

# THE ORPHAN ONCOLOGY INNOVATOR

A *société anonyme* (limited liability company) with a share capital of 11,760,851 Euros Registered Office: 49, boulevard du général Martial Valin – 75015 Paris 410 910 095 R.C.S. Paris

# 2016 REGISTRATION DOCUMENT

# INCLUDING THE ANNUAL FINANCIAL REPORT AND THE MANAGEMENT REPORT



This document was submitted to the Autorité des Marchés Financiers (AMF) on 24 April, 2017 in accordance with Article 212-13 of its General Regulations. It may be used in connection with a financial transaction only if it is accompanied by a memorandum duly approved by the AMF. This document has been prepared by the issuer under the responsibility of its signatories.

Copies of this Registration Document are available free of charge at Onxeo's registered office located at 49, Boulevard du Général Martial Valin – 75015 Paris, France, on Onxeo's website: <a href="www.onxeo.com">www.onxeo.com</a> and on the website of the Autorité des marchés financiers: <a href="www.amf-france.org">www.amf-france.org</a>.



#### **IMPORTANT NOTICE**

This document is a free translation (the "Translation") of Onxeo's "Document de Référence 2016", dated 24 April, 2017.

This Translation is provided for convenience only.

IN THE EVENT OF ANY AMBIGUITY OR CONFLICT BETWEEN THE STATEMENTS OR OTHER ITEMS CONTAINED HEREIN AND THE CORRESPONDING STATEMENTS IN THE FRENCH LANGUAGE "DOCUMENT DE REFERENCE 2016", THE "DOCUMENT DE REFERENCE 2016" SHALL PREVAIL.

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#### Note

In this Registration Document, unless it is provided otherwise:

- The term "Registration Document" means this Registration Document;
- The terms "Company" or "Onxeo" mean the company Onxeo whose registered office is situated at 49, boulevard du Général Martial Valin, 75015 Paris, France, registered with the Paris trade and companies register under number 410 910 095;
- The term "Group" means the group consisting of the Company and its subsidiaries.

A glossary defining certain terms used in the Registration Document is set forth in Chapter 12.

#### Disclaimer

# Market and competition information

The Registration Document contains, in particular in chapter 2 "Company activity in 2016", information relating to the Group's markets and its competitive position. This information derives, in particular, from studies conducted by external sources. The publicly available information which the Company believes to be reliable has not been verified by an independent expert, and the Company cannot guarantee that a third party using different methods to collect, analyze or compute data on these markets would obtain the same results.

#### Forward-looking information

The Registration Document contains information on the Group's prospects and development strategies. This information is sometimes identified by the use of the future or the conditional tense or forward-looking terms such as "consider", "envisage", "think", "aim to", "expect", "intend", "should", "aspire to", "estimate", "believe", "wish", "could", "promising", "encouraging", "interesting" or, where appropriate, the negative of the terms thereof or any other similar variation or terminology. This information is not historical data and should not be interpreted as a guarantee that the facts and data set out herein will occur. This information is based on data, assumptions and estimates considered as reasonable by the Company. It is subject to change or is likely to be modified due to uncertainties related, in particular, to the economic, financial, competitive, and regulatory environment. This information is mentioned in various chapters of the Registration Document and contains data relating to the Group's intentions, estimates and objectives, in particular regarding the market in which it operates, its strategy, its growth, its results, its financial position, its cash flow and its forecasts. The forwardlooking information contained in the Registration Document is provided only as of the date of the Registration Document. The Group operates in a constantly changing and competitive environment. It is therefore unable to anticipate all the risks, uncertainties or other factors that may affect its business, their potential impact on its business or the extent to which the occurrence of a risk or a combination of risks could have significantly different results from those stated in any forward-looking information, it being reminded that none of this forward-looking information constitutes a guarantee of actual results.

#### Risk factors

Investors are encouraged to carefully read the risk factors described in section 5.5.1.4 "Risk Factors" of the Registration Document before making any investment decision. The occurrence of some or all of these risks may have a material adverse effect on the Group's business, financial position, results or prospects. In addition, other risks, not yet identified or deemed immaterial by the Company at the date of registration of the Registration Document, could also have a material adverse effect.



# ESSENTIAL INFORMATION ABOUT THE GROUP

# 1.1 PROFILE AND STRATEGY

Onxeo is a clinical-stage biotechnology company specializing in the development of innovative drugs for the treatment of orphan diseases, in particular in oncology, driven by high therapeutic demand in one of the fastest growing segments of the pharmaceutical industry.

The Group's objective is to become a major international player in the field of rare cancers. The Group's growth strategy is founded on the development of innovative drugs based on breakthrough technologies that can make a real difference in the treatment of orphan oncology diseases and considerably improve the quality of life of patients affected by rare and aggressive cancers.

Deployment of this strategy includes notably external growth (M&A) to accelerate development and extend the Group's product portfolio and growth. In 2014, the Group acquired Topotarget, a Danish biopharmaceutical company based in Copenhagen, specializing in the development of oncology products and developer of Beleodaq®, a pan-HDAC inhibitor.

In 2016, the Group acquired DNA Therapeutics and through it, a new drug class derived from the revolutionary technology of DNA repair inhibition in cancerous cells.

The acquisition of this new "first-in-class" product named AsiDNA reinforces the Group's product portfolio, positioning the Group at the forefront of scientific and clinical progress in oncology, DNA repair, thus increasing its scientific renown and, ultimately, its attractiveness on the international market.

The Group's strategy is built on solid assets and distinctive expertise that form the foundation for the Group's future growth:

- A unique biotechnology company profile with a large and diversified product pipeline composed of products developed from extremely promising and diversified technologies, with a balanced distribution between products on the market generating revenue and those in advanced clinical programs and preclinical studies.
   Used as a single-agent therapy or in combination with other anticancer drugs, these programs offer prospects of clinical development for several indications;
- A highly experienced European team of scientists, divided between Paris and Copenhagen, which has repeatedly led programs in Europe and the United States through to the approval stage. The teams are led by a management team and a high-profile Board of Directors with international experience;
- With its international scope and clinical studies conducted in Europe and the United States, it has commercial partners respected throughout the pharmaceutical industry as well as links with the leading academic and scientific opinion-formers in Europe and the United States.

To support the development and marketing of its products, the Group has opted for a selective partnership strategy via co-development agreements for its products in the clinical phase or via licensing agreements for its registered products.

The Group's orphan oncology product portfolio comprises 3 products (Livatag®, Beleodaq®, and AsiDNA™), ranging from preclinical to advanced phases of clinical development, as detailed in the graph below:





Detailed information on these two portfolios can be found in Section 4.2.1 of this Registration Document.

# 1.2 MANAGEMENT AND CONTROL BODIES

# 1.2.1 BOARD OF DIRECTORS

Joseph Zakrzewski Chairman of the Board of Directors and independent Director

Judith Greciet

Chief Executive Officer

Independent Directors:

Russell Greig

Danièle Guyot-Caparros

Thomas Hofstaetter

David H. Solomon

Jean-Pierre Kinet

Jean-Pierre Bizzari

Director, major shareholder representative:

Financière de la Montagne, represented by Mr. Nicolas Trebouta

# 1.2.2 MANAGEMENT COMMITTEES

#### **Executive Committee**

Through the leadership of Judith Greciet, Chief Executive Officer, the Executive Committee prepares the Company's strategy, its major policies and growth scenarios. It takes all decisions pertaining to strategy, defines priorities, and allocate resources, in relations with the Company Board of Directors. It reviews and validates



development plans and oversees their implementation. It reviews all strategic decisions impacting projects and timelines, and validates all strategic and/or financial decisions based on recommendations of the Operations Committee, with a specific focus on critical issues and risks. It also defines the Company's HR policy. It meets once a week to ensure that the Company is being managed in a collective and cross-functional manner.

#### **Operations Committee**

Composed of the operational R&D departments, the Project Coordinator and ad hoc project team members, it sets the operating strategy, systematically reviews and validates the progress of projects, and coordinates the teams. It takes all operational decisions on specific projects and prepares recommendations for the Executive Committee. A specific emphasis is given to adhering to corporate goals and respecting projects' timelines. The committee meets once a week.

# **Risk Management Committee**

This committee updates the Company's risk mapping and monitors action plans with the departments concerned.

# 1.2.3 STATUTORY AUDITORS

#### **Grant Thornton**

French member of Grant Thornton International 29 rue du Pont 92200 Neuilly / Seine

Represented by Mr. Samuel Clochard, a member of the Regional Association of statutory auditors of Versailles.

# **Ernst & Young Audit**

Tour Ernst & Young, Faubourg de l'Arche, 1/2 place des Saisons, 92400 Courbevoie

Represented by Mr. Frank Sebag a member of the Regional Association of statutory auditors of Versailles.

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# 1.3 KEY FIGURES

The table below presents selected financial data extracted from the Company's consolidated financial statements prepared under IFRS for the years ended 31 December 2015 and 31 December 2016.

Notes on the key figures are found in Section 3 of this Registration Document and should be read in relations with Section 6 of this Registration Document.

Consolidated Accounts (IFRS) In thousands of Euros.	31/12/2016	31/12/2015
Net Sales, of which	4 423	3 481
Recurring sales	3 454	<i>2 733</i>
Non-recurring sales	969	749
Operating Expenses, of which	(27 591)	(25 657)
R&D Expenditures	(18 075)	(16 350)
Research tax credit	3 955	<i>3 718</i>
Other Expenses	(13 471)	(13 025)
<b>Current Operating Income</b>	(23 168)	(22 365)
Non-Current Operating Income	(43)	(189)
Financial Income	1 106	602
Taxes	(566)	2 353
Net Income	(22 671)	(19 409)
Net Cash	29 243	33 793



# COMPANY ACTIVITY IN 2016

# 2.1 SIGNIFICANT EVENTS IN 2016

#### 2.1.1 GROUP COMPANIES DU GROUPE

As of the date of the Registration Document, the Group is comprised of the Company, which concentrates the majority of its business in Paris and at its Danish establishment in Copenhagen, and its subsidiaries, most of which have limited activity:

- Onxeo US, newly established in 2016;
- Topotarget UK;
- BioAlliance Pharma Switzerland;
- Topotarget Switzerland;
- SpeBio

During FY 2016, BioAlliance Pharma and DNA Therapeutics both had their assets transferred 100% to Onxeo, and were indeed dissolved. Furthermore, Topotarget Germany, a non-active 100% subsidiary of Onxeo SA, was liquidated in 2016.



#### 2.1.2 CHANGES IN ACTIVITY AND SIGNIFICANT EVENTS DURING THE FINANCIAL YEAR

Onxeo's objective is to become a major international player in the field of orphan and rare cancers. The Company's strong assets and distinctive expertise form the foundation of its future growth:

- A diversified portfolio of products in clinical development with three independent but synergistic programs
   Livatag®, Beleodaq®, and AsiDNA™¹ dedicated to cancer pathologies for which medical needs are important;
- Innovative therapeutic approaches, founded on technologies and differentiated mechanisms of action, with strong competitive advantages that can be available in multiple types of cancer;
- Programs that target significant and growing medical indications, with an estimated global market potential of several billion dollars;
- A skilled team of high-level scientists, working in Paris and Copenhagen, repeatedly leading programs in Europe and the United States through to the approval stage;
- An anchor in the United States with a subsidiary and three products sold by international partners;
- An experienced management team, backed by a high quality international Board of Directors.

The Company's growth strategy relies on the development of innovative drugs, based on unique action mechanisms and breakthrough technologies that make a difference in the treatment of cancer, in particular rare cancers or those resistant to other treatments. In 2016, the Group's three flagship programs, AsiDNA™, Livatag®, and Beleodaq®, advanced significantly.

The primary operational advances and organizational changes of the Group during the financial year are set out below.

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<sup>&</sup>lt;sup>1</sup> AsiDNA™, Livatag®, and Beleodaq® are registered trademarks of Onxeo SA



# 2.1.2.1 R&D Programs

# 2.1.2.1.1 Livatag®

During 2016, the Company accelerated recruitment in the Phase III trial of "ReLive" to assess the efficacy of Livatag, its most clinically advanced product in the 2nd line treatment of advanced hepatocellular carcinoma. ReLive is an international multicenter randomized study assessing the intravenous efficacy of Livatag (Doxorubicin Transdrug™) compared to the available standard of care chosen by physicians for patients with advanced hepatocellular carcinoma (primary liver cancer) after failure or intolerance to sorafenib.

In parallel, the independent follow-up study committee - the Data Safety and Monitoring Board (DSMB) who reviews the study's safety data, met twice in 2016 issuing on each occasion a recommendation of further study without modification.

In addition, the Company introduced at the annual conference of the American Association for Cancer Research (AACR) the results of a study on Livatag's active mechanism that shows a preferential affinity for the liver, confirming its potential in advanced hepatocellular carcinoma.

The Company, in 2016, actively continued its development program in other indications for this asset and/or in combination with other agents. In particular, it announced encouraging preclinical results for Livatag in combination with new immuno-oncology agents of different classes such as checkpoint inhibitors PD-1 and CTLA-4, as well as monotherapy in pancreatic cancer.

To carry out this new preclinical activity, in 2016 Onxeo began collaborating with recognized institutions such as the immunology research program of the Center for Applied Medical Research (CIMA) and the Liver Unit of the Navarre University Clinic in Spain, in addition to other collaborations already in place in France and Germany.

# 2.1.2.1.2 Beleodag® (intravenous belinostat)

As with Livatag, belinostat has been undergoing a program to develop its clinical potential, in particular in combination with immune checkpoint Inhibitors. In 2016, the Company announced preclinical study results for belinostat in combination with immuno-oncology agents revealing that this association could be an appropriate treatment option.

Beyond the peripheral T-cell lymphoma (PTCL) for which Beleodaq is already approved in the US, the Company aims to evaluate other potential tumor indications for Beleodaq in combinations, in order to further the potential of its drug.

In parallel, the Company announced in 2016 the development of an oral formulation for belinostat, which up to now was provided intravenously (IV). Such a formulation would be a clear benefit for patients and physicians alike in terms of ease of administration, compliance, and lack of assistance from medical personnel. It would also enable Onxeo the possibility of extending its patent protection for belinostat and increase interest in developing the product with other drugs for new indications.

Finally, in 2016, the Company continued the geographic expansion of Beleodaq for its PTCL indication by signing an exclusive licensing agreement with Pint Pharma to market Beleodaq (belinostat) in the field of T cell peripheral lymphoma in several key countries in South America.

Pint Pharma will handle the registration, marketing, and promotion of Beleodaq in seven countries: Argentina, Brazil, Chile, Colombia, Ecuador, Peru, and Venezuela.

In addition to an initial payment upon signature, the agreement includes payments based on regulatory and revenue milestones, as well as royalties on net sales of Beleodaq®, for a total value greater than \$20 million.

#### 2.1.2.1.3 AsiDNA™

On 25 March 2016, the Group announced the completion of the DNA Therapeutics acquisition for an initial amount €1.7 million in common shares of Onxeo, thus obtaining innovative technology on the DNA repair mechanisms of tumor cells (siDNA).



Additional milestone payments will be made, namely €1 million in shares or cash at Onxeo's discretion, if the product enters Phase II in a selected indication. Also anticipated is the payment of royalties on sales if the product goes to market, worth up to €25 million per indication.

This acquisition strengthens the Group's portfolio of orphan oncology products and positions the Company in the new field of DNA repair at the forefront of scientific and clinical oncology research. Indeed, the technology developed by DNA Therapeutics interferes with the DNA repair process of tumor cells.

It acts in advance of multiple DNA repair pathways detecting and signaling damage, and thus breaks the DNA repair cycle of the tumor cells, without negatively affecting the healthy cells.

A first-in-class product originating from this new class of drugs, formerly known as DT01, and today referred to as AsiDNA, has already demonstrated its good tolerability profile and intratumoral and peritumoral safety in combination with radiotherapy in a Phase I / IIa in patients with metastatic melanoma. This clinical trial has shown promising results in treated patients, thus evidencing AsiDNA's potential for the future.

The Group systemically pursues the development of this drug as a single therapy or in combination with other treatments in various types of solid tumors and has identified several key steps:

- Optimization of the product manufacturing process begun in 2016 in order to improve costs and production lead times for future clinical development and ultimate large-scale industrialization;
- Preclinical studies in order to better define the pharmacokinetic / pharmacodynamic profile following intravenous infusion (IV) and determine the most relevant indications;
- Research of biomarkers that would help identify the best indications for AsiDNA, alone or in combination with other treatments.

Based on these elements, the start of a Phase I clinical study through systemic administration is expected by the end of 2017.

In July 2016, the Company also received notification of the issuance by the US Patent Office of a key patent on AsiDNA, extending its protection to 2031 in the United States.

The Group is convinced of the significant therapeutic potential of this technology of signal interference to the DNA tumor repair and the innovation that such a potential new cancer treatment paradigm represents.

AsiDNA is the frontrunner of a therapeutic class which could be applied to a broad spectrum of indications that the Group could develop alone or in partnership. AsiDNA™ thus has the potential to generate in the short and long term many catalysts of growth and value creation for the Company and its shareholders.

# 2.1.2.2 Other products dedicated to partnerships<sup>2</sup>

After positive results at the end of 2015 on the Phase II study of Validive® in the prevention of severe oral mucositis induced by radiotherapy and/or chemotherapy in patients with ENT cancer, US regulatory authorities indicated that conducting two Phase III studies was necessary to obtain an eventual approval in the United States. Given the delays and additional development costs that such a program would represent, the Company made the strategic choice not to pursue Validive® development alone, but rather seek a partner to do so.

During 2016, Onxeo continued the international development of its non-strategic products Sitavig® and Loramyc®/Oravig® through partnership agreements.

# 2.1.2.3 Corporate Governance

# 2.1.2.3.1 Developing and strengthening the Board of Directors

In January 2016, the Company announced the development and reinforcement of its Board of Directors with the arrival as permanent guests of Doctor Jean-Pierre Kinet, a professor at the Harvard Medical School, and

<sup>&</sup>lt;sup>2</sup> Validive, Lauriad, Sitavig, Loramyc et Oravig sont des marques déposées d'Onxeo.



Doctor Jean-Pierre Bizzari, an international expert in the field of oncology. Their appointment as Directors received shareholder approval at the Onxeo General Meeting of April 6, 2016.

These two experts are prominent members of many academic and industrial networks in the United States and Europe, and enhance the current level of the Board's expertise particularly in terms of research and development of innovative compounds.

In addition, Mr. Joseph Zakrzewski was appointed Chairman of the Board of Onxeo as announced in October 2015, replacing Patrick Langlois who resigned. Mr. Joseph Zakrzewski joined Onxeo's Board of Directors as a permanent guest in October 2015. His appointment as Director and Chairman of the Board of Directors was confirmed by the General Meeting of April 6, 2016.

Mr. Zakrzewski has worked over 25 years in the health industry at the global level, particularly in the United States. In particular, he held several management positions with US biotech companies, as well as in the area of venture capital.

# 2.1.2.3.2 Creation of a US subsidiary

The Group announced in March 2016 the opening of an American subsidiary in New York - Onxeo US Inc., marking a new stage in the implementation of its US strategy.

Mr. Philippe Maitre heads the subsidiary as Executive Vice President & Chief of US Operations. Philippe Maitre has over 35 years of experience in the pharmaceutical and biotechnology industries, including over 15 years in U.S. listed and unlisted companies.

# 2.1.2.4 Financing

At the end of September 2016, the Company announced a capital increase through the issuance of new common shares without preferential subscription rights. Pursuant to Article L.225 - 138 of the Commercial Code, this capital increase was reserved for a category of investors defined in the 17th Resolution adopted by the Company's General Meeting of April 6, 2016, namely: "companies and investment funds investing on a regular basis in small-cap growth companies, i.e. their market capitalization does not exceed €1 billion, including, without limitation, all private equity venture capital funds working in the area of health or biotechnology and participating in the capital increase for a unit amount of over €100,000 including premium, within the limit of a maximum of 25 subscribers."

Leading American and European institutional investors, and health and biotechnology sector specialists participated in the raise, thereby strengthening and diversifying the shareholder structure of the Company.

This capital increase resulted in the issuance of 5,434,783 new common shares on September 30, 2016 for an amount of €12.5 million.

The money raised strengthened the Group's cash position, which amounted to €34.9 million at the end of the settlement and delivery of the new shares. The funds raised provide additional means to continue R&D programs in the field of orphan diseases in oncology, and will be used to specifically finance:

- The completion of the Phase III for ReLive of Livatag as well as pre-clinical studies in combination with this product;
- The early stages of the development of AsiDNA, including aspects of production and systemic efficacy evaluation;
- Future developments of Beleodaq® including the PTCL indication on the front line, and
- More generally the business activity of the Company.



# 2.1.2.5 TIMELINE SUMMARY OF SIGNIFICANT EVENTS IN FY 2016

January 25	Onxeo announces the development and strengthening of its Board of Directors
February 22	Onxeo announces a new collaboration to accelerate the development of its flagship orphan
	programs in combination with immuno-oncology products
February 26	Results reported for fiscal 2015 and business update
February 29	Onxeo announces the acquisition of DNA Therapeutics and provides an update on the clinical development of Validive®
March 16	Presentation of a poster showing the unique mechanism of action of Livatag® at the annual conference of the American Association for Cancer Research (AACR)
March 21	Onxeo announces the creation of a subsidiary in New York
March 35	Onxeo announces final completion of the DNA Therapeutics acquisition
April 4	Onxeo announces a new positive recommendation by the Data Safety and Monitoring Board (DSMB) to continue the study on "ReLive" of Livatag® for primary liver cancer
April 18	Results of a study on the mechanism of action of Livatag® show a preferential affinity for the liver, confirming its potential in advanced hepatocellular carcinoma.
June 2	Onxeo announces the development of a new histone deacetylase inhibitor (HDACi) formulation by oral delivery for Beleodag®
June 27	Onxeo announced the development plan for AsiDNA, its first-in-class product from DNA technology.
July 4	Onxeo announces receiving notification of the issuance by the US Patent Office of a key patent on AsiDNA™, extending its protection through to 2031 in the United States.
July 7	Onxeo announced a collaboration with the Royal College of Surgeons in Ireland for a research program on Beleodaq® derivatives.
July 27	Onxeo signed an exclusive license agreement with Pint Pharma for the marketing of Beleodaq® in South America in the field of PTCL.
July 28	Onxeo reviewed it business developments in the 1st half of 2016 and released its financial results.
September 7	AsiDNA showed a synergistic effect in combination with PARP inhibitors, without restrictions related to the tumor's genetic profile.
September 7	Onxeo presents at the Rodman & Renshaw 18th Annual Global Investment Conference in New York.
September 12	Onxeo announces the initial results of the preclinical program of Livatag®.
September 29	Onxeo launches a capital increase.
September 30	Onxeo raises €12.5 million from American and European investors.
October 27	Onxeo announces promising preclinical program results for Beleodaq® in combination with control point inhibitors.
November 4	Onxeo announces promising preclinical results for Livatag® in pancreatic cancer.
November 21	Onxeo announces the 9th positive recommendation by the DSMB to continue the Phase III study on "ReLive" of Livatag® for primary liver cancer.
December 8	The Academy of Sciences bestows the Guy Lazorthes Award to Doctor Marie Dutreix for her innovative work on Dbait technology.

The full text of these press releases can be accessed on the Company website (www.onxeo.com).

# 2.2 IMPORTANT EVENTS SINCE THE CLOSING OF THE ACCOUNTS

January 24, 2017, the Company announced finalizing the recruitment of 390 patients for the ReLive study to evaluate the efficacy of Livatag in the treatment of hepatocellular carcinoma and confirmed its forecast for the availability of initial efficacy results by mid-2017.



On January 31, 2017, in a joint statement with the Curie Institute, the Company announced a partnership to study the interest of combining radiotherapy with AsiDNA, an inhibitor of DNA tumor repair, and immunotherapy in the treatment of cancer.

On February 13, 2017, the Company announced that it was notified by the US Patent and Trademark Office of obtaining a new patent covering the broad claims on AsiDNA and similar molecules.

On March 1, 2017, the Company announced that it has appointed two seasoned executives to lead its preclinical and clinical operations, namely Mrs. Françoise Bono as chief scientific officer and Mr. Olivier de Beaumont as chief medical officer.

# 2.3 FORESEEABLE DEVELOPMENTS AND FUTURE PROSPECTS

The Company will continue in 2017 its value creation strategy based on developing innovative therapeutics for severe and rare diseases, cancer in particular, and is planning on the following major catalysts for growth:

- Livatag<sup>®</sup> (doxorubicine Transdrug)
  - Preliminary efficacy results in the Phase III study of ReLive by mid-2017;
  - Results of preclinical studies on Livatag® to assess the product's potential in new indications.
- Beleodaq® (belinostat)
  - Alongside the American partner, Spectrum Pharmaceuticals, the Company prepares to extend the indication for the 1st line treatment of PTCL;
  - Development of a new oral delivery formulation by the Company and an assessment of the interest in associating Beleodaq with other anti-cancer agents, including immuno-oncology agents in tumors other than PTCL.

