over the last three years;
- the director is not a customer, supplier or banker that is material for the company or its group, or not material, for which the company or its group represents a material proportion of the entity's activity;
- the director is not a major shareholder in the company;
- the director does not have any close family ties with a corporate officer or major shareholder of the company; and
- the director has not been an auditor of the company over the last three years.

Moreover, at least one of the independent members must have specific financial or accounting expertise so that he or she may be named to the audit committee.

At December 31, 2015, the company's board of directors had six directors.

The terms of office of the directors shall expire at the close of the shareholders' meeting called to approve the financial statements for the fiscal year ended December 31, 2016, with the exception of Ekaterina Smirnyagina who was appointed at the combined shareholders' meeting of June 18, 2013. Her term of office shall expire at the close of the shareholders' meeting called to approve the financial statements for the fiscal year ended December 31, 2015.

Name or corporate name	**Title**
Gérard Soula	Chairman of the board of directors and chief executive officer
Olivier Soula	Director and General Deputy Manager
Olivier Martinez	Director
Bpifrance Investissement represented byLaurent Arthaud	Director

Dominique Takizawa	Independent director
Ekaterina Smirnyagina	Independent director

A list of other offices held by the company's directors can be found in section 14.1.2. of the reference document.

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, on which he reports 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 vice-president. The vice-president has the same powers as the chief executive officer with regard to third parties.

On February 25, 2014, the board of directors received the resignation of Mr. Thierry Laugel.
As the minimum number of directors has been met, an ordinary shareholders' meeting does not have to be called to fill this vacancy on the board of directors.

1.2. Roles and responsibilities of the board of directors

The board is subject to the provisions of the French commercial code, articles 11 to 13 of the company's bylaws and the rules of procedure that it has adopted.

These rules can be accessed on Adocia's website (www.adocia.fr).

The board is responsible, among others, for:

- setting 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,
- appointing the chairman of the board, the chief executive officer and the vice-presidents, and determining their compensation,
- authorizing the agreements and commitments referred to in Articles L. 225-38 and L. 225-42-1 of the French commercial code, and
- approving the report of the chairman of the board on corporate governance and internal control.

It monitors the quality of the information provided to shareholders and to the markets.

1.3. Conditions for the preparation and organization of the work of the board

To contribute effectively to the work and deliberations of the board, each member shall receive the documents he or she deems necessary. Requests of this nature shall be made to the chairman or, if applicable, to any other company executive (chief executive officer or vice-president).
Each member of the board is authorized to meet with the company's key executives, provided that he or she so inform the chairman of the board and the chief executive officer in advance.
The board is regularly informed by the chief executive officer of the company's and the group's financial position, cash position, financial commitments and significant events.
Lastly, any new member of the board may request training on the specific aspects of the company and its group, their business lines and their business sectors.

The members of the board may be called to a meeting by any means, even verbally.

All documents or draft documents providing information on the agenda and on all matters submitted to the board for review are sent, delivered or made available to board members within a reasonable time frame before the meeting.

A packet detailing the contents of the items on the agenda, prepared by executive management, is provided to each director during the meeting.

Minutes are drawn up for each meeting, and a draft is sent to the directors for comment. The final version of the minutes is approved at the next meeting and signed by the chairman and another board director who attended the meeting. Representatives of the works council attend the meetings, and the company's statutory auditors also attend meetings dealing with the closing of the annual and interim financial statements. The board of directors is assisted by three standing committees whose responsibilities and operating procedures are specified in the rules of procedure: the audit committee, the compensation committee and the scientific advisory board. The rules of procedure also provide for the possibility of creating any other committee, whose composition and responsibilities it shall determine, as often as the interests of the company so require.

In accordance with recommendation 15 of the MiddleNext Code, the board conducts an annual assessment of its operations. The board of directors, appointed on October 24, 2011, laid down the rules for conducting this evaluation in its rules of procedure.

1.4. Report on the activities of the Board during fiscal year 2015

Over the course of the past year, the company's board of directors met twelve times, on January 30, Feruary 19, March 3, 25, 26 et 31, May 27, July 20, Septmber 22, November 10 novembre and on December 10 and 16, 2015.. The chairman of the board chaired these eight meetings, and the attendance rate for all members was 93%.