# AsiDNA™

- In-vitro proof of concept by systemic delivery (intravenous);
- Assessment of the interest in associating AsiDNA with different anti-cancer agents on various types of tumors in animals and optimal dosing schedules;
- Regulatory toxicity studies prior to the intravenous and repeated administration to humans;
- Implementation of a clinical study by systemic delivery to demonstrate the activity of AsiDNA through systemic delivery.

Onxeo considers that, in light of its current activities, it has no specific comments to make on trends that might affect its recurring revenue and its general operating conditions since the date of the last financial year ending December 31, 2016, up to the publication date of this report.

The Company's main investments will focus on research and development. With a cash position of €29,243,000 at December 31, 2016, the Company has sufficient visibility to carry out its projects through early 2018 and is reviewing the opportunity to put in place new financing, either non-dilutive or by calling on the market, in parallel of its ongoing search for new licensing agreements.

# 2.4 SOCIAL AND ENVIRONMENTAL INFORMATION

In accordance with the provisions of Article L. 225-102-1, R. 225-104, and R. 225-105 of the French Commercial Code, the Registration Document includes information relating to our awareness of the social, environmental, and societal impact of the Company's activities - the "Social and Environmental Responsibility Report".

The information contained in this Social and Environmental Responsibility (SER) Report by Onxeo has been established based on internal contributions from the Human Resource Department and the Quality Department. Activities are coordinated by the Executive Management. The list of indicators was defined in accordance with the French ministerial decree relating to SER matters.

The information published reflects the Company's desire for transparency and its wish to objectively describe its most relevant historic and newly-engaged activities that reflect its commitment to Social and Environmental Responsibility (SER). The process for collecting SER information and indicators will be reviewed and optimized each year.

The company has taken into account the following elements of the aforementioned Decree that are judged to be both relevant and significant in terms of its core business and its current and future challenges:



- Social information: employment, work organization, social relations, health & safety, and training. Societal information: relations with stakeholders.
- Environmental information: pollution and waste management.
- Accordingly, the following sections of the SER Decree of April 24, 2012, are excluded due to a lack of relevance or the information was judged to be insignificant in view of scale or effect:
- Release of greenhouse gases, adapting to climate change: the Group's activities are not subject to the issues raised by greenhouse gases and its sites are not located in areas subject to major climatic constraints.
- Biodiversity: the Group is not directly affected by biodiversity protection issues as the risks associated with raw material used are limited. By way of example, according to tests performed, both Loramyc® and Sitavig® present no risk to the environment due to their patient applications.
- Sustainable use of resources, energy consumption, measures taken to improve energy efficiency and the use of renewables, water consumption and supply based on local constraints: as these products are outsourced, and the Group does not have an industrial site, the impact on these issues is related to the activity of two laboratories and R&D offices and is thus limited.
- Land use: the Group's activities do not have any particular impact in terms of land use.
- Visual and noise impact of the Company's activity on the environment: the impact is limited, as the Group's business causes no visual or sound nuisance. Moreover, R&D activity is strictly supervised to ensure that there are no emissions of aqueous or gaseous waste from dangerous products (see section on Pollution and Waste Management).
- Local, economic, and social impact: Due to the Group's size and limited workforce, the impact in terms of employment and regional development, as well as on neighboring and local populations, is not significant.

**The period covered** by the data collated is the calendar year 2016. In order to provide supplementary data about the development of the activities of the Group, data for 2015 is also presented.

**The scope of consolidation** includes the company Onxeo and its subsidiaries within the meaning of Article L.233-3 of the French Commercial Code.

#### 2.4.1 SOCIAL INFORMATION

With the exception of section 2.4.1.1.5 below relating to the Company's secondary establishment located in Denmark that has four employees as of December 31, 2016, the social information listed here only covers Onxeo's principal place of business located in France; the subsidiaries of the Company have no salaried employees. DNA Therapeutics' employees are recorded among the staff of the Company on 12/31/2016; the absorption of the subsidiary DNA Therapeutics was carried out on 1/11/2016. Onxeo's American establishment, having one employee on December 31, 2016, is not included in the figures below.

#### 2.4.1.1 Employment and remuneration

### 2.4.1.1.1 Human Resources Policies

The Group's human resource policy endeavors to support and accompany its momentum and strategy. By its actions, the Human Resource Department aims at creating the necessary conditions:

- For improving individual and collective performance;
- For employee development by providing access to training;
- And to promote a culture of managerial excellence.

The Group meets all legal requirements for information and consultation of the social partners and maintains a concerted permanent dialogue with them.

The Group's employment policy is based on objective criteria and individual merit. Professional equality is thus granted to employees without distinction of race, color, religion, sex, handicap, family status, sexual orientation, age and national or ethnic origin.

# 2.4.1.1.2 Total headcount of the Company at 31 December 2016

On December 31, 2016, the total number of employees came to 52 salaried employees and 1 corporate executive officer, 51.1 full-time equivalents (46.1 permanent, 3 fixed-term, and 2 trainees). This includes



in full-time equivalents 40.1 managers and 11 other employees including 2 trainees. Onxeo's other subsidiaries do not have any employees.

# Employee breakdown by gender, age, and geographical area on December 31, 2016

The table below details the distribution within the Group between men and women as of December 31, 2016 by category:

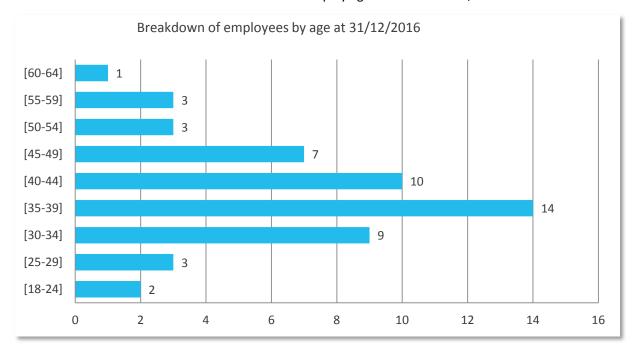
Type of contract:	Women	Men	Total
Fixed term	3	0	3
Permanent	31	16	47
Trainee	2	0	2
Total	36	16	52

CSP:	Women	Men	Total
Managers	27	14	41
Non-managers	7	2	9
Trainees	2	0	2
Total	36	16	52

# Breakdown of the workforce by age, men and women combined, on December 31, 2016

On December 31, 2016, the average age was 40, 39 for women and 42 for men.

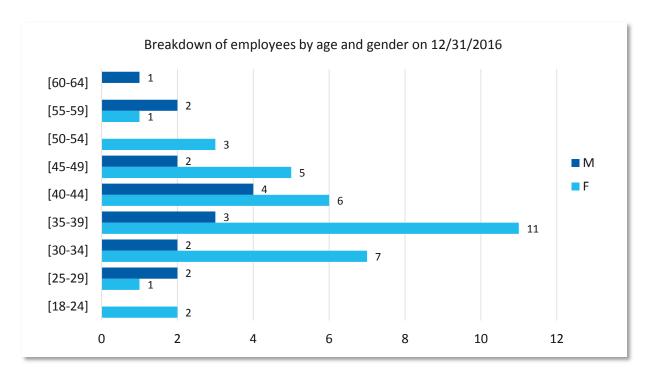
The table below details the distribution within the Group by age on December 31, 2016:



# Breakdown of employees by age and gender on December 31, 2016

The table below details the distribution within the Group between men and women by age category as of December 31, 2016:





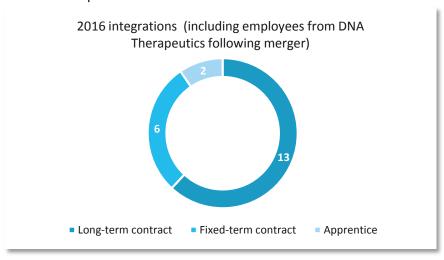
# Breakdown of employees by geographical area on December 31, 2016

All of the above employees are located in France.

# 2.4.1.1.3 Personnel mobility during FY 2016

At the Company level:

- New hires: 21 employees including 13 permanent, 6 fixed-term, and 2 trainees, including the employees from the absorption of DNA Therapeutics



- Departures: 16 employees, including 8 resignations, 2 trial period ruptures at the employer's initiative, 3 fixed-terms ended, 1 conventional termination, and 2 training periods ended.





# 2.4.1.1.4 Remuneration policy within the Company

Onxeo's remuneration policy is based on the following three main principles:

- Performance recognition;
- External competitiveness;
- And experience in the job and function.

All employees receive a fixed salary and variable compensation linked to individual performance, and to the Company's performance.

The table below shows the average increase by status of employees' base salary of the Group, employed full-time, permanent, working as of February 1, 2016, and having more than one year of seniority:

STATUT	Average individual increases in 2016	Average individual increases in 2015
Executive	2%	3.34%
Non-executive	2%	2.68%

A salary benchmark was recognized in 2016 for all Company employees. This benchmark revealed that wages at Onxeo were broadly in line with the market. Random checks were carried out where necessary on certain salaries or when hiring new employees. The aim is to check the relevance, integration, and consistency of proposed salaries with the rest of the team and vice versa.

In 2016, the salary increase for women was slightly higher than for men.

All employees on open-ended contracts with at least four months' service also benefit from stock option plans passed at the General Meeting that are implemented each year by the Board of Directors. During fiscal 2016, the Board of Directors allocated 333,500 stock options to 50 non-executive employees of the Company, including those in Denmark and the United States. These allocations have exercise periods of 4 years, 25% exercisable at the end of each year elapsed from the date of the grant and, at the latest, within 10 years of their allocation by the Board.

Also, an envelope of 134,750 bonus shares was allocated by the Board of Directors.

#### 2.4.1.1.5 Danish establishment

As of December 31, 2016, the permanent Danish establishment based in Copenhagen had four employees, all on permanent full-time contracts.

Their average age is 50 and average experience is 9 years.



The wage and stock option allocation policy is the same as that of Onxeo in France. An employee resigned from the Danish office in 2016.

# 2.4.1.2 Organization of working time and absenteeism

# 2.4.1.2.1 Organization of working time

Under the agreement on the adjustment and reduction of working time of 11 July 2007, working time in the Company is calculated on an annual basis, on the basis of 218 days a year for managers who work a fixed number of days and on the basis of 36 hours 45 minutes per week for non-managerial staff.

Two employees work on an 80% part-time basis as of December 31, 2016.

The Company hires temps during peak business periods.

#### 2.4.1.2.2 Absenteeism

The main reasons for absenteeism in 2015 and 2016 were sickness and maternity leave. They are at parity for 2016.

In 2016, 149 sick days of less than one month were taken against 245 in 2015, while sick days in excess of one month came to 77 working days versus 138 in 2015. Maternity leave represented 206 working days in 2016 compared to 656 in 2015.

The absenteeism rates for sickness and maternity were 1.8% and 1.6% respectively.

As for accidents, Onxeo reports one work accident in 2016 that occurred during a business trip resulting in a day off; the accident involved a fall. In 2016, the Company recorded one work interruption for therapeutic treatment lasting 10 days.

#### 2.4.1.3 Labor relations

# 2.4.1.3.1 Labor relations and description of collective bargaining agreements

Labor dialogue is led by the Executive Management with staff representatives. Employee delegate and Works Council monthly meetings were held during the year ended December 31, 2016.

### 2.4.1.3.2 Staff representative

The Single Delegation of Personnel was renewed in 2016. Professional elections took place in February 2016. The Single Delegation of Personnel includes four members from management and one non-executive member. The Company shall ensure that the rights and freedoms of the staff representatives are strictly respected, and that they have the same prospects for professional development and training than other employees.

The management and staff representatives together freely agree upon common provisions ensuring the development of a social policy of quality and progress through the maintenance of a permanent and constructive social dialogue on subjects relating to the Company and its employees.

#### 2.4.1.3.3 Principal agreements

The main collective bargaining agreements in force within Onxeo are as follows:

- Agreement for the Adjustment and Reduction of Working Time dated 11 July 2007;
- A company charter relating to the system for employee inventors, concluded on March 17, 2006 and updated on February 26, 2013, to encourage innovations, the Company's core business;
- The collective agreement dated July 11, 2007, on the change from the collective agreement that applies to the Company, the Collective Bargaining Agreement for Chemical Industries to that of the Pharmaceutical Industry as of October 1, 2007;
- Company collective agreement of July 11, 2007 covering pension and healthcare schemes.



Finally, each year the company submits a report to the Works Council summarizing part-time work in the company, employment trends, qualifications, training and salaries, the situation compared to general employment and training conditions for men and women, and measures concerning the employment of disabled workers in the company.

In accordance with Article L.225-37-1 of the Commercial Code, this report is presented to the Board of Directors during the first quarter.

# 2.4.1.4 Health and Safety

#### 2.4.1.4.1 Occupational Health and Safety (OH&S)

Group activities include office work and pharmaceutical product research and development. These activities involve general risks applicable to any company - fire, electrical, travel related risks and specific risks related to R&D activities. All these risks are assessed, managed, and controlled by the OH&S system put in place by Onxeo and presented below.

#### 2.4.1.4.2 Health and Safety Department: presentation and mission objective

To guarantee the health and safety (H&S) of its employees, Onxeo has a Health and Safety Department that ensures the prevention of occupational risks and the implementation of H&S actions. It is responsible for the prevention and management of the risks inherent in the Company's business.

# 2.4.1.4.3 OH&S Policy

The Company's occupational health and safety policy is based on the following principles:

- The staff operates responsibly and in complete safety;
- The Company strictly complies with H&S legislation;
- H&S is an integral part of all projects, processes, decision-making and planning activities;
- Any incidents and OH&S issues are deferred and evaluated so that they are accompanied by corrective and/or preventive action;
- The Company promotes a policy of continuous OH&S improvement;

With daily attention to the work, health and safety of its employees, and the environment, and in focusing on spreading good practices and preventive actions, the OH&S policy is an integral part of sustainable development and the corporate social responsibility policy.

In 2015, Onxeo Management set up an Occupational Health & Safety audit, and included it in the 2016 action program on Health, Safety, and Working Conditions. Management wanted to have an outside view of the Company, thus guaranteeing in particular the objectivity of the evaluations carried out during the audit. Thus, a company specializing in the field of Occupational Health and Safety was commissioned for this purpose.

The audit was organized around three main objectives: to take an inventory, make recommendations for action, and establish a safety referent profile.

The restitution of the OH&S audit and its associated action plan were presented to the HSC. The audit revealed the following:

- Workplace health and safety is being managed by involved actors;
- The existing organization is effective;
- The positions taken by the key actors facilitates exchanges at all levels;
- The demands on complying with the regulatory requirements is high.

Several recommendations, none of which are critical, stemming from the action plan defined under the audit became actions in 2016.

Thus, the main actions carried out in 2016 following the audit were:

- Setting up an emergency management procedure;



- The definition and formalization of a Safety Referent job profile and launching the hiring process; the Safety Referent's assignment will primarily be to ensure internal awareness training of the various risks, especially in the laboratory and also to analyze incidents and accidents.
- The definition and development of a Workplace Health and Safety policy for 2016-2017, optimized and formalized with respect to the policies of previous years.
- This policy will generate a specific document.
- It revolves around three axes:
  - Continuously protecting health and ensuring workplace safety;
  - Increased consideration for the quality of working life within the Onxeo organizations and in management actions, including developing means to prevent psychosocial risks.
  - Ensure compliance with the Company's legal and regulatory obligations.
- This would include a policy of dealing with any internal violence especially bullying, sexual harassment, or any deviant behavior, based on the principles of loyalty, respect for the dignity of persons, the rights of persons and individual freedoms within the Company.
  - The Company will make every effort to continue to ensure effective prevention of workplace harassment under the internal provisions defined in a specific document entitled, "Framework for dealing with internal violence".
  - This document mentions the definition of harassment and violence at work, the expectations of the various actors, the sanctions against the perpetrators of workplace violence, and procedures covering harassment and violence at work.

Moreover, within the continuity of the Health and Safety policies of previous years, several actions were taken in 2016:

- The annual update of Onxeo's Occupational Risk Assessment Document;
  - It was optimized following the recommendations of the OH&S audit. The occupational risk analysis was carried out by the unit defined within Onxeo.
  - These work units were reviewed and optimized with respect to 2015.
  - Psychosocial risks were covered by working groups, unit by unit, as recommended by the INRS.
- A new registry of benign accidents and incidents was set up in 2016 at the Company's initiative.
- Audits and regulatory controls of electrical installations and fire extinguishers in accordance with standards and regulations in force. These verifications resulted in the issuance of Q18 and Q4 certifications;
- Training: The training of personnel is important in terms of risk prevention and meeting general safety requirements. The addition of new staff systematically involves OH&S training.
- For staff working in labs, this OH&S training is complemented with a part concerning general laboratory H&S, chemical risk prevention, and especially biological carcinogenic mutagenic reprotoxic substances, and related equipment.
- In addition to training newcomers, OH&S training sessions are carried out by the OH&S Department. The
  purpose of these training sessions is to review laboratory hazards and risks, to train for safe practices and
  manipulations in the laboratory, and to ensure that employees anticipate or respond to a sensitive situation
  or potential risk of an incident.
- The description and training, both initial and renewed, of first responders in the use of fire extinguishers;
- Training of new people in charge of evacuation in addition to the existing team.

For specific projects, Onxeo conducts a study of the impact on hygiene, health, and working conditions. These studies were presented for consultation on three occasions:

- The acquisition and subsidiarizing of DNA Therapeutics, and the integration of its product AsiDNA™;
- The absorption of the DNA Therapeutics subsidiary by Onxeo;
- The establishment of a new management tool, "SAP by design" for accounting, procurement, financial reporting, and budget.

H&S legal and regulatory developments are closely watched at Onxeo. This makes it possible to keep up to date regarding regulatory changes affecting the Company.



Prevention and protection in terms of occupational health and safety receives constant attention at Onxeo; investments have been made in this area, notably concerning the purchase and maintenance of collective and individual protection equipment and expenditures associated with regulatory inspection and assessment. Total OH&S investment amounted to nearly €40,192 in 2016.

### 2.4.1.4.4 2017 OH&S Program

The OH&S program has been established to meet regulatory obligations and is designed to achieve continuous improvement.

The main commitments for 2017 include:

- Risk assessment and prevention approach:
  - The update to Onxeo's Occupational Risk Assessment Document;
  - Monitoring the various prevention plans and risk management situations;
  - Follow-up of the action plans resulting from the Occupational Risk Assessment Document and the OH&S audit;
  - Performing exercises or drafting procedures and specific operating modes;
- Internal communication on OH&S (prevention...);
- The implementation of OH&S training sessions;
- The application of fire regulations:
  - Running fire drills;
  - Regulatory electrical and fire extinguisher controls;
- Continuous and recurring actions involving product management, risk assessment of new activities, updating H&S documents, and regulatory monitoring;
- Verification of protective equipment:
  - Purchase and maintenance of PPE;
  - EPEC maintenance;
- Waste management.

The 2016 annual report on hygiene, safety, and working conditions and the 2017 annual OH&S program were presented to members of the Health and Safety Committee in accordance with Article L4612 of the French Labor Code. The latter were presented to members of the HSC at its regular meeting in February 2017.

# 2.4.1.4.5 Summary of agreement with the OS&S staff at the Company

The updated version of Onxeo Internal Rules was presented on December 18, 2013 by Executive Management to the HSC for advice on hygiene, safety and working conditions in the Company. The members of the HSC issued a favorable opinion on the implementation of the 2014 internal rules on the advice of the Works Council and after the filing and publishing formalities.

No new text was signed in 2015 on Occupational Safety and Health. In 2016, the OH&S policy and the framework for internal violence prevention were presented and signed by management.

# 2.4.1.4.6 Occupational illness and work accidents

In 2016, the work-related accident frequency rate was 10.62 and that of work-related accidents while commuting was 21.24 and the severity rate was 0.01 and the work-related accidents commuting severity rate was 0.01, due to a commuting accident that resulted in a one-day work stoppage.

In 2015, the work-related accident frequency rate, the work-related accidents while commuting rate, the severity rate, and accidents and commuting rates are 0. Indeed, Onxeo is happy to report that there were no work or commuting accidents in 2015.

An accident is considered to be a work accident, irrespective of the cause, if it occurs due to or during work and affects any salaried or other person working for whatever reason and at whatever location, for one or several employers or managers. A work accident is also any travel accident that occurs over the normal route of the employee between:

- The place of work and one's main residence - or secondary residence if this location is stable in nature (a weekend home, for example) or a place at which one stays for family reasons;



- And the place of work and that in which they normally take their meals (restaurant, canteen, etc.).

Onxeo did not register any occupational illnesses. Occupational illnesses are those resulting from exposure to risk at one's workstation.

# 2.4.1.5 *Training*

#### 2.4.1.5.1 Development and training

The Company continually strives to offer its employees quality opportunities for training and development that are adapted to the needs of the Company and the specific requirements of each job. Broken down into two parts: training programs to promote managerial skills and technical training related to the expertise required by different jobs.

#### 2.4.1.5.2 Investment in training and development

In order to enhance individual and collective performance, the Company's training plan sets out the investment levels necessary to meet the strategic needs of the Company in the short and medium term.

In 2016, the focus was placed on the following three areas:

- Updating and acquiring technical expertise and knowledge of scientific and technical regulations; for example, training sessions were held in the new ERP tool "SAP by design".
- The development of language techniques and practices aimed at improving the level of English for employees working in an international environment, which concerns 48% of Onxeo employees.

In 2016, the Company committed a total of €71,819.50 to continuous vocational training, including €52,062.97 on trainings conducted as of December 31, 2016, i.e. nearly 1.21% of the total payroll, in addition to contributions due under Individual Training Leave and professionalization. This represents an investment in training of €1,033 per trained employee; average annual FTE. An important budget optimization effort was made in 2016 without decreasing the overall amount of training relative to previous years.

During the year ending December 31, 2016, 1,235 hours were committed to training for a total of 1,201.50 hours completed (81 individual actions), compared to 755.50 hours in 2015.

In 2016, the focus was placed on business training as well as English language instruction to strengthen skills related to job requirements, and transversal work in a multicultural context.

The Company's annual training program also includes in-house training, especially in the areas of pharmacovigilance, quality assurance, health and safety, and in the laboratory - clearances, and handling...

Training newcomers is systematic and suited to their specialty in these areas.

# 2.4.1.6 Equal treatment

Onxeo is a decidedly feminized Company - 70% women compared to 30% men on December 31, 2016 - and this is representative of its sector.

For information, women represent 56.8% of the workforce in the pharmaceutical industry (source LEEM - Annual Report 2015). The distribution of men/women has been stable for more than 20 years.

According to employment center statistics, the proportion of men/women is very different in other industrial sectors and the trend is reversed: there are 29% women for 71% men.

A strong majority of women executives in key positions:

- 73% of the women at Onxeo have executive status;
- Several key positions at Onxeo are occupied by women:
  - Chief Executive Officer
  - Director of Human Resources
  - Head of Clinical Development
  - Head of Investor Relations and Corporate Communications
  - Head Accountant



- Senior Regulatory Affairs Manager
- Senior Quality Assurance Manager

#### Hires for 2015/2016:

- In 2015, out of 14 permanent executives hired, eleven were women. In addition, 2 women were hired in fixed-term positions.
- In 2016, 13 executives were hired or integrated. These figures include employees of DNA Therapeutics following the absorption of the subsidiary. One man and nine women in permanent positions, and one man and two women in fixed-term positions.

The Company will ensure that it receives an equal number of women and men candidates in 2016, enabling them to interview both men and women for the vast majority of positions. However, as the final choice of candidates was made exclusively based on professional and human skill criteria, actual hires were not at parity in 2016, reflecting a highly-feminized sector trend.

# 2.4.1.6.1 Professional inclusion of people of with disabilities

In 2016, the Company did not have any disabled employees. Nevertheless, the Company's employment policy is based on objective criteria and individual merit. Professional equality is shown to all employees irrespective of disability.

A study was made in late 2013 to define a disability action plan and reference protective workstations or adapt specific work to provide certain services or facilities. This plan of action was carried out since 2014 through the implementation of specific actions in connection with the Establishment and Personal Assistance Services such as: packaging, purchasing supplies (paper), and ordering meal trays. In 2015 and 2016, Onxeo renewed these specific actions in favor of employing people with disabilities by renewing its purchase supply contracts for paper, and its meal tray and buffet orders. Engaging a suitable company specializing in recycling and archiving completed these actions since 2015.

# 2.4.1.6.2 Diversity and non-discrimination

The Company takes care to ensure the equal treatment of its colleagues and a respect for diversity. It refuses any and all discrimination, regardless of the nature, origin, gender, or age, etc. in its hiring practices and during employment. Employee advancement within the Company is linked to merit as well as opportunities and openings that depend on the progress of its projects.

#### 2.4.1.6.3 Fundamental ILO conventions

The Company takes care to ensure that it complies with applicable regulations and is not aware of any particular issues on this matter.