The following main points were addressed at the meetings:

- Updates on financing of the Compnay
- Private placement
- Business discussion with potential partners,
- Update on the business and the status of various projects
- Set up of American subsidiary
- Building acquisition

- Financial updates:

. • Revised quarterly
• Plan for 3 years from 2015 to 2018
• Presentation and approval of the 2016 budget.
• Report of the Remuneration Committee:
• Compensation Approval
• Allocation of stock options to employees of the US subsidiary
• Award BSPCE AGA and the Executives
• Free allocation of shares to employees of the Group
• definitive acquisition of free shares.
• Points to submit to the General Meeting of Shareholders:
• Appointment of New Director
• Setting of attendance fees
• Renewal of delegations and financial authorizations to be granted to the Board of Directors

1.5. Audit committee

The board of directors of the company, in its previous form as a simplified joint-stock company, had established an audit committee. The board of directors of the company, in its new form as a corporation, decided at its meeting of October 24, 2011 to maintain this already-established audit committee.

The audit committee, which is independent from the company's executives, is responsible for assisting the board of directors and ensuring 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 responsible, among others, for:

- monitoring the financial reporting process;
- monitoring the effectiveness of the internal control and risk management systems ;
- monitoring the statutory audit of the annual financial statements and the consolidated financial statements by the statutory auditors;
- making a recommendation concerning the statutory auditors whose appointment is proposed at the shareholders' meeting and reviewing the terms of their compensation;
- monitoring the independence of the statutory auditors;
- reviewing the conditions under which derivatives may be used;
- periodically reviewing the status of significant legal proceedings; and
- in general, providing any advice and making any appropriate recommendations to the board of directors in the above areas.

The audit committee is, if possible, 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 as member 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 filing date of this reference document, the members of the audit committee are:

- Ms. Dominique Takizawa, independent member with financial and accounting expertise, and
- Mr. Olivier Martinez, director.

Ms. Dominique Takizawa chairs this committee.

Ms. Takizawa is the member of the board with "specific financial or accounting expertise," due to her nearly 25 years of experience in the pharmaceutical industry and the executive management positions she held at Sanofi Pasteur, Biomérieux and Institut Mérieux.

Having two members on this committee was deemed sufficient, given the total number of directors of the company. The audit committee's rules of procedure, adopted on October 24, 2011 after approval by the board of directors, specifies the audit committee's roles and responsibilities and its organizational arrangements, including the minimum number of times the committee shall meet each year. It also specifies that the committee may interview any member of the company's board of directors and perform any internal or external audit on any matters it deems to be within its responsibility. The chairman of the audit committee shall so inform the board of directors in advance. In particular, the audit committee has the right to interview those individuals who contribute to the preparation of the financial statements or to the audit thereof (vice-president finance, chief financial officer and key finance department managers). It has the right to direct, independent and confidential consultation with the statutory auditors.

The audit committee met three times in 2015, on January 8, Ferbruary 25, and July 20, 2015.

1.6. Compensation Committee

The board of directors of the company, in its previous form as a simplified joint-stock company, had established a compensation committee. The board of directors of the company, in its new form as a corporation, decided at its meeting of October 24, 2011 to maintain this committee.

The compensation committee is responsible, among others, for:

- reviewing the main objectives suggested by executive management with respect to the compensation of executives of the company who are not corporate officers, including bonus share issues and stock option plans;
- reviewing the compensation of executives who are not corporate officers, including bonus share issues and stock option plans, pension and benefit plans and benefits in kind;
- making recommendations and proposals to the board concerning:
    - compensation, retirement and insurance plans, non-cash benefits, and other financial entitlements, including severance pay, of the members of the board of directors. The committee suggests the amounts and structure of the compensation and, in particular, the rules for determining the variable component, taking into account the company's strategy, objectives and results, as well as market practices, and
    - bonus share plans, stock subscription or purchase options and any other similar profit-sharing program and, in particular benefits granted to specific members of the board of directors,
- reviewing the total amount of directors' fees and how they are allocated among the members of the board of directors, as well as the conditions for reimbursement of any expenses incurred by members of the board of directors,
- preparing and presenting any reports that may be required by the board of directors' rules of procedure, and

- preparing any other compensation-related recommendations that may be requested by the board of directors.

In general, the committee provides any advice and makes any appropriate recommendations in the above areas.

The compensation committee is, if possible, 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 the compensation committee members is concurrent with their term as member of the board of directors.

As of the date of this reference document, the members of the compensation committee are:

- Ms Ekaterina Smirnyagina
- M Laurent Arthaud

In the performance of its duties, the committee may ask the chairman of the board to provide it with assistance from any of the company's senior managers whose expertise may facilitate dealing with a matter of business on the agenda.