# 2.4.2 ENVIRONMENTAL INFORMATION

As product manufacturing is outsourced, the Group does not have its own factories. Business takes place in offices and two R&D laboratories and, consequently the impact of Company activity on the environment is limited.

The Company and the Group operate as a responsible corporate citizen that seeks to limit the potential negative impacts of its activity on the environment and respects the main principles aimed at ensuring the protection of human health and the environment.

# 2.4.2.1 General policy

R&D activity is strictly supervised to ensure that there are no hazardous aqueous or gaseous emissions from dangerous products (see section 2.4.2.2. Pollution and Waste Management).

Internal Onxeo referents are the Health and Safety Department and the Laboratory Manager. Regulatory monitoring is performed jointly by these two departments.



Regular training programs, clearances and workstation notices help maintain the level of security on the activities carried out in the laboratory.

Tracking expenditures linked to air treatment, the accreditation of waste management contractors and the administration of waste monitoring documentation are the responsibility of the Laboratory Manager.

The Company is not subject to the rules applicable to installations classified under environmental protection. An audit made in the fall of 2016 confirmed that the Company did not enter within this scope.

To date, the Company has not initiated any specific voluntary certification process.

# 2.4.2.1.1 Training and information concerning environmental protection:

The training of each new arrival includes environmental awareness. This awareness centers on the management of waste paper and energy savings.

Communication campaigns are also conducted on the theme of sustainable development and energy consumption.

#### 2.4.2.1.2 Resources devoted to the prevention of environmental risks and pollution

The resources devoted in 2016 to the prevention of environmental and pollution risks relating to R&D with costs for:

- Central air treatment and conditioning: €9,097, covering preventive and corrective maintenance activity, support for the improvement of the air treatment system, and qualification of the control and the air handling system;
- Waste management by various service providers: €6,910.

# 2.4.2.1.3 Amount of provisions and guaranties for environmental risks

There are no provisions or guarantees related to environmental risks.

# 2.4.2.2 Pollution and waste management

### 2.4.2.2.1 Prevention and limitation of emission into the air, water, and soil

#### Gaseous emissions

Onxeo facilities meet the recommendations issued by the INRS (national institute for research and safety) concerning emission controls.

The R&D laboratory is equipped with an air treatment unit. The laboratory air is extracted only after having been processed by suitable filters including HEPA (High Efficiency Particulate Air).

Contaminations generated at workstations are confined and the air extracted at these workstations is filtered at a level corresponding to recommendations and guidelines.

The rules of technical controls and maintenance ensure the reliability of the systems in place.

Specific training for the different workstations and procedures put in place are also sufficient to ensure good operating conditions and avoid releases into the environment.

#### **Aqueous** emissions

No aqueous effluent of a hazardous product has been released into the environment by Onxeo: all hazardous waste and unused liquid products are managed and processed by approved service providers.

# 2.4.2.2.2 Preventive measures for recycling and disposal of waste

Data on waste tonnage produced is not consolidated due to their insignificant nature in terms of the company's activities. However, Onxeo has implemented measures aimed at improving waste management.



# 2.4.2.2.3 Circular economy

#### Recycling of waste paper and packaging.

Most waste paper and packaging is sorted and recycled.

#### Disposal of waste (specific pollution).

Laboratory waste is of two types: non-hazardous and hazardous.

Non-hazardous waste does not require special treatment. Hazardous waste, however, is sorted according to the risks presented; it is stored securely in the laboratory before contractors specialized in the treatment of chemical and biological waste come to take it away.

All new Company employees are entitled to a Health & Safety overview. In the laboratory, this overview includes additional training on all instructions and rules specific to the laboratory including waste management. Specific training or clearances are then provided.

#### Fight against food waste

There is no Company cafeteria or restaurant.

# Significant greenhouse gas emissions generated by the Company

The Company's operations are dedicated to research and development. They do not include industrial production or distribution, and therefore have no significant use of raw material for products to be marketed, and no significant releases to the environment, or greenhouse gases.

#### 2.4.3 SOCIETAL INFORMATION

# 2.4.3.1 Relationship with stakeholders

#### 2.4.3.1.1 Shareholder and investor relations

All shareholders have access to full, transparent, and clear information that is adapted to the needs of the individual and can be used to make an objective assessment of Onxeo's growth strategy and results. This financial communication policy aims to ensure that all shareholders have access to information that complies with usual market practices.

A very diverse array of public documents including regulatory information covering the company's business activities, strategy and financial position are available on the company's website under the heading Investors, in French and English, and on request from Onxeo Executive Management. Email us at contact@onxeo.com to directly receive annual reports, institutional brochures, and press releases.

As part of the regulatory information required of a listed company, Onxeo publishes various annual and other periodic information. Financial information is complemented by press releases aimed at the financial community and the wider public, concerning subjects of significant importance to better understand the company's business activities and strategy. The Company holds periodic meetings with fund managers and financial analysts to explain the Company's challenges, products, plans, and results.

In 2016, Onxeo also gave over one hundred and fifty individual presentations to the financial community, primarily in France and the US.

# 2.4.3.1.2 Sponsorship

Currently the Company does not pursue any sponsorship activities.

# 2.4.3.2 Outsourcing

Onxeo focuses its activity, its human resources, and its know-how developing and registering innovative drugs. To this end, it contracts out clinical trial and manufacturing activities, alongside services in the fields of security, premises maintenance, and computer maintenance.



In fact, the Company's products require ever more extensive, and therefore ever more costly, clinical trials as development progresses. Accordingly, any product evolving in the various stages of its clinical development and moving ever closer to the marketing stage will require increasingly significant resources. Clinical trials conducted thus far, notably in Europe and the United States, have therefore been mostly performed using the services of subcontractors. The industrial development phase enables production processes developed during preclinical and clinical trials to be reproduced on a large scale, in readiness for product commercialization. This phase is generally initiated only when the products have proved their efficacy. The Company uses certified subcontractors to carry out these scale changes.

The supplier selection and audit process is carried out in line with pharmaceutical industry regulations, Good Manufacturing Practice, Good Clinical Practice, and Good Laboratory Practice.

The Company's subcontractors are audited following contract signature and are also a contractual requirement for key production stages and the delivery of outsourced products.

The Company, in its subcontractor selection criteria, aligns adequacy with need, quality, and the associated cost - social and environmental criteria, however, are not decisive at this time.

# 2.4.3.3 Fair commercial practices

The risk of corruption deemed is low or zero vis-à-vis Onxeo or coming from its employees. The Company is not involved in winning public market contracts or tender offerings. For this reason, the following ethical elements were developed.

### 2.4.3.3.1 Adoption of a code of ethics

Onxeo shares trade on the Euronext Paris Stock Exchange. Accordingly, all activities affecting Onxeo shares are regulated, notably the purchase, sale, and free allocation of shares and stock options.

Onxeo has implemented several years ago a code of ethics. The code of ethics is currently reviewed in accordance with the AMF recommendation-position no. DOC-2016-08 of October 26, 2016 relating to inside information, insider's duties, and prevention tools were put in place by the Company.

This code applies:

- To all employees whether or not included on the list of insiders, permanent, or temporary;
- To third persons or companies, service providers, and consultants working on behalf of Onxeo when they were notified of their inclusion on a list of external insiders, permanent or temporary;
- To Directors, the Chairman of the Board of Directors, the General Manager, and Executive Vice Presidents.

#### 2.4.3.3.2 Managing conflicts of interest

As provided for in the Board's internal rules, each Director shall endeavor to avoid any conflict that may exist between his moral and material interests and those of the Company. He fully and in advance informs the Board of any actual or potential conflict of interest in which he could be directly or indirectly involved.

In case of a potential conflict of interest occurring after the start of his mandate, the Director concerned must inform the Board immediately upon becoming aware, refrain from participating in discussions and decision making on the issues concerned and, if applicable, resign.

A lack of notification by the Director concerned is a recognition that no conflict of interest exists.

# 2.4.3.3.3 Consumer health and safety measures

Measures taken to ensure the integrity of consumer health and safety are covered by the Company's compliance with Good Manufacturing Practice and Good Laboratory Practice, as well as with French and international regulations relating to clinical trials and the rules of pharmacovigilance. The Company therefore follows a number of rules: statutory and regulatory provisions defined by the National Agency for the Safety of Medicines (ANSM) in France, the European Commission and European Medicines Agency (EMA) in Europe, the Food and Drug Administration (FDA) in the USA and equivalent regulatory authorities in other countries, all of which govern research and development work, preclinical trials, clinical trials, regulation of pharmaceutical



establishments, and the manufacture and marketing of the drugs. Such regulation in the main countries in which the Company operates is based on the procedures defined by the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). This regulatory framework is broadly described each year in the Registration Document.

# 2.4.3.3.4 Actions taken in support of human rights

The Company takes care to ensure that it complies with applicable regulations and is not aware of any particular issues on this matter.

# RESULTS AND FUNDING

#### **Historical financial situation**

The information describing the evolution of the financial situation and the results of operations performed during the exercises corresponding to historical financial information are included in the Registration Document as follows:

- Chapter 3 « Management report and financial situation », pages 37 to 43 of the Registration Document of the financial period ending 2015 filed with the AMF on April 29, 2016, under number D 16-0452.
- Chapter 3 « Management report and financial situation », pages 34 to 41 of the Registration Document of the financial period ending 2014 filed with the AMF on April 14, 2015, under number D 15-0336.

This chapter is extracted from the management report authorized by the Board of Directors on March 7, 2017. The numbers therein must be read in connection with those presented in chapter 6 of the Registration Document.

# 3.1 RESULTS

# 3.1.1 PRESENTATION OF ONXEO'S FINANCIAL STATEMENTS AND ALLOCATION OF INCOME

The Company's annual financial statements have been prepared in accordance with the rules of presentation and assessment methods prescribed by the legislation in force.

# 3.1.1.1 Review of the financial statements and results

For the financial year ended December 31, 2016, the Company's revenue came in at €557,000 compared to €810,000 for the financial year ended December 31, 2015. This revenue corresponds mainly to sales of finished products of Loramyc®, Oravig® and Sitavig® made to license partners and to intermediaries rebilled to third parties.

Other income totaled €3,485,000 up from €2,898,000 recorded for 2015. This includes the royalties calculated on sales made by licensing partners for €2,150,000 and the proportionate share of payments received on the signing of partnership agreements spread over time in the amount of €749,000.

Operating expenses for the past year amounted to €29,512,000, compared to €29,231,000 for 2015. Despite this apparent stability, R&D spending was up mainly due to the increase in patient recruitment for the Phase III trial of Livatag and the impact of the new AsiDNA program, the cost of which rose to €17,325,000 compared to €16,232,000 for the previous year. These expenses were offset by a lower payroll related mainly to the reduction in bonus premiums paid on employee targets and an improved control over other operating expenses.

Operating revenue showed a loss of €25,393,000 compared with a loss of €25,399,000 for fiscal 2015.

Financial income turned a profit of €21,673,000 against a loss of €2,986,000 in fiscal 2015. This increase comes mainly from the provision reversals on securities and receivables of the subsidiary Topotarget Germany that was liquidated during the year. This income was offset by the recording of a €21,742,000 technical liquidation loss listed under extraordinary charges. In fiscal 2016, the Company also recorded provisions on foreign



subsidiary equity holdings of €291,000 against €3,688,000 in 2015, positive net currency exchange differences of €145,000 compared to €838,000 in 2015, investment income of €113,000 against €334,000 in 2015, as well as financial expenses of €267,000 against €572,000 in 2015.

Current income before taxes was a loss of €3,722,000 compared with a loss of €28,384,000 in fiscal 2015.

The exceptional result showed a loss of €21,469,000 essentially made up of the technical liquidation loss described above.

The Company recorded in the year 2016 a €3,955,000 research tax credit.

As a result of these various revenue and expense items, the net P&L for the period showed a loss of €21,236,000 against a loss of €25,163,000 in 2015.

# 3.1.1.2 Allocation of income

It is proposed to the general meeting of April 26, 2017, to allocate in full the loss for the year amounting to €21,236,246 to the 'losses carried forward' account, which will thus increase from €141,544,626 to €162,780,872.

In accordance with the provisions of Article 243a of the General Tax Code, we remind you that no dividend was distributed during the three preceding financial years.

# 3.1.1.3 Non-deductible expenses

In accordance with the provisions of Article 223c of the French General Tax Code, we inform you that no non-deductible tax expense was incurred during the financial year.

Furthermore, no overheads as per Articles 39-5 and 223d of the [French] General Tax Code which are not listed in the special statement have been noted.

# 3.1.1.4 Financial summary

In accordance with Article R 225-102 paragraph 2 of the Commercial Code, we attach the table showing the Company's results over the last five years in section 6.3 of the Registration Document, p. 157.

# 3.1.1.5 Equity investment and controlling interests at year-end

In accordance with the provisions of Article L 233-6 of the Commercial Code, we inform you that during the financial year, the Company did not invest in any company having its registered office in France.

# 3.1.1.6 Statement related to payment periods

In accordance with the provisions of Article L.441-6-1 of the French Commercial Code, in the table below we specify the payment deadlines for the Company's suppliers for the past two financial years.

	31/12	/2016	31/12/2	2015
Amounts payable to suppliers	9 116 052		7 689 488	
Including allowances for unforeseen invoices	5 107 074		3 128 472	
Including accounts payable to suppliers	4 008 979	100%	4 561 016	100%
- Outstanding invoices	2 087 542	46%	2 056 286	45%
Including intragroup	23 956	1%	23 956	1%
- Invoices payable within 15 days	405 085	9%	314 248	7%
- Invoices payable between 15 and 30 days	1 516 352	33%	2 190 482	48%
Including intragroup		0%	1 379 534	30%

#### 3.1.2 PRESENTATION OF THE GROUP'S CONSOLIDATED FINANCIAL STATEMENTS

The Onxeo Group's consolidated financial statements have been prepared in accordance with the International Financial Reporting Standards (IFRS).



The consolidated financial statements posted revenues of €4,423,000 compared to €3,481,000 in 2015. This increase comes from the sales growth of licensed partners, in particular those of Beleodaq in the United States enabling the Group to receive higher amounts of royalties on sales. Recurring revenue increased from €2,733,000 in 2015 to €3,455,000 in 2016. The increase in non-recurring revenue (+€220,000) that corresponds to recognizing income in the year payments are received upon signature of license agreements and spread out over time, stems from the signature of the agreement with Pint Pharma. Operational charges amounted to €27,591,000 against €25,657,000 in 2015, as a direct result of increases in R&D including the Livatag® and AsiDNA® programs. After recording non-current operating expenses of €43,000, financial income of €1,106,000 and a tax expense of €566,000, the net result was a loss of €22,671,000 compared to a loss of €19,409,000 for the previous year.

The contribution made by the consolidated companies to the overall result (before IFRS adjustments) is as follows:

- Onxeo is the main contributor with revenue of €4,013,000, mainly consisting of revenue related to Beleodaq® as part of the agreement with Spectrum. The Company covered all research and development expenditures as well as overhead costs, generating a consolidated loss of €21,149,000.
- The contribution of the English subsidiary Topotarget UK, which as the holder of certain patents receives a proportionate share of Beleodag® income, showed a profit of €10,000.
- The Group's other subsidiaries had limited activity and their contribution to consolidated income was a loss of €117,000.

The impact related to the Group's financial restatements under IFRS rules was a loss of €1,415,000, primarily broken down as follows:

- A €853,000 charge corresponding to the restatement DNA Therapeutics acquisition, resulting from the discrepancy between the date when Onxeo took control over this company under IFRS rules and the date of the simplified merger between the two companies under French GAAP;
- A €538,000 charge resulting from an increase in deferred tax liabilities;
- A €482,000 charge corresponding to the warrants and stock options as well as the bonus shares granted during the year;
- A €42,000 charge representing a change in pension liabilities for the year,
- Income of €530,000 from foreign currency translation differences,
- €31,000 charge from the recognition of a technical loss on the liquidity contract.

## 3.2 CASH POSITION AND FINANCING

This section is to be read jointly with the numbers presented in chapter 6 of the Registration Document and, in particular, in connection with the table related to cash flow and the table regarding shareholder equity.

#### 3.2.1 GROUP'S FINANCIAL PROFILE

As a biotech company focused on the development of innovative drugs, the Group must finance trials which may be long and costly, which in turn results in a specific financial profile generally characterized by negative cash flow over a number of years. The orphan oncology products developed by the Group should nonetheless lead to a strong growth in the medium/long term and yield high profits, through a partnership covering the advanced stages of clinical development and the marketing phase. These partnerships with more influential pharmaceutical groups could thus result in payments to Onxeo during key stages of the development and marketing of products.

# 3.2.2 FINANCIAL POSITION WITH RESPECT TO THE VOLUMENT AND COMPLEXITY OF ITS BUSINESS

The Group had a cash position of €29,243,000 at year-end and did not contract any financial debt, except for repayable public grants amounting to €5,348,00.

# 3.2.3 R&D EXPENDITURES



The evolution of R&D expenditure over the five previous years is presented in the table below:

R&D Expenditure	In thousands of euros
2012	9,258
2013	9,978
2014	14,834
2015	16,350
2016	18,075

The bulk of R&D expenses are related to clinical trials as well as the industrial development of drugs.

The cost of a clinical trial may vary but will remain, as a general rule, proportionate to the number of individuals involved. When the development strategy of a new product is defined, trials are first carried out on a small number of patients and, in absence of any contraindication, extended to a larger population.

The development of the Group's products requires ever more extensive, and consequently ever more costly, clinical trials as development progresses. Accordingly, any product evolving in the various stages of its clinical development and moving ever closer to the marketing stage will require increasingly significant resources. Clinical trials conducted thus far, notably in Europe and the United States, have therefore been carried out by relying on internal resources, partnerships with public research institutes and, to a large extent, the services of subcontractors.

The industrial development phase enables production processes developed during preclinical and clinical trials to be reproduced on a large scale, in readiness for product commercialization. This phase is generally initiated only when the products have proved their efficacy. The Group uses certified subcontractors to carry out these scale changes and, depending on the contracts with the latter, it is susceptible of taking charge of specific investments.

# 3.2.4 WORKING CAPITAL REQUIREMENT (WCR)

The working capital requirement is negative as of December 31, 2016, totaling €5.8 million compared to - €2.6 million for the previous year. This variation is essentially linked to the increase of accounts payable to suppliers (+ €2.9 million), and is a result of the deployment of R&D programs, the acquisition of DNA Therapeutics, and deferred income stemming from the signature of the license agreement with Pint Pharma (+ €2.2 million), compensated by a drop in in tax receivables after the reimbursement of withholding tax (- €1.4 million).

The evolution of R&D expenditure and the new license agreements that the Group will be led to sign on its products are amongst the principal factors which will influence the WCR evolution in the coming years.

#### 3.2.5 INVESTMENTS

The Group's main historical investment is its 2014 acquisition of the company Topotarget, by way of fusion, for €88 million (IFRS rules). This policy of external growth was again pursued in 2016 as illustrated by the completion of the acquisition of DNA Therapeutics in March of the same year for €1.7 million. The two operations were financed in their entirety by the issue of new shares.

Beyond these exceptional operations and R&D expenses incurred by the Company – which are commented above and counted as debt insofar as the Group has not obtained an MA – the investments are limited and will remain so in the coming years. Indeed, the Group has made the strategic choice of working with external partners for the entirety of its fundamental research activities, for part of its development activities (clinical trials), as well as for the production, storage and distribution of its products. For this reason, the Group's activity is far from being capital-intensive, the only fixed assets being miscellaneous chattels, in addition to office supplies, laboratory equipment, hardware and office furniture. On December 31, 2016, the entirety of tangible assets was valued at € 0.7 million.

In order to prevent its financial resources being tied up too heavily, the Group gives priority to rental, in particular for the premises of its registered office in Paris, its establishment in Copenhagen and its laboratory. Accordingly, no heavy capital expenditure is currently planned that would give rise to fixed assets being booked.



No firm commitment has been made by the Group regarding investments.

# 3.2.6 FUNDING

# 3.2.6.1 Funds raised – equity contributions

To this day, existing and new shareholders' cash contributions have been the Company's favored form of financing.

Capital increases carried out since the formation of Onxeo total € 190.9 million as of the end of December 2016. Three private financing rounds took place between 1999 and 2004, contributing € 27 million to the Company. The Company carried out an IPO in December 2005 on Euronext Paris, raising € 30 million on this occasion. Between 2007 and 2016, the Company carried out a number of secondary financing operations (capital increases with retention or removal of preferential subscription right) raising an additional sum of over € 130 million.

To the abovementioned operations must be added the capital increases benefitting the Company through the conversion of the warrants/options issued or partnership contracts.

# 3.2.6.2 Research Tax Credit

In the light of the amount of research and development costs incurred, the research tax credit (credit d'impôtrecherche, or CIR) is an important mechanism for the Company in terms of financing.

During the last five years, the amount declared for CIR in France and on account of a similar mechanism in force in Denmark revealed the following trend:

In thousands of euros	2012	2013	2014	2015	2016
CIR France	1,979	2,389	2,083	3,508	3,769
CIR Denmark				306	186
Total	1,979	2,389	2,083	3,814	3,955

In accordance with legal provisions in France and Denmark, the Company expects to receive the 2016 research tax credit reimbursement before the end of 2017.

# 3.2.7 GRANTS

In order to optimize and diversify its funding sources, the Company also uses public grants. These are either outright grants received from various French or European organizations or reimbursable advances mostly granted by BPI France. In general, the grants obtained by the Company are paid in accordance with the progress made on R&D projects, on the basis of expenditure actually incurred. Thus, the various tranches of funding are paid on the basis of financial assessments that the Company regularly submits to the organizations concerned. In the case of refundable advances, a reimbursement timetable is drawn up based on the achievement of the milestones set forth in the R&D programs being financed. In the event of a total or partial failure, the sums generally do not have to be reimbursed by the Company.

The amount of subsidies and reimbursable advances as of December 31, 2016, is of € 534,800, of which € 625,000 are payable in the next few years according to the contractual payment schedule. In light of the development milestones reached by the Company, the reimbursement of some grants is expected and will amount to payments totaling € 831,000 between 2017 and 2021.

#### 3.2.8 DETAIL OF CASH FLOW

Over the course of 2016, cash flow from operating activity totaled -17.1 million euros, compared to -23.1 million euros in 2015. This decrease, despite an increased net loss (-22.7 million euros in 2016 compared to 19.4 million euros in 2015), is owed to the changes in working capital requirement.



Cash flow related to investment activities rose to 1.8 million euros during FY 2016 and corresponds largely to the acquisition of DNA Therapeutics. Onxeo has no other capital-growth strategy as reflect by in net flow of -0.2 million euros recorded for FY 2015.

Cash flows from financing activities were increased in 2016 as they were driven by the Company's equity raising: in 2016, the cash flow was of 12.0 million euro, mirroring the year's financing operations, whereas the similar cash flow for 2015 was at 0.1 million euros.

# 3.2.9 INTRA-GROUP CASHFLOW

Information related to the loans and advances granted by the Company to its subsidiaries are presented in section 7 of the notes to the Company financial statements presented in section 6.3 of the Registration Document.



# FROM RESEARCH TO DEVELOPMENT

# 4.1 RESEARCH AND DEVELOPMENT (R&D)

#### 4.1.1 PRINCIPLES AND ORGANISATION

The Group currently has fifty salaried employees with a high level of expertise, of which nearly two thirds are in R&D and who carry out various activities related to research, development, quality assurance, registration and industrial protection, in addition to various strategic marketing activities, market surveys, corporate development and support services (finance and human resources).

R&D is at the very heart of the Group's activities. For these activities (preclinical, clinical and regulatory), the Group uses its own internal resources and exploits partnerships with research institutes and specialist subcontractors.

The Group has research laboratories at two sites (at the Faculty of Pharmacy in Châtenay-Malabry and at the Company's head office site in Paris).

#### 4.1.2 REGULATORY FRAMEWORK

The Company is subject to the legal and regulatory requirements defined by the Agence Nationale de Sécurité du Médicament (ANSM) in France, the European Commission and European Medicines Agency (EMA) in Europe, the Food and Drug Administration (FDA) in the USA and equivalent regulatory authorities in other countries, all of which govern research and development work, preclinical trials, clinical trials, regulation of pharmaceutical establishments and the manufacture and marketing of the drugs. The Company also complies with the guidance defined by the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) which apply in the main countries in which the Group operates.

Health products may not be offered for sale within a jurisdiction without having received technical and administrative authorization from the authorities of the country in question, in the form of a MA. In order to obtain a MA for a product, the Group must demonstrate its quality, safety and efficacy, and provide detailed information on its composition and manufacturing process. This forms the framework for conducting a comprehensive pharmaceutical development, and preclinical and clinical studies.

Broadly outlined, the development of a new drug involves five stages, from basic research up to its launch on the market: (1) research (discovery); (2) pharmaceutical development, preclinical studies and manufacture; (3) clinical trials on humans; (4) application for MA and (5) marketing. The regulatory authorities require a follow-up process to be performed after marketing in order to continue to monitor the effects and safety of authorized products (pharmacovigilance). They may also demand supplementary post-approval safety or efficacy studies involving particular populations or impose conditions susceptible of restricting the commercial development of the products.

The deadlines imposed by the regulatory approval process may de facto reduce the period of exclusive exploitation of patented technologies or products.

# 4.1.2.1 Clinical trials

Human clinical trials are usually conducted in three phases: Phase I, Phase II and Phase III, which are generally sequential, but may also overlap.

**Phase I:** Phase I consists in administering the product, most often to healthy subjects, in order to start defining its safety profile and its distribution and metabolism.

**Phase II**: in Phase II, the drug is studied within a restricted population of patients suffering from the targeted disease in order to establish its preliminary efficacy, its optimum dosage and better define its tolerance profile.

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**Phase III**: Phase III trials are conducted with a larger number of patients suffering from the targeted disease in order to compare the study treatment with a reference treatment and generate sufficient data to be able to demonstrate a positive benefit/risk ratio.

Clinical trials can sometimes be required after the products have been commercialized in order to explain certain side effects, to explore a specific pharmacological effect or to obtain additional and more accurate data. These are known as post-approval Phase IV trials.

Clinical trials must comply with strict legislation and follow Good Clinical Practices (GCP) standards defined by EMA, the FDA and ICH, alongside ethical standards defined by the Helsinki Declaration of June 1964<sup>3</sup>.

In Europe, the carrying out of a Phase I, Phase II or Phase III clinical trial requires prior authorization from a competent authority within the country or countries in which the research is being conducted, alongside an opinion issued by an ethics committee (in France, the Comité de Protection des Personnes, or CPP), in accordance with European Directive 2001/20/EC and Regulation (EU) No 536/2014. The regulatory authorities may either accept or block clinical trial protocols proposed by Companies seeking to test their products, or demand that changes be made to such protocols. Additionally, any ethics committee with authority over at least one clinical site may delay or momentarily or definitively interrupt a clinical trial if it judges that patient safety is being compromised or in the event of non-compliance with any regulatory provisions.

In the USA, an application to conduct a clinical trial (Investigational New Drug, or IND), notably including a preclinical file for the product and the clinical protocol of the proposed trial, must be submitted to the FDA. In the absence of any objection from the FDA within 30 days of receipt of the IND application, authorization to commence the clinical trial is deemed to have been given. At any time during this 30-day period or subsequent to it, the FDA may demand the interruption of the ongoing or proposed clinical trial ("clinical hold"). This temporary interruption is maintained until the FDA obtains a response to its request for further information. In parallel, approval from an ethics committee (Institutional Review Board, or IRB) regarding the clinical protocol is also required before a clinical trial may commence in the USA.

# 4.1.2.2 Marketing authorization

In order to be marketed, any drug must be granted a MA issued by the competent national or supranational health authorities (ANSM in France, European Commission, FDA, etc.) which assess the quality, safety and efficacy of the product.

The application for a MA must include extremely detailed technical information about the new product, notably its quality, toxicity, efficacy and safety. The accuracy of this information is guaranteed by carefully monitored preclinical and clinical trials. The extent and nature of the trials vary according to a number of factors such as the nature of the assessed product, the developed treatment, the sought-after indications and healthcare standards.

The MA application must include the results of preclinical and clinical trials supported by detailed information about the composition, manufacturing process and quality control procedures for the product. The preparation of these applications and their subsequent review by the competent authorities is a costly process which can take several years.

In the European Union, MA applications may be submitted to the regulatory authorities of a Member State of the European Union (the Reference State) in order to be recognized within the framework of mutual recognition or decentralized procedures in other Member States. For certain products, the application files can be submitted directly to EMA within the context of the so-called centralized procedure. The centralized procedure foresees an application, an assessment and a single authorization to market a particular drug in all European Union Member States.

In the United States, the FDA is the competent authority for the grant of a MA, otherwise known as a New Drug Application (NDA) or Biological License Application (BLA).

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<sup>&</sup>lt;sup>3</sup> World Medical Association (WMA), Declaration of Helsinki, "Recommendations Guiding Physicians in Biomedical Research Involving Human Subjects".



Prior to giving marketing authorization for a product in the USA, the FDA inspects the clinical studies and production sites in order to verify that the data included within the MA application meet the Good Manufacturing Practices (GMPs or Good Clinical Practices). Following issue of the MA, the authorities regularly inspect the production sites to verify that regulations are being complied with. Failure to comply with these regulatory requirements may result in criminal or administrative penalties, such as the suspension of production and product recalls.

Various European and American regulations promote the development of treatments for rare diseases. The FDA grants orphan drug status to any drug aimed at treating diseases affecting fewer than 200,000 people a year in the United States. This status is also available in Europe under a similar law for drugs intended to treat diseases that affect up to five persons out of 10,000 in the European Union and for which there is no satisfactory treatment.

## 4.1.2.3 Product pricing and reimbursement

In many markets, drug pricing is controlled by the state which either fixes it or prevents community buy-ins beyond a given amount. Medico-economic evidence is increasingly requested by health authorities in order to determine benefit/cost effectiveness versus existing health technology alternatives. International price referencing is also increasingly used as a price control mechanism.

In France, effective market access requires that the Group's products be reimbursed at hospital level (via local authority approval) or reimbursed through the social security system. Drug prices are negotiated with the Comité Economique des Produits de Santé (economic committee for healthcare products) after the Commission de Transparence (transparency commission) has given its opinion.

In the United States, although pharmaceutical laboratories may freely establish prices for their products, federal and local initiatives aim to lower the overall cost of healthcare. The American Congress and the lawmakers of each State are likely to continue their efforts towards reforming the healthcare system, controlling the cost of prescription drugs and reforming Medicare and Medicaid.

The development of private health maintenance organizations (HMOs), which have a substantial influence on the purchase of healthcare services and therapeutic products, could also contribute to lower prices by imposing discounts or special price reductions on the Group's products in order to avoid their exclusion from the lists of recommended products drawn up by HMOs.

## 4.1.2.4 Environmental, health and safety regulations

The Group is also subject to laws and regulations concerning the environment, health and safety, which apply to aspects such as the utilization, storage, handling, unloading and disposal of hazardous products, notably chemical and biological products. The impact of such regulations on its activities is therefore highly significant. National authorities have extensive powers in each of these areas and have the right to impose sanctions in the event of any violation.

#### 4.1.3 R&D PROJECTS

The Group develops products in the field of orphan oncology diseases. This involves innovative products for the treatment of resistant cancers or severe diseases for which new therapeutic approaches are needed and which constitute markets of high potential. As of the date of this Registration Document, the portfolio consists of the following main products.

## 4.1.3.1 Products in clinical phase I, II or III

 AsiDNA<sup>TM</sup>: first-in-class product originating from DbAit technology of signal interference to DNA repair in tumor cells. Positive results in Phase I/lia (proof concept trial) when intravenously applied to metastatic melanoma in combination with radiotherapy. Trials are ongoing in order to assess the best combinations with other anti-cancer agents administered intravenously.



- Beleodaq® (belinostat) for the treatment of peripheral T-cell lymphoma (PTCL): positive results in Phase I trials in association with CHOP (Cyclophosphamide, Hydroxyadriamycine, Oncovin, Prednisone) treatment. A Phase III trial with this combination is being prepared with Spectrum, a partner holding a MA in the United States. An oral formulation is currently being developed in parallel to an assessment of interest in associating Beleodaq with other anti-cancer agents.
- Livatag® (Doxorubicine Transdrug™) for advanced primary liver cancer treatment: having commenced in June 2012, Phase III is underway. The completion of the recruitment and randomization of the anticipated 390 patients was announced on January 24, 2017. The preliminary results on efficacy are expected mid-2017.

## 4.1.3.2 Registered products

- Beleodaq® (belinostat), for the treatment of peripheral T-cell lymphoma (PTCL) in relapse or refractory, registered and marketed in the USA by Spectrum Pharmaceuticals. (Conditional MA)
- Loramyc®/Oravig® (miconazole Lauriadfor the treatment of oropharyngeal candidiasis, marketed in France, Italy, and the US.
- Sitavig®/Labiriad® (acyclovir Lauriad®) for the treatment of recurrent labial herpes, registered and marketed in the USA and Italy and registered in several other European countries (France, United Kingdom, Spain, etc.).

Each of these products is presented in detail in section 4.2 of this Registration Document.

## 4.1.4 INTELLECTUAL PROPERTY, PATENTS AND LICENSES

### 4.1.4.1 Patents

Intellectual property is a key asset of the Group and lies at the core of its R&D projects. As of December 31, 2016, the Group's patent portfolio consists of 26 families of published patents concerning innovative products or technologies. The 26 patent families cover 518 patents and patent applications, of which 467 are delivered patents – i.e. nearly 90 % of the portfolio - which provide international and long-term protection for the Group's assets.

The Group's policy regarding intellectual property consists of (i) submitting new patent applications regularly in order to protect its technologies, products and manufacturing processes, (ii) extending this protection to the countries likely to constitute a favorable market or a generic risk and (iii) continuous monitoring in order to take action against any breach of its patents or trademarks.

The length of protection conferred by a patent family is twenty years as of the date of submission within a given jurisdiction, typically the date of the international patent application. This protection may be amended or extended in certain territories, including the United States and Europe, depending on the currently applicable legislation. The protection conferred can vary from one country to the next depending on the examination procedure, specific to each State.

Finally, in the specific case of orphan medicines, the authorities have scheduled additional protection in the form of commercial exclusivity for ten years in Europe and seven years in the United States in order to encourage laboratories to intensify investment and developments in areas where the number of patients is limited.

The Group has ensured that it enjoys robust intellectual property rights protecting its products that have been marketed or are in clinical development. The patent portfolio presented below specifies the various protections and their expiry dates. The Group has also granted marketing rights ("Out-licensing") on the products Loramyc®/Oravig®, described in Section 4.2.2 of this Registration Document.

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# <u>Patents for products that are marketed or undergoing clinical development</u>

Products	Main therapeutic applications	Protections	Expiry date	Status			
Transdrug™ technology: nanoparticle technology							
		i) Livatag® nanoparticles (first generation)	Q1 2019	Delivered (EP, US, JP,)			
Livatag®	Treatment of primary liver	ii) New route of administration of the Livatag® nanoparticles	Q1 2032	Delivered (EP, JP,) Pending (US).			
	cancer	iii) Specific composition of nanoparticles resulting from a selection of particular poloxamer (second generation)	Q3 2036	Pending (EP, US, JP,)			
	Histo	one deacetylase inhibitor (HDACi) t	echnology				
		i) Active substance (belinostat)	Q3 2021	Delivered (EP, US, JP,)			
Beleodaq®	Beleodaq® Peripheral T-cell lymphoma (PTCL)	ii) Formulation IV of the active substance	Q4 2027 US Otherwise Q2 2026 elsewhere	Delivered (EP, US, JP,)			
		iii) Production of the active substance	Q2 2030 US Otherwise Q3 2028 elsewhere	Delivered (EP, US)			
	Dbait techr	nology: « DNA strand break bait » (	Dbait) molecul	les			
		i) Treatment of cancer via administration of Dbait molecules in combination (radio/chemotherapy)	Q3 2024	Delivered (EP, US, JP,)			
		ii) Particular Dbait molecules	Q3 2027	Delivered (EP, US, JP,)			
AsiDNA™	Treatment of cancer	iii) Treatment of cancer via standalone administration of Dbait molecules	Q1 2028	Delivered (EP, US, JP,)			
		iv) Optimized Dbait molecules for an improved in vivo delivery (AsiDNA™ and other Dbait conjugate molecules)	Q2 2031	Delivered (US) Pending (EP,)			



Lauriad® technology: prolonged-release oral mucoadhesive tablet						
Loramyc® / Oravig®	Oropharyngeal candidiasis	(i) Lauriad® technology (ii) Treatment of oral candidiasis	Q3 2022	Delivered (EP, US, JP,)		
Sitavig® / Labiriad®  Prevention and treatment of herpes labialis	(i) Process for the production of the Sitavig® tablet	Q4 2027 US Otherwise Q1 2027 elsewhere	Delivered (EP, US, JP)			
		(ii) Treatment of herpes via a single administration of Sitavig®	Q4 2029 US Otherwise Q4 2030 elsewhere	Delivered (US) Pending (EP)		
Validive <sup>®</sup>	Treatment of oral	(i) Clonidine in the treatment/prevention of mucositis	Q3 2029	Delivered (EP, US, JP)		
	mucositis	(ii) Clonidine in the decrease of adverse effects related to radiotherapy	Q2 2036	Pending (EP, US, JP,)		

## 4.1.4.2 Trademarks

The protection of trademarks varies from country to country. In some countries, this protection is essentially based on the use of the trademark whereas in others, it only results from registration.

Rights on trademarks are obtained through national trademarks, through international registrations or through community trademarks. Registrations are usually granted for a period of ten years and are indefinitely renewable although, in some cases, the persistence of their validity depends on the continuous use of the trademark.

The Group holds trademarks consisting of the names of its marketed products or that of products undergoing clinical development as well as the names of its proprietary technologies Lauriad® and Transdrug™, the name of the Company and its logo.

These trademarks benefit from a protection for the pharmaceutical products included in Class 5 of the international classification for products and services.

<u>Trademarks portfolio for products that are marketed or under clinical development</u>

Trademarks	Products	Main countries in which the trademark is registered or pendin registration	
Livatag®	Doxorubicine Transdrug™	United States, Europe, France, Japan	
Beleodaq®*	Belinostat	United States, Europe, Japan, China, Australia, Russian Federation, Mexico, Norway, Oman, Serbia, Singapore, Switzerland, Turkey, Vietnam, Israel, India, South America (Argentina, Brazil, Chile, Colombia, Ecuador, Peru, Venezuela)	
Validive®	Clonidine Lauriad®	United States, Europe, Japan, China	

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Trademarks	Products	Main countries in which the trademark is registered or pending registration
Loramyc®		Europe, United States, China, Japan, India, Singapore, South Korea, Hong Kong, Malaysia
Oravig <sup>®</sup>	Miconazole Lauriad®	United States, China
Oravi <sup>®</sup>		Japan
Sitavig®	Acyclovic Lauriad®	Europe, United States, Australia, New Zealand, South Korea, Brazil
Labiriad®	Acyclovir Lauriad®	Europe
AsiDNA <sup>TM</sup>	AsiDNA <sup>TM</sup>	France

<sup>\*</sup> The trademark Beleodaq® is held by Spectrum Pharmaceuticals, the exclusive licensee of the Group for the marketing of Belinostat in the US, Canada, Mexico and India.

The Group defends its trademark rights by opposing identical or similar trademark registration applications and, if necessary, will initiate lawsuits in order to have its rights recognized.

## 4.2 PRODUCTS AND MARKETS

### 4.2.1 DEVELOPMENT MODEL

The Company has embraced a biotechnology company model dedicated to the development of innovative drugs in the field of orphan pathologies in oncology by creating value through the application of the expertise of its teams on promising programs in order to bring them to a value turning point in their development plan.

The Company applies this strategy in its flagship programs, notably Livatag®, developed to combat primary liver cancer, and seeks to strengthen its portfolio through M&A or external partnership operations, as has been the case with the 2014 acquisition of Topotarget and Beleodaq®, and the 2016 acquisition of DNA Therapeutics and the product AsiDNA<sup>TM</sup>.

Legacy products, notably those based on the Lauriad® technology, are no longer at the heart of Onxeo's activities, which has been implementing its strategic transformation since 2014. Formerly, the assets and knowhow of the Company essentially relied on original reformulations of already approved treatments with wide indications (herpes, candidiasis, etc.) in order to gradually improve their efficacy or tolerance, with the objective of taking them to the registration and marketing stage via partners. While they represent an undeniable knowhow of the teams, they are no longer capable of driving the Company's growth in and of themselves.

Today, Onxeo's primary objective is to evaluate its three main oncology candidates in new indications, in monotherapy but also in combination with other compounds or treatments against rare or resistant cancers, when a synergistic effect may provide greater efficiency.

This strategy involves preclinical and clinical targeted activities, which are rigorously carried out and will allow to highlight and confirm the clinical interest of a program in one or more indications, in order to subsequently find a partner that will pursue the development of the product on large-scale trials through partnership agreements equally permitting to generate income for the Company.

## 4.2.2 ORPHAN DRUGS IN ONCOLOGY

Focusing on orphan drugs in the treatment of cancer, the Group is targeting a particularly attractive market, incorporating pathologies with significant unmet medical need.

In Europe, the orphan status is obtained for a medicine used in a pathology affecting less than 5/10,000 people, namely some 250,000 people for the EU 28. This status allows favorable measures to be applied in terms of clinical development (optimized development regarding time and cost), additional protection with a

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commercial exclusivity of 10 years after MA and a favorable price, generally identical or similar in major European countries.

In the United States, the orphan status is obtained for pathologies affecting less than 200,000 people and the commercial exclusivity is for seven years.

The orphan drugs and oncology drugs markets currently represent the most dynamic of the pharmaceutical sector. To this day, 7,000 rare or orphan diseases have been identified, of which less than 5% benefit from treatment: it is thus necessary to strengthen the development of orphan drugs to meet the needs of those affected and seeking medical solutions.<sup>4</sup>

The market for anti-cancer drugs reached \$78.9 billion in 2015, in a 14% increase from 2014. It henceforth represents 8.3% of the pharmaceutical market total, and anti-cancer remains the first therapeutic category in sales, followed by anti-diabetics (\$71.4 billion) and analgesics (\$56.2 billion)<sup>5</sup>. The growth forecasts for the anti-cancer market remain strong, with \$100 to \$200 billion worth of sales expected by 2020<sup>6</sup>.

EvaluatePharma® forecasts that the orphan drugs market – all pathologies – could reach \$176 billion in 2020. And among the 20 main products in terms of sales, 15 are anti-cancer products, confirming the importance of orphan drugs in oncology<sup>7</sup>.

## 4.2.2.1 Livatag® (doxorubicine Transdrug™)

## 4.2.2.1.1 Livatag®

Livatag® (doxorubicine Transdrug™), the most advanced candidate among the Company's orphan products in oncology, corresponds to a doxorubicin formulation in the form of lyophilized nanoparticles of PEBCA (Poly-Ethyl-Butyl-Cyanoacrylate).

This new therapeutic approach allows drug resistance to be avoided by short-circuiting the mechanisms of multi-drug resistance developed by tumor cells through the masking of the anti-cancer agent. Acting as a Trojan horse, the nanoparticle formulation avoids rejection of doxorubicin outside the cell so that it can exert its cytotoxic action. By preferentially targeting tumor cells in the liver and overcoming resistance to doxorubicin, Livatag<sup>®</sup> (Doxorubicin Transdrug<sup>™</sup>) represents a significant breakthrough in the treatment of this cancer. The first indication of this product is hepatocellular carcinoma (CHC), the sixth most widespread cancer in the world and the second cause of cancer-related death<sup>8</sup>.

In July 2013, Onxeo obtained financing from bpifrance of nearly €9 million of which €4.3 million was awarded directly to the Company via an Industrial Strategic Innovation (ISI) program, payable over 5 years and enabling the acceleration of the industrial development of Livatag®. This financing supported the establishment of the NICE (Nano Innovation for Cancer) consortium, the first consortium with the objective of establishing a nanomedicine sector in France and more specifically focused on the characterization and industrialization of production processes specific to nanomedicines. The Company has already received €3.6 million in 2016, based on the progress of the Livatag® as per schedule.

Livatag® benefits from orphan drug status in Europe and the United States, enabling optimization of the product's development plan in terms of cost and duration, as well as strengthening its protection (market exclusivity). In May 2014, it also received fast-track status from the Food and Drug Administration in the treatment of hepatocellular carcinoma after treatment with Sorafenib. This status acknowledges that a drug is being developed for a severe life-threatening disease for which the medical need is important. It will allow enhanced interaction with the FDA and optimize the evaluation schedule of the product during development right up to registration

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<sup>&</sup>lt;sup>4</sup> Evaluate Pharma, Orphan Drug Report 2015

<sup>&</sup>lt;sup>5</sup> IMS Health MIDAS, December 2014

<sup>&</sup>lt;sup>6</sup> Global Use of Medicines in 2020. Report by the IMS Institute of Healthcare Informatics

<sup>&</sup>lt;sup>7</sup> Evaluate Pharma, Orphan Drug Report 2015

<sup>&</sup>lt;sup>8</sup> Globocan 2012, Liver Cancer: incidence and mortality



## 4.2.2.1.1.1 ReLive phase III trial in treatment of advanced stage HCC

The efficacy of Livatag® has been demonstrated in preclinical models of resistant cancers in vivo and in vitro, its superiority over free doxorubicin having been established.

In a Phase II trial, Livatag®, administered by hepatic intra-arterial route in the form of repeated treatment in HCC patients has been assessed in comparison with the existing standard of care, essentially consisting of intra-arterial chemoembolization. The endpoints concerned efficacy and tolerance, with efficacy being judged by the absence of progression at three months, and survival.

On July 16, 2008, Onxeo announced the suspension of this trial, in accordance with the opinion of the independent committee, the Drug Safety Monitoring Board (DSMB), which had been monitoring the progress of this trial. The committee has observed acute pulmonary intolerance of a higher frequency and severity than anticipated. It therefore recommended the suspension of the trial.

In accordance with the decisions of the DSMB, the Group has continued follow-up of patients included in this trial between 2009 to 2011, which revealed positive results in terms of survival with a median survival of 32 months in patients who had received Livatag® by the hepatic intra-arterial route versus 15 months in patients having received the standard treatment (arterial chemoembolization). These results were presented at the ILCA Congress (International Liver Cancer Association) in September 2011 and the AASLD Congress (American Association for the Study of Liver Diseases) in November 2011.

At the same time, Onxeo pursued studies designed to improve control of the secondary respiratory effects observed in 2008. The Group has developed a new and validated administration scheme in animals allowing the significant reduction of acute side effects in the lungs, which had led to the interruption of the trial.

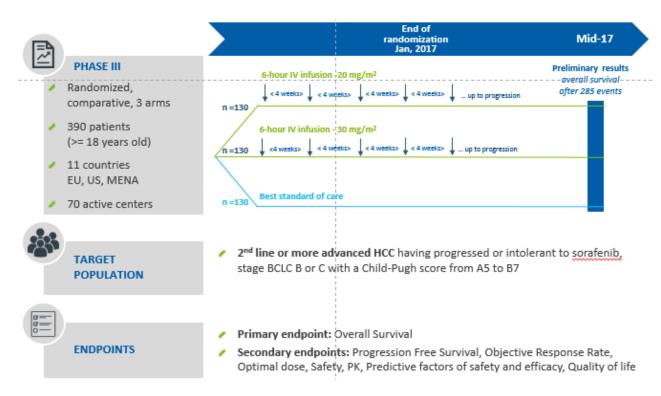
In view of this new data, the ANSM has given its authorization for a Phase III clinical trial in patients with advanced stage HCC, after failure with or intolerance to sorafenib (ReLive study). The first patient was included in the Phase III study in June 2012.

In November 2012, an independent European experts committee (Data Safety Monitoring Board) was established to provide ongoing monitoring of the safety of patients included in the ReLive study, as specified by the protocol. Since its creation, the committee has met twice a year and, up to the date of this Registration Document, has issued positive recommendations regarding the continuation of the study without modification on 9 separate occasions since the start of the trial.

The ReLive study is being conducted in 11 countries in total (Europe, US and countries in the MENA region). The recruitment of 390 patients was completed on January 24, 2017, with 260 patients treated with Livatag® and 130 with the standard of care. The completion of the randomization phase constitutes an important milestone which allows to confirm the trial calendar expecting the publication of the preliminary results in mid-2017.

The development of the ReLive study is illustrated in the following figure.





## 4.2.2.1.1.2 Other preclinical developments

At the end of 2015, the Group launched an ambitious preclinical program to expand the potential of Livatag® through various combination programs with cancer agents (classical cytotoxics, targeted therapies and immunotherapies) in HCC and other solid tumors. Three partnership agreements have been put in place to date, the first with the Hepato-Oncology Team at the Croix-Rousse Hospital in Lyon (France) and the and the Centre de Recherche en Cancérologie of Lyon, Inserm U1052, led by Professor Philippe Merle, principal investigator of the ReLive study and an internationally-recognized expert in HCC; the second with Synovo, a CRO (Contract Research Organization) specializing in immunotherapy and based at Tübingen (Germany) and the third with the Centro de Investigación Médica Aplicada (CIMA) of the University of Navarra (Spain), under the leadership of Professors Bruno Sangro and Pablo Sarobe, two recognized experts in the field of liver disease.

Within the framework of this program, Onxeo assesses the potential of Livatag® when it is administered alongside the new immuno-oncology agents of different categories such as PD-1 and CTLA-4 checkpoint inhibitors currently being developed. The ongoing trial has demonstrated, on mouse orthotopic models of hepatocellular carcinoma (HCC), that the association of Livatag® with these immuno-oncology agents increases anti-cancerous activity (reduction of tumor volume). More precisely, the administration of Livatag® combined with these antibodies is associated to an increase of the population of circulating T-cells, which is consistent with the observed tumor volume reduction.