The committee has two phone calls on June 23, and December 15, 2015.

1.8. Principles and rules that determine corporate officer compensation

The company has implemented all the MiddleNext Code recommendations regarding the compensation of corporate officers and non-executive directors.

Compensation is presented in detail in chapter 15 of the 2015 reference document.

For fiscal year 2015, the variable component of the compensation of the chief executive officer and vice-president depended on several qualitative objectives relating to oversight of financial management, the development of collaborations, the launch of certain clinical trials, the signature of feasibility contracts and the acceleration of the company's business development.

The board of directors evaluated the extent to which these objectives had been met at its meeting of December 16, 2015 and determined, on the proposal of the compensation committee, the amount of compensation to be awarded for the year.

1.9. Other elements of governance

Provisions relating to attendance at shareholders' meetings are included in Article 19 of the bylaws available on the company's website. Information referred to in Article L. 225-100-3 of the French commercial code that is likely to have an impact in the event of a public offering is detailed in the reference document.

2. Risk management and internal control procedures implemented by the company

When preparing this part of the report, the company followed the implementation guide for the reference framework on internal control adapted for midcaps and small-caps published by the AMF on July 22, 2010.

2.1. General risk management principles

A) Definition

Adocia continues to formalize its risk management system. This system seeks to identify all the risks and risk factors that could affect the company's activities and processes and to define the resources to be used to manage these risks and keep them at or reduce them to an acceptable level for the company. It is intended to cover all types of risks and to apply to all of the company's and the group's activities.

B) Goals of risk management

Adocia has adopted the definition of risk management proposed by the AMF [71], which states that risk management is a management tool of the company that helps:

- create and preserve the company's value, assets and reputation;
- secure decision-making and the company's processes to attain its objectives;
- encourage consistency between the company's actions and its values; and
- ensure that the company's employees have a shared vision of the main risks.

C) Components of the risk management system

The risk factors the company has identified to date are detailed in chapter 4 of the 2015 reference document.

2.2. Coordination of risk management with internal control

Risk management aims to identify and analyze the main risks and risk factors that could affect the company's activities, processes and objectives and define the resources to be used to keep these risks at an acceptable level, in particular by implementing the preventive measures and controls that are part of the internal control system.

At the same time, the internal control system relies on risk management to identify the main risks that need to be controlled. The company has been preparing and developing an internal control system since its founding, while the formalization of the risk management system is more recent. The company is now implementing 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."

2.3. General principles of internal control

A) Definition

Adocia has adopted the definition of internal control proposed by the AMF72, which states that internal control is a system that the company implements in order to ensure:

[71] Implementation guide for the reference framework on internal control adapted for midcaps and small-caps and updated on July 22, 2010

- compliance with laws and regulations;
- implementation of the instructions and directions given by executive management;
- proper functioning of the company's internal processes;
- reliability of financial information; and

in general that contributes to control over its activities, the efficiency of its operations and efficient use of its resources.
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 to the company's activities."

B) Components of internal control and stakeholders

Organization

The internal control system is based on a clear organization of responsibilities, standards, resources and procedures implemented. The company has had a quality assurance system since its founding. The processes for all business segments are described in procedures (*Standard Operating Procedures, or SOPs)*, operating methods, 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.

In 2006, the company also established a scientific advisory board which is responsible for reviewing the company's major scientific directions. It proposes methods and strategies for achieving the company's scientific objectives. It evaluates the work conducted by the company and the results obtained.
The scientific advisory board meets one to two times a year. The work of the company's scientific department is presented at these meetings. Based on the data presented, the board's members make recommendations to the R&D director, Mr. Olivier Soula.

The external members of the scientific advisory board are Mr. Jean-Marie Lehn and Mr. Bernard Cabane.

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, 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

C) 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 evaluate complex accounting items,
- A chartered accountant is asked to verify the half-yearly and annual work, for the individual financial statements and the financial statements presented under IFRS,
- Payroll management is subcontracted to an independent specialized firm,

<u>Oversight of internal control, regular reviews</u>

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 and reconciles the data with the reporting. The aim of these reviews is to ensure that the information for each of the items in the scope fairly reflects the group's activity and position.

The operations committee also reviews the key information for each activity. It meets every three weeks 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 therein. 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 individual financial statements of the companies in the group.

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 founding, executive management has played a leading role in defining and implementing the internal control system and subsequently risk management.

2.4. Limitations on risk management and internal control and areas of improvement

In 2014, the company will continue to implement 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 to reflect changes in its internal organization and its business as well as closer coordination with the risk management process.