Lastly, the Company announced at the end 2016 encouraging results of a series of preclinical trials aiming to assess the potential of Livatag® in the treatment of pancreatic cancer. The conducted trial revealed that, on a mouse syngeneic model of pancreatic cancer, Livatag as monotherapy had an efficacy either comparable or superior to that of comparator standard treatment, notably gemcitabine, paclitaxel and erlotinib. Furthermore, the trial showed that Livatag could be associated with these three chemotherapies, with a good tolerance and superior effect (supra-additive) than that of the agents on a standalone basis.

## 4.2.2.1.2 Hepatocellular carcinoma (HCC)

#### 4.2.2.1.2.1 Pathology



Hepatocellular carcinoma (HCC) develops from liver cells (hepatocytes) and represents 85% of primary liver cancers <sup>9</sup>. In the great majority of cases (>90%), HCC occurs when the liver is already abnormal (cirrhosis)<sup>10</sup>. Risk factors are well established:

- Infection with hepatitis B and C viruses is the source of 80% of liver cancers. This is why the areas where the
  infection is endemic, such as Asia, are the most affected by HCC;
- Consumption of large amounts of alcohol, another important cause of cirrhosis, is also an HCC risk factor which contributes more extensively in Western than in Asian countries;
- Metabolic diseases, and in particular obesity, are a growing cause of cirrhosis and HCC.

Most HCCs are diagnosed at an advanced stage because the tumor progresses without any visible clinical manifestations in the early stages. In addition, the first symptoms or signs are usually not specific to HCC but to the associated cirrhosis and may suggest other pathologies.

#### 4.2.2.1.2.2 Epidemiology

Liver cancer is the 6th most common cancer in terms of incidence (782,000 new cases in the world, 5.6% of all new cancer cases) with the 2nd highest mortality rate (746,000 deaths, 9.1% of the total), after lung cancer<sup>11</sup>.

It is the most aggressive form of cancer – alongside pancreatic cancer – with a lethality rate of 95% (relationship between mortality and incidence for a given year).

While Europe (UE28) and the USA see a total of 82,000 new cases each year (10% of the global incidence), it can be said that liver cancer is a public health problem that particularly effects the less developed countries (648,000 new cases) and especially Asia, including China, which alone sees one-half of global cases<sup>12</sup>.

The concentration of cases in Asia, and particularly in China, is of course explained by demography but also and above all by a high prevalence of viral hepatitis B and C.

The incidence rate for liver cancer varies greatly by geographical area: while the average global rate is 11.1/100,000, it approaches 30/100,000 in the Far East (China, Japan, and Korea). In Western countries, its incidence is aligned with that of the global average: 10.2/100,000 in the EU and 9.6/100,000 in the USA<sup>13</sup>.

The 5-year survival rate remains extremely low, even in the most medically advanced countries such as the US, where it is 17% for all patients but only 11% for those diagnosed at an advanced stage (regional invasion) and 3% at the metastatic stage <sup>14</sup>.

The sales potential of Livatag® in HCC, including 2nd line treatment and an extension of 1st line treatment, is estimated at €800 million for the world¹5.

## 4.2.2.1.2.3 Competition

#### Existing forms of treatment

The only possible curative treatment for HCC is surgical resection to remove the whole tumor. However, due to late diagnosis of HCC, the tumors are often large and numerous and only 15 to 20% of patients can undergo such surgical treatment.

Liver transplantation is rarely offered because of the scarcity of grafts and the very strict allocation rules applied.

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<sup>&</sup>lt;sup>9</sup> Kelly J. Lafaro et al, Epidemiology of Hepatocellular Carcinoma – Surg Oncol Clin N Am 24 (2015) 1-17

<sup>&</sup>lt;sup>10</sup> Liver Cancer Treatments (Oct 2011, Institut National du Cancer)

<sup>&</sup>lt;sup>11</sup> Globocan 2012, Incidence et Mortalité du Cancer du foie

<sup>12</sup> Globocan 2012, World Population Prospects, the 2012 revision (United Nations, Department of Economic and Social Affairs)

<sup>13</sup> Idem

<sup>&</sup>lt;sup>14</sup> Rapport « Facts & Figures 2015 » de l'American Cancer Society

<sup>15</sup> Données internes



Radiofrequency is an alternative to surgical resection, bringing about the thermal destruction (via electric current) of the tumor, although the technique is usually limited to tumors no greater than 3cm and in limited number (less than 3).

For patients who cannot benefit from surgical or radiofrequency treatment, there are four alternative therapies:

- Intra-arterial chemoembolization: arterial injection of an obliterating agent in tumor blood vessels whether
  or not associated with doxorubicin (or cisplatin) allows the survival time to be prolonged by around 4-6
  months in certain categories of patients. This is associated with complications that lengthen hospital stays
  in over 30% of patients;
- Sorafenib (Nexavar®, Onyx / Bayer), a product from biotechnologies active on multiple kinase targets (including RAF and VEGFR) is indicated in the treatment of HCC (as well as renal cancer). It prolongs survival of about 3 months compared to the placebo in patients with compensated cirrhosis who cannot receive any other form of treatment;
- Systemic (intravenous) chemotherapy has limited efficacy due to chemo-resistance and systemic toxicity. It is seldom used nowadays.

The problems involved with the treatment of HCC and the associated high mortality rate are attributable to various factors, in particular the diseases associated to HCC, such as liver cirrhosis, which limit treatment options. In addition, primary liver cancer is a cancer that is resistant to chemotherapy. Cancer resistance, whether arising spontaneously or acquired over time, represents a major challenge in the fight against this type of disease. Currently, multi-drug resistance is the principal reason for failure of chemotherapy. Multi-drug resistance of certain tumor cells after repeated cycles of chemotherapy makes these cells insensitive to any other form of therapy.

One of the causes of this type of multi-drug resistance is the activation of a family of transmembrane transport proteins. These proteins are activated under the influence of the multi-resistance gene called MDR-1. The proteins actively reduce the intracellular concentration of cytotoxic agents by expelling them from the target cell on entry. These proteins act as veritable "pumps" preventing the cytotoxic agent from exerting its therapeutic action.

There is therefore an unmet medical need for effective therapy and new treatment strategies for the management of HCC. In preclinical trials, Livatag® has shown its ability to circumvent this efflux pump, allowing the product to permeate and remain in the cancer cell to exert its action.

Products currently at the same stage of development as Livatag® (Phase III) in 2nd line treatment of HCC

clinical trials.gov Reference	Molecule	Company (Sponsor)	Trial Title	Positioning	Phases
NCT01908426	cabozantinib	Exelixis	Study of Cabozantinib (XL184) vs Placebo in Subjects With Hepatocellular Carcinoma Who Have Received Prior Sorafenib (CELESTIAL)	2 <sup>nd</sup> line	Phase III
NCT02435433	ramucirumab	Eli Lilly	A Study of Ramucirumab (LY3009806) Versus Placebo in Participants With Hepatocellular Carcinoma and Elevated Baseline Alpha-Fetoprotein (REACH-2)	2 <sup>nd</sup> line	Phase III
NCT01774344	regorafenib	Bayer	Study of Regorafenib After Sorafenib in Patients With Hepatocellular Carcinoma (RESORCE)	2 <sup>nd</sup> line	Phase III completed, positive results

Non-exhaustive list (research in the Clinical Trials.gov website of ongoing clinical trials using HCC, Hepatocellular Carcinoma as key words)

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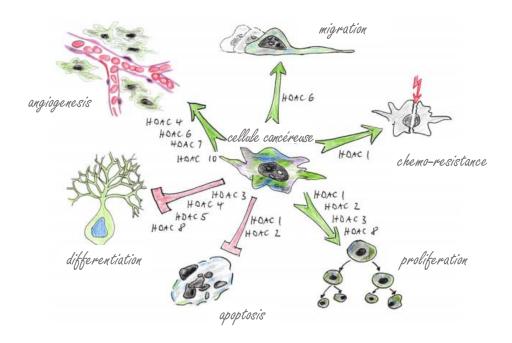


## 4.2.2.2 Belinostat et Beleodag® (intravenous belinostat)

## 4.2.2.2.1 Belinostat, HDAC inhibitor with high potential

Belinostat is a histone deacetylase inhibitor (HDAC) which, via an enzymatic process (acetylation), typically normalizes genetic dysfunctions which are characteristic of cancer cells. It acts via the inhibition of these enzymes (HDAC), notably involved in cellular proliferation.

Belinostat acts on several HDAC types (HDAC 1, 2, 3, 6), thus harnessing a potential of activity on the different processes of tumor development, as illustrated below 16.



Thanks to their pleiotropic action, HDAC inhibitors can simultaneously target several crucial channels for the survival of the cancer cells. In preclinical studies, HDAC inhibitors have already shown antineoplastic activity in vitro and in vivo, as well as synergy with other anticancer agents by killing off the cancer cells and inhibiting tumor growth. 17,18

Nowadays, HDAC are essentially used as monotherapy in the treatment of liquid tumors. This is why the first sought-after indication of belinostat was treatment of peripheral T-cell lymphoma (PTCL) with Beleodaq® (intravenous belinostat), already approved and marketed in the United Stated in this indication, detailed hereafter.

However, belinostat distinguishes itself from the HDAC group due to its action mechanism on the multiple cellular processes of tumor development and has already revealed anti-cancerous activity in solid tumors<sup>19</sup>, with an excellent tolerance profile.

With a view to extend the potential of this key asset beyond PTCL, the Company announced in June 2016 the commencement of the development of an oral formulation of belinostat. This oral formulation holds several advantages:

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<sup>&</sup>lt;sup>16</sup> Adaptation of Olaff, Witt et al., Cancer Letters 277 (2009) 8-21

<sup>&</sup>lt;sup>17</sup> Bolden JE, Peart MJ, Johnstone RW. Anticancer activities of histone deacetylase inhibitors. Nat Rev Drug Discov. 2006;5(9):769-84

Minucci S, Pelicci PG. Histone deacetylase inhibitors and the promise of epigenetic (and more) treatments for cancer. Nat Rev Cancer. 2006;6(1):38-51

<sup>&</sup>lt;sup>19</sup> CuraGen Corporation (CRGN) and TopoTarget A/S Announce Presentation of Belinostat Clinical Trial Results at AACR-NCI-EORTC International Conference. October 2007.



- an extension of patent protection up until 2037;
- a benefit for the patients as well as the doctors in terms of ease of use and painless administration without the assistance of medical personnel;
- a simplified association with other anti-cancerous agents, offering a range of new indications, notably in solid tumors.

The Company has secured several collaborations with leading scientific institutions to study, starting now, the association of intravenous belinostat with anti-PD-1 and anti-CTLA-4 checkpoint inhibitors, with which it could have an important synergistic effect.

Encouraging initial preclinical data carried out on a mouse model of primary liver cancer were reported in October 2016. A complete cessation of tumor growth was observed in all mice (100%) treated with intravenous belinostat in combination with checkpoint inhibitors. This effect was prolonged roughly for a week after the last dose of belinostat was administered. In comparison, the administration of a treatment uniquely on the basis of checkpoint inhibitors revealed an inhibition of tumor growth for only 30% of the mice. The Company pursues these preclinical activities on other solid tumor models.

Subject to a favorable proof of clinical concept, belinostat by oral delivery in combination with checkpoint inhibitors could contribute to indications with strong potential such as head and neck cancer or non-small cell lung cancer. The market size for these two indications is estimated at € 7.7 million in 2016, with a strong growth forecast to reach € 19.1 billion in 2025 (on the territories EU + EU5 + Japan + China)<sup>20</sup>.

(a) Peripheral T-cell Lymphoma, in relapse or refractory (Beleodaq®: intravenous belinostat)

## (i) Pathology

Peripheral T-cell lymphoma (PTCL) is a sub-type of non-Hodgkin lymphoma (NHL). Non-Hodgkin lymphoma occurs as a result of a neoplastic transformation of the lymph cells. In 90% of cases it is associated with cells from the B-cell lymphoma line, in less than 10% of cases with cells from the T-cell lymphoma line and in very rare cases with cells from the NK-cell lymphoma line. The prognosis for T-cell lymphoma is generally worse than for B-cell lymphoma.

The treatment of PTCL is broadly similar to the standard therapeutic treatment for non-Hodgkin lymphoma. In the very rare cases of localized tumors, the treatment used is radiotherapy (with or without chemotherapy) but with most patients the disease has already spread and chemotherapy is therefore used as first-line treatment. Chemotherapy agents are mainly the alkylants, vinca-alcaloids, anthracyclines and corticosteroids, notably such as the CHOP protocol (Cyclophosphamide, Hydroxyadriamycine, Oncovin, Prednisone) or other similar combinations. Protocols based on anthracyclines, such as the CHOP protocol, remain the reference treatment for most sub-types of PTCL. Most patients suffering from a PTCL relapse after a first treatment and require a second therapeutic treatment.

### (ii) Epidemiology

NHL is a rather rare condition worldwide (incidence of 5 / 100,000, 386,000 new cases in 2012), yet they are rather frequent in countries with an aging population. The incidence of NHL is  $20.1 / 100\,000$  in North America (70,000 new cases) and 15.6/100,000 in the European Union (79,000 cases)<sup>21</sup>.

PTCL cases account for between 10 and 15% of NHL cases, namely between 38,000 and 58,000 new cases globally each year. In Western countries, proportions are lower (5 to 10% of all NHL) than in Asian countries (15 to 20%)<sup>22</sup>.

<sup>&</sup>lt;sup>20</sup> GlobalData

<sup>&</sup>lt;sup>21</sup> Globocan 2012 and World Population Prospects, the 2012 revision (United Nations, Department of Economic and Social Affairs), Peripheral T-Cell Lymphoma Facts (July 2014, Leukemia & Lymphoma Society)

<sup>22</sup> Idem



In the main pharmaceuticals markets (US, Europe, Japan and China) there are an estimated of 17,000 to 27,000 new cases each year. As PTCL is a type of cancer the incidence of which increases with age, the ageing population should bring about a consistent increase in the number of new cases, with estimates amounting to between 22,000 and 36,000 by 2030<sup>23.</sup>

The indication approved in the USA concerns refractory patients or those in relapse following 1st line treatment (CHOP) and candidates to 2nd line treatment, namely around 60% of patients treated for PTCL.

For the US, the market is valued at roughly \$187 million in 2015, according to a market study commissioned by the Company in 2016<sup>24</sup>).

#### 4.2.2.2.1.1 Competition

In the US, three products have been approved by the Food and Drug Administration for 2nd line treatment of PTCL: Beleodaq®, Istodax® and Folotyn®. In Europe, no drug has, to this day, obtained a MA in this indication.

In addition to the 3 products approved for PTCL, we should mention Adcetris® which is approved (in the US and the EU) for a sub-type of PTCL, systemic anaplastic large-cell lymphoma where relapsed or refractory in adults.

The products in advanced clinical development (Phase II/III) in the 2nd line treatment indication of PTCL are:

clinical trials.gov Reference	Mollecule	Society (Sponsor)	Trial Title	Phases
NCT02464228	tipifarnib	Kura Oncology	Study of Tipifarnib in Subjects with Relapsed or Refractory PTCL	Phase II
NCT02495415	fenretinide	CerRx	Trial of Intravenous Fenretinide Emulsion for Patients With Relapsed/Refractory Peripheral T-cell Lymphomas	Phase II
NCT02653976	darinaparsin	Solasia Pharma	A Phase 2 Study of SP-02L in Patients With Relapsed or Refractory Peripheral T-cell Lymphoma (PTCL)	Phase II
NCT00406809	ABT-263 (navitoclax)	AbbVie	A Study of ABT-263 in Subjects With Relapsed or Refractory Lymphoid Malignancies	Phase II
NCT01431209	ruxolitinib	Incyte Corporation (University of Nebraska)	Ruxolitinib Phosphate (Oral JAK Inhibitor INCB18424) in Treating Patients With Relapsed or Refractory Diffuse Large B-Cell or Peripheral T-Cell Non-Hodgkin Lymphoma	Phase II
NCT02535247	MK-3475 (pembrolizumab)	Merck Sharpe & Dohme Corp. (Fox Chase Cancer Center)	Study of MK-3475 in Relapsed or Refractory Peripheral T-cell Non-Hodgkin Lymphoma	Phase II
NCT01998035	Romidepsin + azacitidine	Celgene Corporation (Columbia University)	Romidepsin Plus Oral 5-Azacitidine in Relapsed/Refractory Lymphoid Malignancies	Phase I/ Phase II

Non-exhaustive list (research in the Clinical Trials.gov website on ongoing clinical trials using PTCL, Peripheral T-Cell Lymphoma, Relapsed, Refractory as key words)

## 4.2.2.2.1.2 Partnerships

As part of a license and collaboration agreement concluded in 2010, Spectrum Pharmaceuticals is co-developing Beleodaq® in partnership with the Group and is in charge of its promotion before oncology and hematology specialists in the United States.

This agreement provides for milestone payments by Spectrum Pharmaceuticals to the Company when certain regulatory stages have been reached and for royalties and milestone payments on sales.

In February 2014, the FDA granted the admissibility of the U.S. registration dossier for Beleodaq® coupled with a priority review program to allow conditional approval for a drug that treats a life-threatening disease, based

Navigant Consulting Inc

<sup>23</sup> Ibid

IDIO



on clinical benefit predictors. This admissibility triggered both the payment of \$10 million by Spectrum Pharmaceuticals, and the granting of one million of their shares to the Company.

In July 2014, Beleodaq® received MA from the FDA for the treatment of peripheral T-cell lymphoma. This registration is based on the results of the BELIEF Phase II clinical trial which included 129 patients suffering from peripheral t-cell lymphoma which is resistant or in relapse after at least an initial systemic treatment.

Since August 2014, the teams of Spectrum Pharmaceuticals have been promoting Beleodaq® to hematologists, generating the first sales during the second half of 2014 and giving rise to royalty payments to the Group. A second milestone of \$25 million was paid to the Group in November 2014, once FDA approval was obtained.

In order to meet the FDA requirements within the framework of the conditional MA obtained in 2014, Onxeo collaborates with Spectrum Pharmaceuticals to prepare a Phase III clinical trial that would allow to extend the indication of belinostat as a 1st line treatment for PTCL. As the holder of the marketing authorization in the United States, Spectrum Pharmaceuticals will be the promoter of this trial.

Prior to the abovementioned trial, a trial assessing the tolerance of the association of Beleodaq with CHOP (Phase I) (belinostat plus cyclophosphamide, hydroxydaunorubicine, oncovin and prednisone) was conducted by Spectrum and the results published in December 2015, on the occasion of the 57th ASH Annual Meeting.

Other than the fact that the maximum tolerated dose was identified (1000 mg/m², i.e. the same dose as is authorized in monotherapy), the Group announced promising results in terms of response with an 86% global response rate and 67% of complete responses.

The table below provides a summary of the license agreements concluded by the Group for the marketing of Beleodag®.

Partner	Territory	Phase	Amount already generated by the Company	Total to be generated from the agreement
Spectrum Pharmaceuticals License and collaboration agreement in 2010	United States, Canada, Mexico, and India	Marketed in the US as a 2 <sup>nd</sup> line treatment for PTCL. Undergoing development in other indications	\$65 million + 1 million Spectrum shares + royalties on sales	> \$320 million + royalties on sales
Pint Pharma License agreement	LATAM (Argentina, Brazil, Chile, Colombia, Ecuador, Peru, and Venezuela)	Pre-registration	Initial payment of \$3 million received in 2016	> \$20 million + royalties on sales

## 4.2.2.3 AsiDNA™ and the signal interfering DNA (siDNA) technology

## 4.2.2.3.1 A "first-in-class" product acquired through DNA Therapeutics

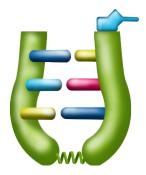
AsiDNA™ is the first product of a new line of drugs (« first in class ») resulting from the signal-interfering DNA (siDNA) technology. The prevention of DNA repair mechanisms in tumor cells is acknowledged today as one of the most promising avenues for cancer treatment.

Cancer cells indeed possess biological defense mechanisms enabling them to react to DNA mutations either spontaneously caused in the case of some genetically unstable tumors, or resulting from treatment by genotoxic agents (chemotherapies or radiotherapy by way of example).

These repair processes contribute to cancer aggressiveness and resistance to treatment.

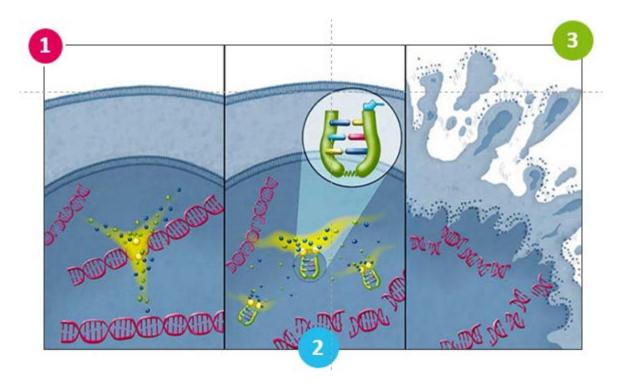
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AsiDNA™ is a double-stranded DNA molecule that acts as a decoy to break the cycle of DNA repair in tumour cells by sending a false lesion signal which mobilises the enzymes (proteins) of detection, signaling and repair of DNA breaks and thus preventing the repair of actual DNA damage induced by genotoxic anti-cancer treatments. Having lost the ability to interrupt cell division, cancer cells continue to divide with damaged DNA, ultimately leading to cell death. In contrast, healthy cells preserve the ability to halt their devision until compound is no longer present, and can later resume their repair cycle.

This unique action mechanism, known as Dbait, was created by Marie Dutreix, Research Director at the Centre National de Recherche Scientifique (CNRS), and Jian-Sheng Sun, Professor at the Muséum national d'Histoire Naturelle in Paris, and largely developed in Professor Dutreix's lab at the Institut Curie. It is illustrated below.



- Several DNA repair avenues are activated in cancer cells via the recruitment of enzymes enabling them to efficiently repair their damaged DNA and avoid cell death;
- AsiDNA mimics a DNA break in the cancer cells and activates the enzyme signaling DNA damage, thus inducing a false damage signal preventing repair enzymes from being recruited on the site where they should act in order to repair damage on the tumour cell's chromosomes;
- Cancer cells are no longer able to divide with damaged DNA, which ultimately leads to cell death.

## 4.2.2.3.2 Competition

The therapeutic field of inhibition of DNA repair mechanisms was first undertaken by PARP inhibitors (poly ADP-ribose polymerase) which count several developing compounds as well as products already on the market such as Lynparza® (olaparib) of Astra Zeneca and Rubraca (rucaparib) of Clovis Oncology, both registered for advanced and recurrent ovarian cancer in patients presenting a BRCA mutation.

Other products are currently undergoing clinical development at varying stages of progress – see table below.

AsiDNA™ differs from other products acting on tumor DNA repair currently being developed, notably PARP inhibitors, thanks to a unique action mechanism that, instead of blocking a repair enzyme or particular mutation, acts upstream of DNA repair, at the level of damage detection and signaling, thus allowing it to interfere with the



multiple DNA repair pathways. The table below illustrates the progress of other products acting on tumour DNA repair.

Molecule	Company (sponsor)	Indications	Phase
niraparib	Tesaro	Ovarian cancer	Registration
talazoparib	Medivation / Pfizer	Breast cancer	Phase 3
veliparib	AbbVie	Lung cancer	Phase 3
lurbinectedin	PharmaMar SA	Small-cell lung cancer ; platinum-resistant ovarian cancer	Phase 3
TRC-102	TRACON Pharmaceuticals Inc (Case Western Reserve University)	Glioblastoma, mesothelioma Lung cancer	Phase 2 Phase 1

Non-exhaustive list (research in the Clinical Trials.gov website on ongoing clinical trials)

#### 4.2.2.3.3 Product development to date and next stages

Preclinical trials undertaken on different types of animal solid tumors revealed that the product enhanced the efficacy of radiotherapy<sup>25</sup>, radiofrequency ablation<sup>26</sup> and that of chemotherapy<sup>27</sup>. The trials also attested to the product's safety throughout several repeated treatments, thus confirming that the product is a promising candidate for both monotherapy and combination therapy.

An AsiDNA concept proof was similarly obtained at local level within the framework of a first Phase I/IIa clinical trial (DRIIM; NCT01469455) on patients affected by metastatic melanoma.

The trial revealed the product's good tolerance and safety both at local and immune level when administered intratumorally and subcutaneously in combination with radiotherapy.

The Group is pursuing the development of this first-in-class product by systemic delivery, and will assess its safety and tolerance level in monotherapy and in combination with other treatments in diverse types of solid cancers.

This development will be launched after the first optimization of manufacturing procedures, undertaken after the DNA Therapeutics buyback in 2016. Among other potential indications, the Group has identified to date two pathologies treated by systemic delivery and for which there is a significant medical need:

- In 2nd line triple-negative breast cancer, known for being genetically unstable for which AsiDNA™ could be used in monotherapy;
- In recurrent ovarian cancer, for which AsiDNA™ would be used in association with the standard of care which carries platinum salt.

The triple-negative breast cancer market is estimated at € 0.8 billion in 2016 with a forecast of € 2.1 million in 2025 in key pharmaceutical markets (EU, EU5, Japan and China)<sup>28</sup>. The market for recurrent ovarian cancer remains to be validated, but could reach equivalent amounts by 2035.

It is however noted that the Group has not yet finalized the clinical development plan for AsiDNA™, which will be defined based on the first current preclinical and clinical (Phase I) future trials' results.

In September 2016, Onxeo unveiled a preclinical trial's interesting results demonstrating the synergistic effect of AsiDNA™ in combination with several products of the category known as PARP inhibitors (Poly ADP-Ribose Polymerase) and allowing to bypass the restrictions associated with the tumor's genetic profile.

#### 4.2.3 OTHER PRODUCTS BASED ON LAURIAD® TECHNOLOGY

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<sup>&</sup>lt;sup>25</sup> Quanz et al., 2009, Berthault et al., 2011, Coquery et al., 2012, Biau et al., 2014

<sup>&</sup>lt;sup>26</sup> Devun et al., 2014

<sup>&</sup>lt;sup>27</sup> Devun et al. 2011, Herath et al., 2016

<sup>28</sup> GlobalData



## 4.2.3.1 *Validive*®

The Group developed Validive® (clonidine Lauriad®) for the treatment of oral mucositis induced by radiotherapy or chemotherapy in patients suffering from a head and neck cancer. It consists of a novel therapeutic application of clonidine, patented by the Group and based on Lauriad® mucoadhesive technology.

In addition to being an agonist of the alpha-2 adrenergic receptors traditionally used to counter hypertension, clonidine also acts as agonist of the alpha-2 adrenergic receptors with an anti-inflammatory effect, which was sought after.

The Group conducted a Phase II randomized clinical trial, double-blinded against placebo, comparing the efficacy and tolerance of the Validive® (clonidine Lauriad®) mucoadhesive tablet in doses of 50  $\mu$ g and 100  $\mu$ g, administered once a day, with those of a placebo in the prevention of severe oral mucositis induced by radiotherapy and/or chemotherapy in 183 patients suffering from head and neck cancer in the post-chemotherapy and radiotherapy mucositis. The trial was conducted in Europe and the United States and the patient recruitment was completed in May 2014.

In terms of efficacy, the Phase II trial revealed:

- Reduction in the incidence of severe oral mucositis (grades 3 and 4) in the group of patients treated with Validive® compared to the control group. The onset of severe oral mucositis after a higher dose of radiotherapy in patients treated by Validive® compared to the placebo group.
- Later onset of severe oral mucositis in patients treated with Validive® compared to placebo.
- No significant difference in terms of efficacy between the 50μg and 100μg Validive® groups.
- In terms of tolerance, Validive® showed a very favorable profile without any major differences in the type, incidence and severity of adverse effects between the Validive® and placebo groups.

Compliance with treatment was very good, with over 80% of patients having effectively used the Validive® or placebo tablet on their gums every day during radiotherapy, as specified by the trial protocol.

A committee of European and US experts established on account of this trial had recommended the continuation of Validive®'s development program, with the conduct of Phase III trial in the same group of patients. The Group then reached out to US and European health agencies in order to validate this plan. Despite acknowledging Validive®'s value and the related benefits to patients, the health agencies considered that future development stages required two Phase III trials for registration in the United States. In light of the additional delays and costs that such a program would represent, the Company estimated that it was in the best interests of its shareholders to move these programs forward to Phase III with the support of a partner.

## 4.2.3.2 Loramyc<sup>®</sup> / Oravig<sup>®</sup> and oropharyngeal candidiasis

Loramyc® (Oravig® in the USA) is an original mucoadhesive gingival tablet of miconazole. It provides early and prolonged release of an efficient concentration of miconazole that impregnates the oral mucosa with little or no systemic transfer. Loramyc® is the first antifungal pharmaceutical specialty to use this mucoadhesive gingival technology. Loramyc® sticks to the gum and disintegrates progressively while releasing miconazole for more than 12 hours on average. Loramyc® is indicated in Europe for the treatment of OPC in immunosuppressed patients. In the United States, Oravig® is indicated for the treatment of OPC in adults.

Oropharyngeal candidiasis (OPC) is a mycosis of the oropharynx induced by yeast-type fungi: Candida albicans and non-albicans. The most common species is Candida albicans. OPC is an opportunistic disease that takes advantage of a deficiency in the immune system and/or a local imbalance in order to infect patients. The conditions associated with its development are often physiological, associated with a local trauma (irritation of the mucous membranes, poor dental hygiene) or with immune anomalies (advanced HIV infection, bone marrow or organ transplant, diabetes, severe malnutrition and debilitating age-related conditions). Furthermore, treatments such as immunosuppressive therapies, radiotherapy, chemotherapy, long-term antibiotic therapy and chronic or inhaled corticosteroids promote the development of fungal infections.



In oncology, the incidence of OPC varies according to the tumor location, the type of drugs and the therapeutic protocol being used: meta-analysis estimates the median incidence of candidiasis in oncology at between 30% and 70%, reaching nearly 100% in patients with a head and neck cancer<sup>29</sup>.

Loramyc®/Oravig® is the first product developed and registered with health authorities (in Europe and the United States) by the Group's personnel. The Lauriad® technology allows a single application per day of the Loramyc® tablet and maintains adequate levels of miconazole in the saliva for the treatment of OPC. The treatment therefore meets a real need for local treatments administered once a day and targeting the affected mucous membrane, with a broad spectrum of activity covering all Candida, thus avoiding drug resistance and clearly reducing the risk of drug interactions. Positioned in a very competitive market with high price pressures, Loramyc® does not significantly contribute to the earnings of the Group. However, its merits in terms of efficacy and ease of administration makes it an attractive product for licensing agreements with international partners.

Furthermore, the clinical development of Loramyc® is ongoing in Japan and China with a phase III study in each country, the final stage prior to registration as required by the regulatory authorities. In Japan, the study is being conducted by the partner Sosei and in China by SciClone Pharmaceuticals. Sosei has announced the submission of a registration dossier to the Japanese health authorities in early 2017.

The table below gives a summary of the licensing agreements signed by the Group for the marketing of Loramyc®/Oravig®.

Partner	Territory	Phase	Amount already generated by the Group	Total to be generated from the agreement
Sosei Co., Ltd Licensing agreement of May 2011	Exclusive marketing license for Japan	Ongoing clinical development	\$3 million	\$14.5 million + royalties on sales
Groupe Therabel Pharma Licensing agreement of March 2010	Exclusive marketing license for Europe (including Switzerland)	Marketing in France and Italy	€9.5 million + royalties on sales	€45.5 million + royalties on sales
Handok Licensing agreement of March 2008	Exclusive marketing license for Korea, Taiwan, Singapore and Malaysia	MA for Korea withdrawn	€1 million	\$12 million + royalties on sales
ScliClone Licensing agreement of June 2008	Exclusive marketing license for China	Ongoing clinical development	€0.6 million	\$4 million + royalties on sales
Dara Biosciences (now Midatech US) Marketing agreement of March 2015	MA + Marketing license for the United States	Marketing in the United States	Undisclosed	Undisclosed

# 4.2.3.3 Sitavig®/Labiriad® (acyclovir Lauriad®) and the labial herpes market

Sitavig®/Labiriad®, the second product developed and registered in Europe and the USA by the Group's personnel, is an original mucoadhesive gingival tablet containing acyclovir. It has been developed for the

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<sup>&</sup>lt;sup>29</sup> Yeung-Yue KA Herpes simplex viruses 1 and 2 Dermatol Clin 2002; 20(2):249-66.; G. Lorette JADD 2006, Vol. 55, n°2, p.225-31



treatment of recurrent herpes labialis with the administration of a single tablet at the first signs of infection.

Caused by herpes simplex virus 1, herpes labialis, often called "cold sores", is the most common form of herpes. This virus causes the appearance, on and around the lips, of transparent vesicles the size of a pinhead, surrounded by a red areola. The blisters burst fairly quickly, become ulcerated and eventually form scabs. Healing takes place without consequences within 7 to 14 days on average.

The herpes virus can be found in vesicular lesions but also in saliva, nasal secretions and tears. Contamination occurs through direct contact with lesions or contaminated secretions. Self-contamination is also common. Transmission can occur as soon as the first symptoms appear and until the scabs dry up.

Over 80% of the global adult population carries HSV-1, the main labial herpes virus<sup>30</sup>. Each year, about 14% of the adult population has at least one episode of herpes labialis<sup>31</sup>. Acyclovir Lauriad<sup>®</sup> targets patients with at least four outbreaks per year, which represents roughly 35% of patients suffering from recurrent labial herpes according to a study of patients conducted by Nielsen for the Group. In addition, HSV-1 infection is often associated with HIV infection, in which case patients have about twelve outbreaks a year.

Like Loramyc®, Sitavig®/Labiriad® shows merit in terms of efficacy and ease of administration being taken just once for the entire herpes episode, making it an attractive product for licensing agreements with international partners. A first exclusive licensing agreement was signed in June 2012 with Abic Marketing Limited, a Teva group subsidiary, to market Sitavig® in Israel. In 2014, new agreements were concluded: with Daewoong Pharmaceutical Co. Ltd and EMS S/A for South Korea and Brazil respectively for the registration and marketing of Sitavig® in each of these territories. In the United States, where the product has been registered since 2013, the Group signed a licensing agreement with Innocutis Holding LLC, a dermatology specialist, for the marketing of Sitavig® which commenced in July 2014. Innocutis has since been acquired by Canadian group Cipher Pharmaceuticals.

Lastly, in July 2015, the Group signed a licensing agreement with pharmaceutical company Bruno Farmaceutici for the marketing of Sitavig<sup>®</sup>. Bruno has launched the marketing of Labiriad<sup>®</sup> (Sitavig<sup>®</sup>'s name in Italy) in the Italian market under its current regulatory status (prescription product) and will assess the feasibility of obtaining over the counter (OTC) status which would allow direct delivery from pharmacists to patients.

The table below gives a summary of the licensing agreements signed by the Group for the marketing of Sitavig®.

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<sup>&</sup>lt;sup>30</sup> Yeung-Yue KA Herpes simplex viruses 1 and 2 Dermatol Clin 2002; 20(2):249-66.;

<sup>&</sup>lt;sup>31</sup> G. Lorette JADD 2006, Vol. 55, n°2, p.225-31



Partner	Territory	Phase	Amount already generated by the Group	Total to be generated from the agreement
Daewoong Pharmaceutical Licensing agreement of April 2014	Marketing license for South Korea	Undergoing registration	€0.148 million	€1.3 million + royalties on sales
EMS S/A Licensing agreement of June 2014	Marketing license for Brazil	Undergoing registration	\$30,000	\$0.12 million + royalties on sales
Cipher (formerly Innocutis) Licensing agreement of March 2014	Marketing license for the United States, Canada, Mexico	Marketed in the United States, undergoing registration in Canada	\$2 million + royalties on sales	\$5 million + royalties on sales
Bruno Farmaceutici Licensing agreement of June 2015	Marketing license for Italy	Launched Q1 2016	€0.5 million + royalties on sales	€2.5 million + royalties on sales
Teva Licensing agreement of June 2012	Marketing license for Israel	Compilation of OTC file	\$0.15 million	\$0.35 million + royalties on sales



# CORPORATE GOVERNANCE

## 5.1 THE BOARD OF DIRECTORS

Sections 5.1, 5.5 and 7.2.2 of the Registration Document reproduce the Chairman of the Board's report on corporate governance, internal procedures and risk management as required under Article 225-37 of the French Commercial Code (Code de commerce). This report was approved by the Board of Directors at its meeting on 7 March 2017; and was submitted to the AMF simultaneously with this Registration Document. It is available on Onxeo's website: <a href="https://www.onxeo.com">www.onxeo.com</a>.

This report, prepared by the Chair of the Board of Directors, relates the composition, preparatory and organizational conditions of the works of the Board of Directors for the financial year 2016 as well as internal control and risk management procedures established by Onxeo.

The report further indicates the limitations that the Board of Directors have imposed on the powers of the Chief Executive Officer and presents by reference the principles and rules adopted by the Board of Directors to determine the remuneration and benefits granted to executive officers, the methods related to the participation of shareholders in general meetings as well as the elements likely to have an influence in case of a public offering.

This report was prepared and written in accordance with French law no. 2008-649 of 3 July 2008 covering various provisions for adapting French company law to EU law, and with the Code of Corporate Governance for Listed Companies issued by MiddleNext, the code selected by the Board of Directors as a benchmark code, which may be viewed at the MiddleNext website: <a href="https://www.middlenext.com">www.middlenext.com</a>. The Board acknowledges having taken note of the elements at "points to be watched" sections of the Code.

#### 5.1.1 COMPOSITION AND SCOPE OF THE BOARD

#### 5.1.1.1 Composition of the Board of Directors

According to the legal, regulatory and applicable statutory provisions, the Board of Directors must be composed of at least three members, 18 at the most, appointed by the General Shareholders' Meeting for a three-year period.

During its meeting on 22 January 2016, the Board of Directors took note of the resignation of Mr. Pierre Langlois as Director and chairperson of the Board of Directors with effect after said meeting of the Board and appointed, as his replacement, Mr. Joseph Zakrzewski. The appointment of Mr. Joseph ZAKRZEWSKI as Director was ratified by the General Meeting of shareholders dated April 6, 2016 and his mandate was renewed for a period of three years expiring at the end of the Ordinary General Meeting to be held in 2019 in order to approve the financial statements for the year ended December 31, 2018.

This same General Meeting:

- Renewed the directorships of Mrs. Danièle Guyot-CAPARROS and Mr. Russell GREIG;
- Appointed as Directors Messrs. Jean-Pierre KINET and Jean-Pierre BIZZARI for a period of three years expiring at the close of the Ordinary General Meeting to be held in 2019 in order to approve the financial statements for the year ended December 31, 2018.

At the time of this document, the Board of Directors is composed of nine members:

Mr. Joseph ZAKRZEWSKI
Independent Director, Chairman
Mrs. Judith GRECIET
Director, Chief Executive Officer
Independent Director

Mr. David SOLOMON
 Mr. Jean-Pierre KINET
 Mr. Jean-Pierre BIZARRI
 Independent Director
 Independent Director



- Financière de la Montagne

Director and Shareholder, whose permanent corporate representative is Mr. Nicolas TREBOUTA

The Board of Directors also appointed among its members a senior independent Director, Mrs. Danielle Guyot-Caparros. This Director shall ensure that the Company complies at all times with the practices of good governance applicable to it, particularly in respect of French regulations. She will also be responsible for providing the Board with ongoing assistance to ensure the proper functioning of the Company's governance bodies and to offer her perspective on the operations on which the Board is called upon to deliberate.

In accordance with the provisions of the law of January 27, 2011 referring to proportionate gender balance on corporate boards, stipulating that the percentage of either sex may not be less than 20% as of January 1, 2014, and increasing to 40% on January 1, 2017, the Board of Directors has elected two women who make up 22% of its members. It will be proposed to the General Meeting of Shareholders called to approve the accounts for the financial year ended December 31, 2016 to appoint Mrs. Christine GARNIER and Mrs. Elvira SANZ, bringing to four the number of women on the Company's Board of Directors, or 40% of its members, given the non-renewal of the mandate of Mr. David SOLOMON.

With a Director representing the major shareholder of the Company, the Board believes that its composition appropriately takes into account the shareholders' participation in its capital.

The Board members bring together essential top-level skills, thereby enriching the work and deliberations of the Board and the specialized committees with varied experience in their fields of expertise, particularly in the health and biotech sectors. They are mindful of all shareholder interests and engage fully in the deliberations, participating effectively in the Board's decisions and validly supporting them.

Detailed information about each member of the Onxeo Board including details about the directorships held by them is provided in Section 5.1.2.1 of this Registration Document.

## 5.1.1.2 Mandate of the Board of Directors

The Board of Directors is responsible for determining the direction of the business of the Company and the Onxeo Group in terms of strategic, economic and financial policies. It oversees their proper implementation.

Subject to the powers expressly granted by General Meetings and within the limits of its corporate purpose, the Board handles all matters affecting the smooth operation of the Company and takes decisions about the more pertinent subjects by deliberation, including all strategic decisions affecting the company and the Group, at the initiative of its Chief Executive Officer.

The Board's rules of procedure, which are available to shareholders at the head office and on the Company's website <a href="www.onxeo.com">www.onxeo.com</a>, determine the mission of the Board, its committees and organizes their work.

These rules specify the Board's operating methods and the procedures for implementation of the legal and statutory provisions regarding its role in the management of the Company and the Group. It also specifies the rights and duties of the Board members, mainly regarding the prevention of conflicts of interest, multiple directorships, the strict confidentiality of deliberations and due diligence in participating in the work of the Board. Finally, it deals with AMF rules relating to Onxeo share transactions.

The Board's rules of procedure clearly state that in order for it to exercise fully its mandate:

- (i) The Chief Executive Officer and the Chairman of the Board, as well as the Chairman of each committee, shall convey useful information to other members of the Board;
- (ii) Board and Committee meetings are preceded by notification, within a reasonable time, of the items on the agenda that require reflection and special analysis, where appropriate this information should be accompanied by documentation;
- (iii) The Board must be regularly informed of any significant event related to Company business;
- (iv) In order to enable easy consultation and, in some cases, facilitate Directors' decision-making, as well as in accordance with the law, the Board's rules of procedure authorize the use of videoconferencing and teleconferencing systems.

Finally, the Board of Directors decides freely on the procedures pertaining to the Company's general management. These can be assumed under the responsibility of either the Chairman of the Board of Directors



or by another individual appointed by the Board and given the title of Chief Executive Officer. Onxeo's Board currently separates the functions of Chairman and Chief Executive Officer.

## 5.1.1.3 Organization and report on the Board's activities in 2016

The Board of Directors met when convened by its Chairperson who set the agenda for each session. In order to better prepare decision-making concerning the different mandates under its responsibility, Onxeo's Board of Directors has established four committees:

- The Compensation Committee,
- The Appointments and Governance Committee,
- The Audit Committee, and
- The Business Development Committee

#### 5.1.1.3.1 The Board's activity report

Seven board meetings were held in 2016. The participation rate was 93%.

At each of these meetings, the Board of Directors took note of the progress of projects and the prospects of activities and results and paid particular attention to financing and Company strategy. Beyond these recurrent themes, the Board made the following key decisions during 2016:

At its meeting of January 22, 2016, the Board approved the 2016-2020 strategic plan as well as the budget for 2016. It determined (i) the percentage of corporate and individual objectives that the Chief Executive Officer achieved for determining the amount of her variable compensation for financial year 2015, (ii) the compensation of the Chief Executive Officer for the financial year 2016, as well as the 2016 objectives for the Chief Executive Officer. The Board also:

- Recognized the lapsing of stock options and bonus shares, due to the departure of certain employees of the Group,
- Appointed Mr. Joseph ZAKRZEWSKI as an independent Director and Chairman of the Board of Directors, replacing Mr. Patrick Langlois who resigned. Mr. Joseph ZAKRZEWSKI was also appointed a member of the Audit Committee,
- Designated Mrs. Danièle GUYOT-CAPARROS as an Independent Director.

Finally, the Board of Directors approved a new warrant plan for Mr. Joseph ZAKRZEWSKI, Board member who is not an employee or officer.

At the Board meeting of February 26, 2016, the annual and consolidated accounts for 2015 were approved alongside the terms of the associated press release. It approved the annual report, including the report of the Chairman on corporate governance, internal control and risk management, as well as special reports on the allocation of stock options or purchase of shares and the bonus shares. The Board reviewed newly concluded regulated agreements or those that are still being negotiated during financial year 2015. It approved the draft resolutions and convened the Annual General Meeting and decided on the policy of the Company towards professional and wage equality. The Board also ruled on the decisions to be taken concerning the DNA Therapeutics acquisition - contribution of shares, capital increase remunerating the contribution of DNA Therapeutics shares, and completion of a private placement, etc. Finally, the Board approved a revised 2016 budget and reviewed the composition of the Board committees.

**The Board meetings of April 27-28, 2016** sales figures for Q1 2016 were approved alongside the terms of the associated press release.

The Board meetings of July 27-28, 2016 approved the half yearly accounts at June 30, 2016 and approved the half yearly financial report alongside the terms of the associated press release. It noted the cancellations of securities giving access to capital during the course of the first half of 2016.

Finally, the Board:

- Adopted a new stock option plan and a new allocation of bonus shares to employees and the Chief Executive
   Officer,
- Adopted a new warrant plan for non-salaried non-executive Board members.



- Noted a capital increase resulting from the exercise of stock options and amended Article 6 of the by-laws.

The Board meeting of September 20, 2016 approved the principle of a capital increase through the issuance of new shares without preferential subscription rights in favor of a category of persons under the authorization granted to the Board by the General Meeting of April 6, 2016 under its seventeenth resolution and subdelegated to the Chief Executive Officer all powers to carry out the planned new issue.

The Board meetings of October 24-25, 2016 recorded the completion of the capital increase, the principle of which was approved on September 20, 2016 and approved the terms of its supplementary report on the said capital increase. The Board approved the sales figures for Q3 2016 alongside the terms of the associated press release. The Board determined that the performance conditions for the executive stock option plan were met for the period from October 27, 2015 to October 25, 2016.

The Board approved a new warrant plan for a consultant of the Company.

Finally, the Board noted the vesting of the bonus shares granted by the Board of Directors on September 22, 2014, approved the increase in share capital by issuing 137,761 new shares with a nominal value of €0.25 each, and amended Article 6 of the by-laws.

**At its meeting of 21 December 2016**, the Board approved the 2017-2020 strategic plan as well as the budget for 2017.

The Board also:

- Recognized the lapsing of stock options and bonus shares, due to the departure of certain employees of the Group,
- It determined (i) the percentage of corporate and individual objectives that the Chief Executive Officer
  achieved for determining the amount of his variable compensation for financial year 2016, and (ii) the
  compensation of the Chief Executive Officer for financial year 2017, as well as the 2017 objectives for the
  Chief Executive Officer.

## 5.1.1.3.2 Audit Committee

#### Composition

Audit Committee members are selected from among the directors. They are appointed on a personal basis and cannot be represented. The term of office of the committee members coincides with that of their directorship.

The committee may only include members of the company's Board of Directors, excluding those in management positions.

It is composed of two or three members, of whom one at least must have specific financial or accounting skills and be independent.

The Audit Committee is presently composed of three members: Mrs. Danièle GUYOT-CAPARROS, who chairs it, Mr. Joseph ZAKRZEWSKI and Mr. Nicolas TREBOUTA, permanent representative of Société Financière de la Montagne. Mrs. Judith GRECIET, Chief Executive Officer, attends the meetings as an invitee of the Audit Committee.

As of the date of this report, the Committee has two independent Directors including its Chairman.

#### Mission objective

The Audit Committee's overall mission is to assist the Board of Directors in monitoring issues related to the development and control of semi-annual and annual accounting and financial information as well as elements to assess the risks incurred by the Group.

It examines the accounts prior to their presentation to the Board and gives views on the appointment and remuneration of the auditors as well as elements relating to their independence.

As part of its review of the company's consolidated financial statements, the Audit Committee ensures that the adopted accounting principles, which have a significant impact on the presentation of the financial statements of the company, have been formally validated by the executive management and the auditors and that they are brought to the knowledge of the Board of Directors. It also ensures that the main accounting options and



choices made have been explained and justified by the executive management to the Board and reviewed by the Auditors. Finally, it ensures that the Auditors have access to all information necessary to carry out their responsibilities and that they were able to present all their material observations.

Within the framework of internal control, the Audit Committee ensures the monitoring of the effectiveness of the internal control systems.

The Company became aware of the final AMF report concerning the 22 July 2010 Audit Committee and has used it to complete the role of the Committee.

#### **Organization and minutes**

The Audit Committee meets at least twice a year in advance of the approval of yearly and half-yearly financial statements. In 2016 three sessions were held with a 100 % participation rate.

The Committee met on **February 26, 2016** at which time the 2015 consolidated financial statements and the audit of the 2015 accounts were presented and thoroughly reviewed. It also reviewed the Company's risk management process and the Chair's report on corporate governance, risk management and internal control.

During its July 26, 2016 meeting, the Committee reviewed all documents related to the half-year results.

At its meeting of **October 21, 2016,** the Committee reviewed the ERP project to implement SAP Business by Design.

At its various meetings, the Audit Committee heard from the Group's CFO and the auditors who submitted their comments.

#### 5.1.1.3.3 Compensation Committee

## Composition

The members of the Compensation Committee are selected from among Onxeo directors or external experts. They are appointed on a personal basis and cannot be represented. The term of office of the committee members coincides with that of their directorship.