The board of directors has approved this report which will be presented to the shareholders' meeting called to approve the financial statements for fiscal year 2015.

3. Representation of men and women on the board of directors

In accordance with Act no. 2011-103 of January 27, 2011 on the balanced representation of men and women on boards of directors and supervisory boards and on gender equality, currently two of the six members of the board of directors are women, Ms. Dominique Takizawa and Ms. Ekaterina Smirnyagina.

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Chairman of the Board of Directors

ODICEO ERNST & YOUNG et Autres

Adocia
Fiscal year ended December 2015

Statutory auditors' report, prepared in accordance with Article L. 225-235 of the French Commercial Code (*Code de commerce*), on the report of the Chairman of the board of directors of Adocia

ODICEO
115, boulevard de Stalingrad
B.P. 52038
69616 Villeurbanne Cedex
Corporation with €275,000 in share capital

Statutory Auditor
Member of the Compagnie
Régionale de Lyon

ERNST & YOUNG et Autres
Tour Oxygène
10-12 boulevard Marius Vivier Merle
69393 Lyon cedex 03
Simplified joint stock company with variable capital

Statutory Auditor
Member of the Compagnie
Régionale de Versailles

Adocia

Fiscal year ended December 31, 2015

Statutory auditors' report, prepared in accordance with Article L. 225-235 of the French Commercial Code (*Code de commerce*), on the report of the chairman of the board of directors of Adocia

Dear Shareholders:

In our capacity as statutory auditors of Adocia and in accordance with the provisions of Article L. 225-235 of the French Commercial Code (*Code de Commerce*), we present to you our report on the report prepared by your company's chairman as provided by Article L. 225-37 of the French Commercial Code for the fiscal year ended December 31, 2015.

It is the chairman's responsibility to prepare and submit to the board of directors for approval a report that describes the internal control and risk management procedures implemented at the company and provides the other information required by Article L. 225-37 of the French Commercial Code related, in particular, to the corporate governance scheme.

It is our responsibility:

- to give you our observations based on the information contained in the chairman's report regarding the internal control and risk management procedures related to the preparation and treatment of accounting and financial information, and

- to certify that this report contains the other information required by Article L. 225-37 of the French Commercial Code, it being understood that it is not our responsibility to verify the fairness of this information.

We have performed our work in accordance with the accounting standards applicable in France.

Information regarding the internal control and risk management procedures related to the preparation and treatment of accounting and financial information

The accounting standards require that we follow certain procedures to assess the fairness of the information regarding the internal control and risk management procedures related to the preparation and treatment of accounting and financial information contained in the chairman's report. These procedures entail:

- reviewing the internal control and risk management procedures related to the preparation and treatment of accounting and financial information that forms the basis of the information provided in the chairman's report and the existing documentation;

- reviewing the work involved in preparing this information and the existing documentation;

- determining whether any major weaknesses in internal control related to the preparation and treatment of accounting and financial information identified by us in the course of our audit have been properly disclosed in the chairman's report.

Based on this work, we have no observation regarding the information about the company's internal control and risk management procedures related to the preparation and treatment of accounting and financial information contained in the chairman of the board of directors' report, which was prepared in accordance with the provisions of Article L. 225-37 of the French Commercial Code.

Other Information

We certify that the chairman of the board of directors' report contains the other information required by Article L. 225-37 of the French Commercial Code.

Villeurbanne and Lyon, April 7, 2016

The Statutory Auditors

ODICEO	ERNST & YOUNG et Autres
Sylvain Boccon-Gibod	Sylvain Lauria

APPENDIX III – INDEPENDENT VERIFIER'S REPORT ON CONSOLIDATED SOCIAL, ENVIRONMENTAL AND SOCIETAL INFORMATION PRESENTED IN THE MANAGEMENT REPORT.

Adocia

Year ended the 31 December 2015

Independent verifier's report on social, environmental and societal information presented in the management report

ERNST & YOUNG et Associés

Adocia

Year ended the December 31, 2015

Independent verifier's report on social, environmental and societal information presented in the management report

To the shareholders,

In our quality as an independent verifier accredited by the COFRAC5, under the number n° 3-1050, and as a member of the network of one of the statutory auditors of the company Adocia, we present our report on the social, environmental and societal information established for the year ended on the 31 December 2014, presented in chapters 8.3, 8.4 and 17.7 of the management report, hereafter referred to as the "CSR Information," pursuant to the provisions of the article L.225-102-1 of the French Commercial code (*Code de commerce*).