At the time of this report, the Compensation Committee comprises four members:

Mr. David SOLOMON as it Chairman, Mr. Nicolas TREBOUTA representing Société Financière de la Montagne, Mr. Russell GREIG and Mr. Jean-Pierre KINET. It is made up of three independent Directors including its Chairman. Mrs. Judith GRECIET, Chief Executive Officer, attends the meetings as an invitee of the Audit Committee.

#### Mission objective

The Compensation Committee is responsible for preparing the decisions of the Board of Directors in particular on (i) the determination of the main annual objectives of Management and, where applicable, the Deputy Managing Director, (ii) the initial level and any increase in Management and possibly the Deputy Managing Director (including the fixed and variable portions and benefits in kind, including stock options or share purchase or bonus shares), (iii) the distribution of attendance fees allocated to directors, (iv) any exceptional remuneration of directors for specific tasks or duties assigned by the Board.

Moreover, Management informs it of the Company's remuneration policy and proposes draft allocation plans of stock options, share purchase warrants and bonus shares.

## **Organization of works**

The Compensation Committee meets at least once a year. In 2016, it held four sessions with a 100% participation rate.

At its meeting on **January 21, 2016**, the committee examined the variable remuneration of the Chief Executive Officer for 2015 and her objectives for 2016. It also discussed the Chief Executive Officer 's remuneration for the financial year 2016.

At its meeting of **July 26, 2016**, the Committee reviewed the beneficiaries of the new stock option and bonus share plans.



At its meeting on **October 26, 2015**, the Committee reviewed the attainment of the performance conditions of the stock option allocation plans and 2014 bonus shares for the Chief Executive Officer. It examined the conditions for granting new stock options and bonus shares to executives and employees of the Company. The Committee also reviewed the conditions of the warrant plan for non-salaried non-executive Board members.

At its meeting on **December 20, 2016**, the committee examined the variable remuneration of the Chief Executive Officer for 2016 and her objectives for 2017. It also discussed the Chief Executive Officer's remuneration for the financial year 2017.

#### 5.1.1.3.4 The Appointments and Governance Committee

#### Composition

The members of the Appointments and Governance Committee are selected from among Onxeo Directors or external experts. They are appointed on a personal basis and cannot be represented. The term of office of the committee members coincides with that of their directorship.

At of the date of this report, the Appointments and Governance Committee is composed of three members:

Mrs. Danièle GUYOT-CAPARROS as chairman, Mr. Thomas HOFSTAETTER and Mr. Jean-Pierre BIZZARI. It is composed of three independent Directors including its Chairman. An additional member may be appointed on a temporary basis to the Appointments and Governance Committee if his profile is suited to the subject at hand. Mrs. Judith GRECIET, Chief Executive Officer, attends the meetings as an invitee of the Audit Committee.

#### Mission objective

The Appointments and Governance Committee's mandate is to prepare the decisions of the Board of Directors in case of changes to the composition of the Board of Directors or Management.

In particular, it is responsible for:

- Presenting to the Board of Directors recommendations on the composition of the Board and its Committees, in particular on its changes;
- Preparing succession plans for the Board and Management;
- Annually reviewing of the list of the members of the Board who may be qualified as an 'independent member';
- Organizing any selection and evaluation process with a view to recommending to the Board of Directors the final list of candidates for a Director position; and
- Reviewing, alongside Management, the profiles of candidates for a position on the Executive Committee and participating, if necessary, in the interview process.

## Organization of works

The Appointments and Governance Committee meet on an ad hoc basis, but in any event no less than once a year. In 2016, it held two sessions with a 100% participation rate.

#### 5.1.1.3.5 The Business Development Committee

### Composition

The Business Development Committee members are selected from among the directors. They are appointed on a personal basis and cannot be represented. The term of office of the Committee members coincides with that of their directorship.

This Committee comprises Mr. Thomas HOFSTAETTER as Chair, Mr. Russell GREIG, Mr. Jean-Pierre BIZZARI and Mr. Jean-Pierre KINET. There are thus four independent directors including the Chairman. Mrs. Judith GRECIET, Chief Executive Officer, attends the meetings as an invitee of the Audit Committee.

#### Mission objective

The Business Development Committee supports and assists the executive management on matters of business development, namely on acquisition projects and strengthening the product pipeline as well as the Company's strategic direction.

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It prepares the Board's deliberations relating to the Company's strategic direction. It makes proposals and gives opinions and recommendations in its field of competence.

As such, it must:

- Discuss beforehand the strategic plan proposed by the Chief Executive Officer to the Board of Directors including research program issues and associated strategic choices with regard to the external and internal business context; and
- Study, propose targets and present its recommendations on the acquisition of new business projects, whether in the form of acquisitions of assets or companies (as well as their related financing) on any proposed the sale of assets, or investments belonging to the Company.

#### Organization of works

The Business Development Committee meets at least once a year. In 2016, it met on one occasion with a 100% participation rate.

## 5.1.1.4 Assessment of the Board of Directors

In accordance with recommendation No. 15 of the MiddleNext corporate governance code to which the Company adheres, the Chairman of the Board requests, once a year, that each member expresses their opinions on the Board's functioning and the preparation of its work.

The assessment completed in 2016 gave the Board the opportunity to review and amend the organization of the specialized committees, and to review more generally the organizational rules of the meetings of the Board to ensure greater fluidity of information and greater responsiveness of Directors.

## 5.1.2 INFORMATION ON THE DIRECTORS

The board does not have a director elected by employees or an observer.

Apart from Mrs. Judith Greciet, who is also the CEO of the Company, no Director exercises any executive or salaried function for Onxeo or for any company directly or indirectly controlled by Onxeo.

No family relationship exists between any Directors.

No Director has been sentenced for fraud, none has been involved in a management or director capacity in any corporate bankruptcy, receivership or liquidation during the past five years and none has been the subject of any official public incrimination and/or sanction that has been definitively issued by a statutory or regulatory authority. None of them has been prevented by a court from acting as a member of an administrative, management or supervisory body of an issuer or of taking part in the management or the running of the business of any issuer during the past five years. The other mandates/functions of the Directors noted hereunder are based on the interest declaration made by the Directors. The Company emphasizes that it disclaims any liability arising out of the information given by the Company management or its corporate officers.

## 5.1.2.1 Corporate offices

As of the date of the Registration Document, the Company Board of Directors comprises the following members:



#### Joseph ZAKRZEWSKI

Joseph Zakrzewski was appointed Chairman of Onxeo's Board of Directors on January 22, 2016. His mandate will expire at the shareholders' general meeting of 2019.

At 55 years old, Joseph Zakrzewski has over 25 years' experience as an executive in the biotechnology and pharmaceutical industry, serving on the board of directors of publicly and privately held companies, being advisor to a number of entities, and being involved in a number of philanthropic activities.

Mr. Zakrzewski was also a Venture Partner at Orbimed in 2010-11, the largest investment fund target at healthcare in the world. From 1988 to 2004, Mr. Zakrzewski took up different functions at Eli Lilly & Company, notably in R&D, manufacturing, finance and business development for the biotechnologies and proteins divisions.

Business Address 715 Street Road, New Hope, PA 18938 USA

## Terms of office and duties

## Within the Company

Chairman of the Board of Directors of Onxeo

## Outside the Company

At 31 December 2016, Joseph Zakrzewski is also:

- Director, Acceleron Pharmaceuticals (US)
- Director, Amarin Pharmaceuticals (US)
- Director, Insulet Corporation (US)

Over the past years, Joseph Zakrzewski has also hold, amongst others, the following post outside the company, which he no longer holds:

Director, Liposcience (US)



#### **Judith GRECIET**

Judith Greciet joined Onxeo on 1 March 2011, as Chief Operating Officer in charge of R&D and Operations. She has been CEO and a director of the company since 29 June 2011. Her term of office will expire at the annual shareholders' general meeting of 2017.

Age 48, Judith Greciet's career has been spent in various laboratories (including Zeneca, Wyeth), occupying important managerial and strategic international positions in the growing field of Oncology and Immunology, working on innovative products. She has a doctorate in Pharmacy and is a graduate in business and administration pharmaceutical marketing.

#### **Business address**

ONXEO

49, boulevard du Général Martial Valin - 75015 – Paris

France

#### Terms of office and duties

## Within the Company

Director and Chief Executive Officer of Onxeo

#### Outside the Company

As at 31 December 2016, Mrs. Judith Greciet is also:

Chairwoman of the Board of Directors of Onxeo Inc. (US)

Over the past 5 years, Judith Greciet has also performed the following functions and posts which she no longer performs:

- Chairwoman of the Board of Directors, Eisai France
- Director, Theravectys (France)
- Chairwoman of the Board of Directors, Laboratoires BioAlliance Pharma
- Director, France Biotech

## **Russell GREIG**

Russell Greig has been a director of Onxeo since 26 June 2013. His term of office will expire at the shareholders' annual shareholders' general meeting of 2019.

Russell Greig, 64, has over 30 years' experience in the pharmaceutical industry, with expertise in research and development and international business development. Russell Greig spent a significant part of his career at GlaxoSmithKline (USA/UK) where he was Senior Vice President of Worldwide Business Development R&D, President of Pharmaceuticals International and SROone, the investment fund of GSK.

# <u>Address</u>

1241 Karen Lane, Wayne, PA 19087-2759 USA

#### Terms of office and duties

#### Within the Company

- Director of Onxeo

## Outside the Company

At 31 Decembre 2016, Russell Greig is also:

- Chairman of the Board of Directors, AM Pharmaceuticals (Netherlands)
- Chairman of the Board of Directors, Mint Solutions (Netherlands)
- Chairman of the Board of Directors, Sanifit (Spain)
- Chairman of the Board of Directors, eTheRNA (Belgium)
- Director, Ablynx (Belgium)
- Director, TiGenix (Belgium)
- Venture Partner, Kurma Partners (France)

Over the past 5 years, Russell Greig has also performed the following functions and posts which he no longer performs:

- Chairman of the Board of Directors, Syntaxin (UK) now Ipsen (France)
- Director, Isconova (Sweden) now Novavax AB (US)
- Chairman of the Supervisory Board, Novagali (France) now Santen (Japan)

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#### Danièle GUYOT-CAPARROS

Danièle Guyot-Caparros has been a director of Onxeo since 26 June 2013. His term of office will expire at the annual shareholders' general meeting of 2019.

Danièle Guyot-Caparros is 58. After experience with an audit firm carrying out international assignments she joined Rhône-Poulenc, later to become Aventis and then Sanofi, occupying several important posts, notably with responsibilities carried out in France at European level and then in business planning and performance monitoring on a worldwide level.

## <u>Address</u>

4, rue d'Eblé 75007 Paris France

#### Terms of office and duties

## Within the Company

Director of Onxeo

#### Outside the Company

At 31 December 2016, Danièle Guyot-Caparros is also:

Director, Diaxonhit (France)

#### **David H. SOLOMON**

David Horn Solomon has been a director of Onxeo since 29 June 2011. His term of office will expire at the shareholders' annual general meeting of 2017.

Aged 56, David Horn Solomon has been Chief Executive Officer of public BIONOR PHARMA (Norway) since January 2015. A physician-pharmacologist, he was a faculty member at Columbia University from 1994-2001, before joining Carrot Capital Healthcare Ventures, a venture capital investment firm. Since 2006, he has held chief executive positions in Biotech companies, including recently from 2008-2015 as CEO of NASDAQ listed Zealand Pharma.

# Business address: Sund Capital ApS

Havnegade 39,

Copenhagen, Denmark

#### Terms of office and duties

#### Within the Company

Director of Onxeo

## Outside the Company

At 31 December 2016, David H. Solomon is also:

- Director and Chairman of the Remuneration Committee, TxCell SA (France)
- Director, Promosome Inc (US).
- Director of the American Chamber of Commerce in Denmark
- Director, Cass Foundation (UK)

Over the past 5 years, David H. Solomon has also performed the following functions and posts which he no longer performs:

- CEO, Zealand Pharma (Denmark)
- CEO, Bionor Pharma (Norway)



#### Terms of office and duties Thomas HOFSTAETTER Thomas Hofstaetter has been a director of Within the Company la Société Onxeo since 31 May 2012. His term of Director of Onxeo office will expire at the shareholders' annual general meeting of 2018. Over the past 5 years, Thomas Hofstaetter has also performed the following functions and posts which he no longer performs: Age 68, Thomas Hofstaetter holds a Director, Bionor Pharma ASA (Norway) doctorate in molecular biology (University Director, Geron Corporation (USA) of Tubingen, Germany). He has over thirty Chairman and CEO, VaxInnate Corporation (USA) vears' experience in corporate development and mergers and acquisition of pharmaceutical and biotechnology companies, particularly with Wyeth, Inc., Aventis, VaxInnate Corporation and Geron Corporation.

FINANCIERE DE LA MONTAGNE,
represented by Nicolas Trebouta

<u>Business Address</u>: Lindenstr. 37 60325 Frankfurt

Germany

Financière de la Montagne has been a director since 29 June 2011. Its term of office will expire at the shareholders' annual general meeting of 2017.

Age 53, Nicolas Trebouta has managed investments since 2004 directly through his company, Financière de la Montagne, or through biotech funds. Co-founder of Chevrillon and Associates in 2000, he participated via this organization in several LBO operations including Picard Surgeles, the printer CPI and Albingia Insurance. He is a doctor and has been a shareholder of BioAlliance since 2008.

#### **Business Address:**

Financière de la Montagne 4-6, Rond-Point des Champs Elysées 75008 Paris France

## Terms of office and duties

#### Within the Company

Director of Onxeo

# Outside the Company

At 31 December 2016, Nicolas Trebouta is also:

- Manger, SCI du Chardonnet
- Manger, SARL Financière de la Montagne
- Manger, SCI Fleurus Immobilier
- Manger, SCI 5 rue de la Liberté
- Chairman, SAS Dragon 8
- Manger, SC Financière des Associés
- Director, GIE IO
- Chairman of the Supervisory Board, SCA Chevrillon & Associés
- Manger, EARL Ferme de Bissy
- Manger, SC Valois
- Manger, SCI du Trillon
- Co- Manger, SC Aster

Over the past 5 years, Nicolas Trebouta has also performed the following functions and posts which he no longer performs:

- Chairman and CEO, SICAV Mercure Epargne Longue

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#### Jean-Pierre BIZZARI

Jean-Pierre Bizzari has been a director since 6 April 2016. His term of office will expire at the shareholders' annual general meeting in 2019.

Age 63, Dr. Jean-Pierre Bizzari was Executive Vice-President and Head of Clinical Development in Oncology (US, Europe, Asia, Japan) at Celgene from 2008 to 2015. He took part in the clinical development of several anti-cancer compounds such as Taxotere®, Eloxatin®, Abraxane® and Irinotecan® (CPT-11). A renowned oncologist worldwide, he is a member of the Scientific Committee of the French National Cancer Institute ("Institut National du Cancer" (INCa)), of the European Organisation for Reaserch and Treatment of Cancer (EORTC), and Chairman of the New Drug Advisory Committee. Dr. Bizzari is also an active member of the Board of Director of several French and American biotechnology company. He has published over 70 articles un prestigious scientific titles and presented over 160 abstracts at scientific congresses.

<u>Business address</u> 235 Laurel lane Haverford- PA 19041 - USA

#### Terms of office and duties

## Within the Company

Director, Onxeo

#### Outside the Company

At 31 December 2016, Jean-Pierre Bizzari is also:

- Director, Transgene SA (France)
- Director, Halozyme Therapeutics (US)
- Director, Pieris Pharmaceuticals (US)
- Director, iTeos Therapeutics (Belgium)
- Director, Nordic Nanovector ASA (Norway)
- Director, European Organisation for Research and Treatment of Cancer (EORTC)

Over the past 5 years, Nicolas Trebouta has also performed the following functions and posts which he no longer performs:

Director, Celator Pharmaceuticals (US)

#### Jean-Pierre Kinet

M. Jean-Pierre Kinet has been a director since April 6, 2016. His term of office will expire at the annual shareholders' general meeting of 2019.

Age 64, Professor Jean-Pierre Kinet M.D. is one of the world's most eminent immunologist, most widely known for his discovery of genes and proteins in relation to the E-receptor of immunoglobulin. His scientific discoveries have contributed towards new therapies and diagnostic tools for the treat of immune diseases. He is also co-founder and founder of two biotechnology companies and director of several others across Europe.

Business Address 42 rue de Berri 75008 Paris - France

#### Terms of office and duties

#### Within the Company

- Director of Onxeo

### Outside the Company

At 31 December 2016, Jean-Pierre Kinet is also:

- Director, AB Science SA (France)
- Director, Pharmaleads SA (France)
- Chairman of the Board of Director, Vaxon SA (France)
- Chairman, Ixlife Capital SAS (France)

Over the past 5 years, Nicolas Trebouta has also performed the following functions and posts which he no longer performs:

- Chairman of the Board of Director, Theravectys SA (France)
- Chairman of the Board of Director, UCB Pharma SA (Belgium)



## 5.1.2.2 Conflicts of interests

As provided by the bylaws of the Board of Directors, each director must potential avoid any conflict – whether material or moral – between their interests and those of the Company. They must disclose to the Board fully and without delay any conflict of interest – whether actual or potential – that might implicate them directly or indirectly.

In the case of a conflict of interest, even if potential, arising after the start of his term of office, the relevant director must disclose it to the Board of Directors without delay, abstain from any debates and votes on the matters concerned by this conflict and, if relevant, resign.

An omission or silence by a director is treated as a positive affirmation that no conflict exists.

To the Company's knowledge, at the date of the present Registration Document, there are no conflicts of interest between the Directors' duties towards the Group and their private interests and/or other duties.

# 5.1.2.3 Independence

At the date of the Registration Document, the Company estimates that its Board of Directors counts six independent directors as defined in MiddleNext code of governance: Russell Greif, Danièle Guyot-Caparros, Thomas Hofstaetter, Joseph Zakrzewski, David Solomon, Jean-Pierre Kinet and Jean-Pierre Bizzari.

#### 5.1.2.4 Directors' remuneration

The remuneration of corporate officer is generally in the form of a fixed fee, sometimes complemented by benefits in kind (typically a company car) and a variable fee indexed to performance indicators.

This remuneration can be further by allocation of stock-options or free-shares in order to guarantee retention.

Directors' are remunerated in the form of directors' fees paid only to independent directors.

The maximum annual amount of attendance fees was set for 2016, and any subsequent year, by the Combined General Meeting of Shareholders of 6 April 2016 at €220,000.

In accordance with the decision of the Board Meeting, it was paid as follows:

- the directors receive a fixed, prorated remuneration of €36,000 for their position, and variable remuneration of €2,500 per Board meeting;
- the Chairman of the Board receives fixed, prorated remuneration of €9,400 for his position and variable remuneration of €3,000 for each Board meeting;
- committee members who are also independent directors receive additional variable remuneration of 1,000 euros per committee meeting of which they are a member, apart from the Corporate Development Committee where such remuneration has been set at 2,000 euros; and
- committee chairpersons receive additional variable remuneration of 2.000 euros per committee meeting of which they are chairman, apart from the Corporate Development Committee where such remuneration has been set at 3.000 euros.

Directors who exercise a management role or who represent a corporate shareholder shall not receive attendance fees.

The Board of Director agreed to four allocations of share purchase warrants (BSAs) to non-salaries, non-executive directors of the Company. The characteristics of these BSAs are detailed at table 8 of section 5.2.2 of the Registration Document.



Directors' fees and other remuneration received by non-executive corporate officers					
Non-executive corporate officers	Amounts for FY 2016 8 board meetings and 10 committee meetings		Amounts for FY 2015 8 board meetings and 7 committee meetings		
	Directors' fees in €	Other remunerations	Directors' fees in €	Other remunerations	
Joseph Zakzewski	69 000 €	157 500 BSA	N/A	N/A	
Russell Greig	25 400 €	-	19 900 €	15 000 BSA	
Danièle Guyot-Caparros	29 400 €	-	25 400 €	-	
David Solomon	23 900 €	47 500 BSA	18 400 €	20 500 BSA	
Thomas Hofstaetter	27 400 €	20 000 BSA	25 400 €	15 000 BSA	
Financière de la Montagne Represented by N. Trebouta	N/A	47 500 BSA	N/A	20 500 BSA	
Jean-Pierre Kinet	19 550 €	30 000 BSA	N/A	N/A	
Jean-Pierre Bizarri	17 550 €	47 500 BSA	N/A	N/A	
Patrick Langlois	3 556 €	2 000 € (*)	35 400 €	13 000 BSA 24 000 € (*)	
TOTAL	215 756 €	350 000 BSA 2 000 €	124 500 €	84 000 BSA 24 000 €	

 $<sup>(*) \</sup> Consultancy \ contract \ signed \ by \ Onxeo \ and \ PJL \ Conseils \ on \ 1 \ July \ 2012 \ providing \ for \ a \ fixed \ fee \ of \ 2000 \\ \textcircled{$\in$ (excl. VAT)$ per month.}$ 

Directors do not benefit from any deferred indemnity or remuneration on any termination of their term of office.

## 5.1.2.5 Agreement with main shareholders, clients or suppliers

To the knowledge of the Company, at the date of the Registration Document, no deal or agreements exists entered into with the main shareholders, clients or suppliers, whereby a director was designated as member of the Board of directors, management or supervisory body or the general management.

## 5.1.2.6 Restrictions accepted by corporate officers to sell their shares

To the knowledge of the Company, at the date of the Registration Document, there is no restriction accepted by the corporate officers to sell the shares they hold in the Company.

# 5.1.2.7 Information on service agreement between members of the Board of the Directors, Executive Committee, or Supervisory Board of the Company or its subsidiaries

There is no service agreement entered into between members of the Board, management or supervisory body and the Company or one of its subsidiary.

## 5.2 THE EXECUTIVE COMMITTEE

As of the date of this Registration Document, the executive management of this Company is exercised by Judith Greciet, Chief Executive Officer, of whom a presentation is provided in Section 5.1.2.1 above.

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#### 5.2.1 LIMITS PLACED BY THE BOARD ON THE POWERS OF THE CEO AND ITS DEPUTIES

The Board's bylaws, which are available on the Company's website, set out the terms of the CEO's powers and duties.

The Chief Executive Officer and the Chief Operating Officer cannot undertake certain acts, measures, commitments or contracts if they have not obtained prior authorization from the Board of Directors.

Accordingly, in addition to those Company operations that legally require the Board of Directors authorization - including sureties, guarantees, endorsements and the establishment of collateral arrangements for the purposes of ensuring third party commitments – the following require the Board's prior approval:

- Finalization of the annual budget;
- Any decision to acquire or dispose of Company or business assets, or any decision to invest in a company, by any means whatsoever;
- Any decision of acquisition or disposal of assets or investments or any contract that commits the Company for an amount exceeding €400,000 per year for any decision other than those approved in the Company's annual budget; and
- Any decision to make available or grant rights to important intellectual or industrial property or tangible assets owned by the Company.

## 5.2.2 REMUNERATION OF EXECUTIVE COMMITTEE MEMBERS

The remuneration of Executive Committee members is generally composed of a fixed salary supplemented by a benefit in kind (usually a company car) and variable remuneration linked to performance indicators

This remuneration is accompanied by stock options and free shares, which are awarded for retention purposes.

Executive committee members receive no attendance fees for their position as corporate officers.

The Company has not put in place any severance compensation or any supplementary pension plans for corporate officers.

Onxeo complies with the MiddleNext Corporate Governance Code relating to the remuneration of its corporate officers for companies whose securities are admitted to trading on a regulated market.

## **Judith Greciet**

Ms. Judith Greciet joined Onxeo on March 2, 2011, as Chief Operating Officer in charge of R&D and Operations. She was appointed CEO on June 29, 2011.

Annual gross compensation for Ms. Judith Greceit was set at €304,500 for FY 2016 by the Board of Directors on 22 January 2016 upon proposal and recommendation of the Compensation and Appointments Committee.

The fixed compensation collected by Mrs. Judith Greciet was thus set at €304,500 for FY 2016.

On 22 January 2016, the Board of Directors also decided that the variable remuneration of the CEO would in principle represent up to 50 % of the fixed salary and that for FY 2016 it would be subject to the achievement of objectives related to research and development activities, the structuring of Company strategy, and the quality of investor relations. After recognition of the achievement of the objectives, on 21 December 2016, the Board set variable remuneration for Judith Greciet for 2016 at 100% of the envelope, which was subject by the Company's internal weighting of 50%, or €76,125.

In 2016, Ms. Judith Greciet received no attendance fees in accordance with the rules set out in the preceding paragraph and did not receive any other instruments providing access to capital, except for the allocation of stock options and free shares (AGA).

Judith Greciet did not receive any benefits in kind in 2016 other than a company car.

The tables below, pursuant to AMF recommendation n° 2014-14 « Guide d'élaboration des documents de référence adapté aux valeurs moyennes », present a summary of all elements relating to corporate officers' remuneration.