Responsibility of the company

It is the responsibility of the Board of Directors to establish a management report including CSR Information referred to in the article R. 225-105 of the French Commercial code (*Code de commerce*), in accordance with the protocols used by the company (hereafter referred to as the "Criteria"), and available on request at the company's headquarters.

Independence and quality control

Our independence is defined by regulatory requirements, the Code of Ethics of our profession as well as the provisions in the article L. 822-11 of the French Commercial code (*Code de commerce*). In addition, we have implemented a quality control system, including documented policies and procedures to ensure compliance with ethical standards, professional standards and applicable laws and regulations.

Responsibility of the independent verifier

It is our role, based on our work:

- to attest whether the required CSR Information is present in the management report or, in the case of its omission, that an appropriate explanation has been provided, in accordance with the third paragraph of R. 225-105 of the French Commercial code (*Code de commerce*) (Attestation of presence of CSR Information);

- to express a limited assurance conclusion, that the CSR Information, overall, is fairly presented, in all material aspects, in according with the Criteria;

Our verification work was undertaken by a team of four people between February 2015 and March 2015 for an estimated duration of three weeks.

We conducted the work described below in accordance with the professional standards applicable in France and the Order of 13 May 2013 determining the conditions under which an independent third-party verifier conducts its mission, and in relation to the opinion of fairness, in accordance with the international standard ISAE 3000[6].

1. Attestation of presence of CSR Information

5 Scope available at www.cofrac.fr

6 ISAE 3000 – *Assurance engagements other than audits or reviews of historical information*

We obtained an understanding of the company's CSR issues, based on interviews with the management of relevant departments, a presentation of the company's strategy on sustainable development based on the social and environmental consequences linked to the activities of the company and its societal commitments, as well as, where appropriate, resulting actions or programmes.

We have compared the information presented in the management report with the list as provided for in the Article R. 225-105-1 of the French Commercial code *(Code de commerce).*

In the absence of certain information, we have verified that the explanations were provided in accordance with the provisions in Article R. 225-105-1, paragraph 3, of the French Commercial code *(Code de commerce).*

Based on this work, we confirm the presence in the management report of the required CSR information.

2. Limited assurance on CSR Information

Nature and scope of the work

We undertook three interviews with five people responsible for the preparation of the CSR Information in the financial, human resources and health & safety departments, in charge of the data collection process and, if applicable, the people responsible for internal control processes and risk management, in order to:

- Assess the suitability of the Criteria for reporting, in relation to their relevance, completeness, reliability, neutrality, and understandability, taking into consideration, if relevant, industry standards;

- Verify the implementation of the process for the collection, compilation, processing and control for completeness and consistency of the CSR Information and identify the procedures for internal control and risk management related to the preparation of the CSR Information.

We determined the nature and extent of our tests and inspections based on the nature and importance of the CSR Information, in relation to the characteristics of the Company, its social and environmental issues, its strategy in relation to sustainable development and industry best practices.

For the CSR Information which we considered the most important[7] at the level of the entity, we consulted documentary sources and conducted interviews to corroborate the qualitative information (organisation, policies, actions, etc.), we implemented analytical procedures on the quantitative information and verified, on a test basis, the calculations and the compilation of the information, and also verified their coherence and consistency with the other information presented in the management report.

For the other CSR informations, we assessed their consistency in relation to our knowledge of the company.

Finally, we assessed the relevance of the explanations provided, if appropriate, in the partial or total absence of certain information.

7 **Environmental and societal information**: pollution and waste management (preventative measures, recycling and waste management), sustainable use of resources and climate change (energy consumption, measures undertaken to improve energy efficiency and to promote the use of renewable energy), measures undertaken in favour of consumers' health and safety).

Social information: employment (total headcount and breakdown, hiring and terminations), work accidents, notably their frequency and their severity, as well as occupational diseases, training policies, number of days of training.

We consider that the sample methods and sizes of the samples that we considered by exercising our professional judgment allow us to express a limited assurance conclusion; an assurance of a higher level would have required more extensive verification work. Due to the necessary use of sampling techniques and other limitations inherent in the functioning of any information and internal control system, the risk of non-detection of a significant anomaly in the CSR Information cannot be entirely eliminated.

Conclusion

Based on our work, we have not identified any significant misstatement that causes us to believe that the CSR Information, taken together, has not been fairly presented, in compliance with the Criteria.

Paris-La Défense, the March 15, 2016

Independent Verifier

ERNST & YOUNG et Associés

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