Table 1 – Table summarizing the compensation, stock options and free-shares allocated to each executive corporate officer

Summary table of remuneration, options and shares allocated to each executive officer (in €)				
Judith Greciet – Chief Executive Officer	FY 2016	FY 2015		
Remuneration payable in respect of the financial year (broken down in Table 2)	383.603	439.486		
Value of options awarded during the year	42.700	24 600		
Value of performance shares awarded during the year	84.600	N/A		

Table 2 - Summary table of the compensation of each executive corporate officer

Summary of remuneration paid to each executive officer (in €)					
Judith Greciet – Chief Executive Officer	Amounts in 2016		Amounts in 2015		
	Owed	Paid (1)	Owed	Paid (1)	
- fixed remuneration (2)	304.500	304.500	300.188	320.151	
- variable remuneration (3)	76.125	127.500	127.500	137.106	
- exceptional remuneration	N/A	N/A	N/A	86.692	
- directors' fees	N/A	N/A	N/A	N/A	
benefits in kind (4)	2.978	2.978	3.314	3.314	
TOTAL	383.603	434.978	431.002	547.261	

- (1) Payment of variable remuneration for year N to year N + 1
- (2) Fixed compensation includes base salary, the monetary value of paid leave, and any back pay or absences
- (3) Variable remuneration depending on the fulfillment of objectives particularly related to R&D, corporate strategy, financial management, investors relations and the organization of the Company.
- (4) Company vehicle

Table 3 – Directors' fees and other remuneration received by non-executive corporate officers.

Table 3 is provided in Section 5.1.2.4 of this Registration Document.

# Table 4 – Stock options to purchase or subscribe for shares granted during the financial year to each corporate officer

During FY 2016, 70,000 stock options were allocated to Mrs. Judith Greciet in her capacity as executive corporate officer (see table 8 hereinafter). These options were only exercisable from a period of four (4) years, subject to the achievement of performance conditions assessed one year after their allocation and related to (i) continuing the growth strategy by acquisition/licensing of at least two new projects and optimization of the integration of these projects; (ii) the results of Livatag® phase III trial depending on the planning schedule; (iii) successful stock market developments as assessed against a benchmark of comparable companies in the industry.

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Stock-Options allocated during the FY 2016 to each executive corporate officer.								
Name of the executive corporate officer	Allocation date	Category of options	Valuation of the options pursuant to the Black & Scholes method (in euros)	Amount of options allocated in the fiscal year	Exercise price	Expiration date		
Judith Greciet	27/07/2016	Subscription of options		70,000	3.16€	27/07/2026		
TOTAL			70,000					

Table 5 – Stock options to purchase or subscribe for shares exercised during the financial year by each executive corporate officer

No option to purchase or subscribe for shares was exercised by the corporate officers in 2016.

# Table 6 – Performance shares awarded during the financial year to each corporate officer

During FY 2016, 30,000 free shares (AGA) were allocated to Mrs. Judith Greciet in her capacity as executive corporate officers.

These shares will be acquired after a one year delay and subject to certain performance criteria: (i) continuing the growth strategy by acquisition/licensing of at least two new projects and optimization of the integration of these projects; (ii) the results of Livatag® phase III trial depending on the planning schedule; (iii) successful stock market developments as assessed against a benchmark of comparable companies in the industry

# Table 7 - Performance shares that became available during the financial year for each corporate officer

A total of 44,491 free bonus shares (AGA) allocated to Mrs. Judith Greciet in her capacity as executive corporate officer on 22 September 2014, become available during FY 2016.

# Table 8 – History of the allocation of stock warrants and options

As part of its policy of remunerating and motivating its executives and employees, Onxeo regularly establishes plans for awarding special founders' share purchase warrants and free bonus shares.

The independent directors have also benefited from regular plans for the distribution of BSAs. From 2014, these distributions were extended to all non-executive and non-salaried directors of the Company.

Whether for BSAs or SOs, the subscription price is determined as the weighted average by the volume of the past 20 days on the stock market prior to the date of distribution.

The terms of exercise of the SO and BSA distributed to executives and corporate officers, issued at 31 December 2016 are described in Table 8 hereunder.



History of the awards of financial instruments granting rights to the share capital Information on the BSA and SO allocated to corporate officers								
	SO Dir.2011	SO Dir.2012	SO Dir.2014	SO Dir.2015	SO Dir.2016			
Date of AGM	29/06/2011	31/05/2012	30/06/2014	20/05/2015	06/04/2016			
Date of Board of Directors meeting	21/09/2011	13/09/2012	22/09/2014	27/10/2015	28/07/2016			
Exercise terms			1 SO/1 share					
LACICISE (CITIIS		Vesting 4 years s	subject to perforn	nance conditions				
Shares that may be subscribed by executive corporate officers (Judith Greciet) (1)	167,453 <sup>(2)</sup>	56,507	18,871	60,000	70,000			
Start date for exercise	21/09/2015	13/09/2016	22/09/2018	27/10/2015	28/07/2016			
Expiry date	21/09/2021	13/09/2022	22/09/2024	27/10/2025	28/07/2026			
Subscription price (1)	3.63	3.75	6.17	3.61	3.16			
Shares subscribed at 31/12/2014	0	0	0	0	0			
Cancelled or lapsed shares	0	0	7,156	0	0			
Options remaining at 31/12/2014 <sup>(1)</sup>	219,782	103,597	18,871	60,000	70,000			

<sup>(1)</sup> After adjustment of the number and subscription price of warrants following the capital increases of July 2011, July 2013 and December 2014 in accordance with Article L.228-99 of the Commercial Code (Board meeting of 28 July 2011, 14 November 2013 and 22 January 2015)



# Table 8 (continued)

	BSA 2011	BSA 2012	BSA 2013	BSA 2014	BSA 2014-2	BSA 2015-1	BSA 2015-2	BSA 2016-1	BSA 2016-3
Date of AGM	28/07/2011	31/05/2012	26/06/2013	30/06/2014	30/06/2014	20/05/2015	20/05/2015	06/04/2016	06/04/2016
Date of Management Board/Board of Directors meeting	21/09/2011	13/09/2012	19/09/2013	22/09/2014	4/03/2015	27/10/2015	22/01/2016	27/10/2016	21/12/2016
Exercise terms				1 warrant/	1 share - Vesting	/18 months			
Shares able to be subscribed by corporate officers (1)	41,864	41,857	88,490	85,886	19,000	65,000	90,000	190,000	70,000
of which Joseph Zakrzewski	N/A	N/A	N/A	N/A	N/A	N/A	90,000	50,000	17,500
of which David Solomon	15,699	0	15,616	13,013	5,500	15,000	0	30,000	17,500
of which Thomas Hofstaetter	N/A	15,696	15,616	13.013	0	15,000	0	20,000	0
of which Danielle Guyot-Caparros	N/A	N/A	15,616	13.013	0	0	0	0	0
of which Russell Greig	N/A	N/A	15,616	13.013	0	15,000	0	0	0
of which Jean-Pierre Bizarri	N/A	N/A	N/A	N/A	N/A	N/A	N/A	30,000	17,500
of which Jean-Pierre Kinet	N/A	N/A	N/A	N/A	N/A	N/A	N/A	30,000	0
of which Financière de la Montagne	N/A	N/A	N/A	13.013	5,500	15,000	0	30,000	17,500
of which Patrick Langlois	26,165	26,161	26,026	20.821	8,000	5,000	0	N/A	N/A
Starting date for exercise of BSAs	21/03/2012	13/03/2013	19/03/2014	22/03/2015	4/09/2015	27/10/2016	22/01/2016	27/10/2016	21/06/17
Expiry date	21/09/2017	13/09/2018	19/09/2023	22/09/2024	4/03/2025	27/10/2025	22/01/2025	27/10/2025	21/12/2026
Issue price	0.38€	0.39 €	0.40 €	0.64 €	0.63 €	0.36 €	0.33€	0.26€	0.24€
Subscription price (1)	3.78€	3.75 €	3.85 €	6.17 €	6.26 €	3.61 €	3.33€	2.61€	2.43€
Shares subscribed at 31/12/2014	0	0	0	0	0	0	0	0	
Total BSAs cancelled or lapsed	0	0	0	0	0		0	0	
BSAs outstanding at end of period (1)	41,864	41,857	88,490	85,886	19,000	65,000	90,000	190,000	70,000

<sup>(1)</sup> After adjustment of the number and subscription price of warrants following the capital increases of July 2011, July 2013 and December 2014 in accordance with Article L.228-99 of the Commercial Code (Board meeting of 28 July 2011, 14 November 2013 and 22 January 2015)

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Table 9 — Warrants and stock options granted during the financial year to the top ten non-executive employees or exercised by them

Warrants and stock-options granted to the ten employees other than corporate officers receiving the largest number of options	Number of warrants or stock-options granted	Weighted average price	Plan
Stock-options granted, over the fiscal year, to the ten employees other than corporate officers receiving the largest number of stock- options granted (overall information)	245,000	3.16 €	2016 SO Employee Plan

# Table 10 – Free shares allocation history

Free shares allocation history Information regarding the free shares allocated					
	AGA 2016				
Date of General Assembly meeting	6/04/2016				
Date of Board of Directors meeting	28/07/2016				
Total number of free shares (1) allocated	164,750				
Including free shares allocated to executive corporate officers (Judith Greciet) (1)	30,000				
Acquisition date of the free shares	28/07/2017				
End of the conservation period	28/07/2018				
Options cancelled or lapsed	16,700				
Options remaining as of 31/12/2016	148,050				

<sup>(1)</sup> Subject to performance conditions. Performance conditions are related to the progress of R&D programs, company and business development activities, and the performance of the Company stock price.

Table 11 – Other benefits of executive corporate officers

Executive Corporate Officer	Employment contract		Supplementary pension plan		Indemnities or benefits due in respect of termination or change in duties		Indemnities related to a non- competition clause	
	Yes	No	Yes	No	Yes	No	Yes	No
Judith Greciet CEO In office since: 29/06/2011 End of term: Shareholders' meeting called to approve the financial statements for the year ending on 31/12/2016		x	x			x		x

During the Board meeting of 21 May 2014 and on the proposal of the Appointments and Compensation Committee dated 16 May 2014, the board approved the suspension of the employment contract of Judith GRECIET with effect from 1 July 2014 for the duration of her term of office as Deputy CEO.

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All commitments relating to remunerations, indemnities or benefits owed or likely to become owed by the Company as a result of the start, cessation, or change of function by corporate officers:

Within the Group, there are no such commitments subject to the procedure in Article L. 225-42-1 of the French Commercial Code.

During the financial year 2016, the Company has no allocated any capital or debt securities to the executives.

Pursuant to Articles L.225-197-1 & L.225-185 of the French Commercial Code, the Board of Directors, upon recommendation of the Compensation Committee, has decided on a quota of shares (whether allocated or subscribed to as a result of secondary issues) that the executive corporate officers of Onxeo must keep as bearer shares until the expiry of their duties to the Company. This quota was set at 10% of the interests after tax and linked contributions obtained via secondary issues.

Moreover, the Group's pension commitment for its executive corporate officers totals €73,184 as at 31 December 2016 (consolidated accounts IFRS).

# 5.3 INTERESTS HELD BY DIRECTORS AND CORPORATE OFFICERS OF THE COMPANY

Interests held by directors and officers in the Company's share capital at 31 December 2016.

Interests held by directors and officers in the Company's share capital at 31/12/2016	Number of shares	% of share capital	Number of shares resulting from the potential exercise of BSAs	Number of shares resulting from the potential exercise of options	Number of free shares	Total % after potential exercise of warrants and stock options
J. Greciet	44 491	0,09%		374 222	30 000	0,95%
Financière de la Montagne	6 403 379	13,61%	81 013			13,78%
J. Zakrzewski	5 000	0,01%	67 500			0,15%
P. Langlois			112 173			0,24%
R. Greig			43 629			0,09%
D. Guyot-Caparros			28 629			0,06%
T. Hofstaetter			79 325			0,17%
D. Solomon			112 328			0,24%
J.P. Bizarri			47 500			0,10%
J.P. Kinet			30 000			0,06%
Total	6 452 870	13,72%	602 097	374 222	30 000	15,86%

# 5.4 TRANSACTIONS BY DIRECTORS AND CORPORATE OFFICERS IN THE COMPANY'S SHARES

In accordance with the provisions of Article L. 621-18-2 of the French Monetary and Financial Code, we submit to your attention the transactions involving the Company's securities (acquisitions, divestments, subscriptions or exchanges of securities) made, to the best of the Company's knowledge, by Company management or members of the Board of Directors or people with close personal ties in FY 2016. The Company emphasizes that it disclaims all liability regarding information provided by or corporate officers.



Person concerned	Nature of transaction	Date of Transaction	Number of securities	Amount of transaction (In €)
Joseph ZAKRZEWSKI, Chairman of the Board of Directors	Purchase	05 October 2016	5 000	12 899,50
Financière de la Montagne SARL, Director	Subscription	05 October 2016	741 847	1 706 248,10

Some directors have subscribed, entirely or partially, to the share purchase warrants (BSA) that were allocated to them by the Board of Directors meetings on 22 January 2016, 28 July 2016, 25 October 2016, and 21 December 2016, totaling for 380,000 BSAs.

# 5.5 INTERNAL CONTROLS

#### 5.5.1 COMPONENTS OF THE RISK MANAGEMENT SYSTEM

## 5.5.1.1 Definitions and objectives

The process for risk management set up by Onxeo aims to identify the entirety of risks capable of affecting the Company's activities and processes and to define means to control the occurrence of these risks and their consequences, to contain and reduce their probability of occurring as well as their impact on the Company's activity. This process is geared at all types of risks and is applicable to all activities by the Company and the Group.

Onxeo adopts the definition of risk management proposed by the AMF<sup>32</sup> (French Financial Market Authority), according to which risk management is a function of the Company's internal governance which aims to:

- Create and preserver the value, assets and goodwill of the Company;
- Ground the Company's decision-making process to achieve its objectives;
- Facilitates greater coherence between the decisions and values of the Company;
- Rallies the partners towards a common vision of the key risks faced by the Company.

The Company has conducted a review of its risks and considers that there are no other key risks safe for those mentioned hereunder.

# 5.5.1.2 Organizational framework

The Group also ensures there is adequate control of its operational risks. Risk management is steered by the Risk Committee, a management body established by executive management. Its responsibilities include proposing and updating annual risk mapping and subsequently reviewing the execution of the risk monitoring plans with those in charge of the particular activity.

It is the Executive Committee's responsibility to validate the mapping put before them by the Risk Committee and in particular approval of the list of "major" company risks.

The annual risk management and mapping processes are presented each year to the Audit Committee within the context of its mission to review and monitor the effectiveness of internal control and risk management systems.

The Group has adopted a procedure that is intended to frame all the risk management methods and tools implemented and which specifies the terminology adopted in the Group - criteria of likelihood and severity, and types of risks, etc.

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<sup>&</sup>lt;sup>32</sup> Guide de mise en œuvre du cadre de référence sur le contrôle interne adapté aux valeurs moyennes et petites mis à jour le 22 juillet 2010



The objectives of this risk management policy are primarily to preserve the Group's assets and reputation, keep its costs to a minimum and promote the achievement of its strategic objectives.

# 5.5.1.3 Risk management process: identification and analysis of the main risks

The Risk Committee annually updates the mapping of risks in order to take into account the company's strategic objectives as well as the evolution of its activities, its financial situation and its environment.

For each of the identified risks, the Committee analyses its potential impact in terms of its financial effect, work days lost, impact on the company's activity and image, and assigns a probability index and a criticality index from which they deduce a factor from the combining of these two criteria.

Risks are then ranked in order of decreasing importance to categorize them according to the following classification: major risk, high risk, or acceptable risk.

Any major risk falls under a risk management plan specifying actions to be taken, persons in charge, main persons involved, deadlines, and the budget associated with each action.

The following major risk factor descriptions are organized in a manner consistent with this risk mapping.

## 5.5.1.4 Risk factors

## 5.5.1.4.1 Risks related to the Group's activity

#### 5.5.1.4.1.1 Risks related to drug research and development

# The risk of serious side effects in a clinical trial or negative results of a clinical trial could affect the Group's growth

To obtain marketing authorization for a product, the Company must conduct preclinical trials on animals and complete clinical trials on humans in order to demonstrate the product's safety and effectiveness.

If patients are or were to be exposed to unexpected and serious risks, the Company could choose, or the regulatory authorities could ask the Company, to suspend or end clinical trials. Deaths and other undesirable events could occur during a clinical trial because of medical problems, which may or may not be related to the treatment being tested and require the Company to delay or interrupt the trial.

In addition, the Company may decide, in view of negative results, to abandon development projects that it initially considered promising.

The inability of the Company to complete clinical trials successfully could have a material adverse effect on its ability to generate future revenues, its financial condition, and its development.

To minimize risk, the Company conducts its trials by taking maximum precautions, particularly in defining protocols, using associated experts, and studying competing products. In addition, some products developed by the Company are using active ingredients existing on the market, for which the profiles of effectiveness and tolerance are well established.

From a strategic point of view, the Company has organized its portfolio of products in development into several independent lines, each based on a technology or a novel active mechanism. This allows the Company to face the risks inherent in pharmaceutical research and to determine its priorities for accelerating development at any time based on the results obtained, as part of its ongoing search for growth.

## The risk of significant delays in the conduct of its clinical trials could affect the Group's growth

As a general rule, clinical trials extend over several years and are very costly. Their completion depends on a number of important parameters such as the indication, the size of the population affected, the nature of the clinical protocol, the proximity of the patients and the clinical sites, the criteria for eligibility for the trials, competition for patient enrolment, the availability of sufficient quantities of products, assistance from third parties and compliance with regulatory standards.



In 2016, Onxeo continued the Phase III clinical trial of Livatag® in HCC and expects to announce preliminary effectiveness results by mid-2017, in line with the defined schedule.

If, for reasons associated with one or more of the aforementioned parameters, a significant delay were to arise in a trial resulting in development times significantly deviating from estimates, this could have an adverse impact on the Company's ability to generate future revenue, its financial condition, and its development.

This risk becomes less critical as development of the Company's products advances.

#### 5.5.1.4.1.2 Risks related to the market acceptance of the Group's products

The commercial success of the Group strongly depends on its ability to gain and retain the support of the medical community, prescribing physicians and paying agencies. The degree of acceptance by the market depends on several factors, in particular:

- the perception of the therapeutic benefit by the prescribing physicians;
- the possible occurrence of undesirable side effects not detected during the clinical trials;
- the reimbursement policies of different countries and, more generally, of public or private paying agencies; and
- the effective implementation of a scientific publication strategy.

Furthermore, while the Group believes that its products will provide a therapeutic response to a need that is currently unmet, competing therapeutic solutions, whether in existence, under development, or previously unknown, could, in the near or more distant future, gain significant market shares and limit the Group's ability to market its products successfully.

Poor market penetration as a result of one or more of the abovementioned factors could have an adverse effect on the Group's business, prospects, financial position, results and development.

## 5.5.1.4.1.3 Risks related to outsourcing of clinical studies conducted by the Group

The Company is in a situation of dependency in relation to the providers involved in the clinical trials that the Company launches.

The Company uses various providers in France and abroad to carry out its clinical trials. The quality of test results depends mainly on the quality of the desired services and their compliance with the original specifications and applicable standards.

The failure of a subcontractor involved in a clinical trial, the loss of data, delays or errors in data processing could have an adverse effect on the validity of tests and the compilation of regulatory filings for products under development by the Company.

To address this risk, Onxeo audits the processes of its subcontractors and rigorously monitors clinical trials at every stage.

The Company is in a situation of dependency in relation to third parties to manufacture its products, which could affect its ability to develop and market its products in a timely and competitive manner.

As part of its strategy, Onxeo subcontracts the manufacture of its developing products. Although the Company believes that the number of subcontractors who can offer manufacturing capacity is significant, their inability to complete a project or their failure could have an adverse effect on the development of its products, the timing of their release on the market or their compliance, thereby affecting the conduct of its trials or related processes.

In addition, the Company entrusts the manufacture of its marketed products to third parties. In the event of failure of the manufacturers, interruption or quality problems in the provision of products, the Company could be temporarily unable to supply its commercial partners, which would undermine its reputation, affecting both its sales and profitability.

# 5.5.1.4.1.4 Risks of dependence on the subcontractors to which the Group outsources the manufacturing of its products



As part of its strategy, the Group subcontracts the manufacturing of its products under development or already on the market. The manufacturing of the Group's products is a particularly complex and demanding process, in particular due to applicable regulations and specific requirements applicable to the authorization of clinical trials and for MAs.

Although the Group's subcontractors are selected after careful assessment of the performance of their quality department and the transparency of their activities, difficulties could arise during the manufacturing or the distribution of the Group's products. In the event of a failure of a subcontractor, an interruption or a quality issue in the provision of its products, the Group could find itself temporarily unable to supply its commercial partners, which would adversely affect its reputation, affecting both its sales and profitability.

In addition, one or more subcontractors of the Group may unilaterally decide to increase the manufacturing cost of the drugs they manufacture on its behalf, in order to address an increase in the price of the raw materials used. If the Group were unable to pass on such increases in the manufacturing cost of its products to its customers (including due to commercial pressure from its competitors), its gross margin could be significantly reduced.

Moreover, in case of non-compliance of the products manufactured by these third parties with applicable regulatory standards, sanctions could be imposed on the Group including fines, injunctions, orders to pay damages or the suspension or the withdrawal of the granted authorizations.

Furthermore, in the event the Group substitutes a critical subcontractor responsible for manufacturing its products, tests and additional validations could be required to maintain MAs granted for its clinical trials. This could delay the development of the products concerned and increase manufacturing costs.

Finally, even though it considers that the number of subcontractors likely to meet its needs is significant, the Group cannot guarantee that it will be able to enter into new contracts in the desired time periods and on acceptable commercial terms.

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

# 5.5.1.4.1.5 Risks related to drug pricing and reimbursement policies

# Risk associated with a delay in obtaining pricing and rates of reimbursement or lower-than-expected prices and rates

Drug prices are decided by public commissions and agencies in relation to a flat rate deemed acceptable to the community and are therefore largely beyond the control of the Company. Governments and other third party payers actively endeavor to curb healthcare costs by limiting both the coverage and the reimbursement rates applicable to new therapies.

Onxeo's ability to generate sufficient profits on the sale of its products will partly depend on the level at which they are made available and the level of their reimbursement by the public health authorities, private health insurance companies and healthcare management organizations in the various countries where they are marketed. Should the timing of the procedure for price negotiation result in a significant delay in marketing a product, or should the Group be unable to obtain an appropriate level of reimbursement, its profitability would suffer

## Risk that a marketed product will cease to be reimbursed

The Company anticipates constant and increasing changes in proposed legislation to strengthen government controls over drug prices. In the western world, pressure on prices and reimbursement of drugs is generally on the increase, and there is a growing tendency for certain products not to be reimbursed.

The Company cannot, therefore, guarantee that it will succeed over time in maintaining the price level of its drugs or the agreed reimbursement rate. In the circumstances, its sales and profitability could be significantly altered.

The Company works alongside specialized consultants and international medico-economic experts in order to anticipate the information needed to provide effective support to its pricing files in the various countries



concerned and to maintain a level of publication that makes it possible to regularly confirm the medical service rendered.

## 5.5.1.4.1.6 Risks related to the commercial development of the Group

The Group markets its products through a network of partners with whom it has entered into licensing agreements for the marketing of its products having obtained a MA.

Since the summer of 2014, a first product of its orphan oncology portfolio, Beleodaq®, has been marketed in the United States via the company Spectrum Pharmaceuticals. Similarly, the first two products developed by the Group - Loramyc®/Oravig® and Sitavig®, have been respectively sold in Europe by the Therabel Group and in the United States by Cipher Pharmaceuticals. However, these two products, which are not part of the strategic orphan products in the oncology portfolio, do not significantly contribute to either income or results and should not be considered as important elements in the Group's valuation.

The successful marketing of the Group's products via its partners relies, in part, on the financial resources, expertise and customer base of the latter. The Group cannot guarantee that it will be able to keep its existing partners or enter into contracts with new partners in order to market its products on acceptable financial terms in all the countries with a sales potential, nor can it guarantee that its partners will have the necessary expertise in the field of oncology or that they will devote the necessary resources to the commercial success of its products. The future development of the Group will, in part, depend on the pace at which its partners support and use its new products. Indeed, they must be confident in the value, for their market and territory, of the new products offered by the Group, as well as of the acceptability of the prices and sales conditions set by the Group.

The Group could, in the mid and long term, directly market all or part of the products it develops. The success of the direct marketing of the Group's products would then depend on its capacity to implement its own sales and marketing infrastructure and, for that purpose, incur significant costs and recruit a qualified workforce.

Although the Group monitors its partners and strives to retain the in-house expertise needed to coordinate them and monitor their marketing and sales efforts, failure in the efforts of the marketing network of the Group's products and/or the occurrence of one of the risks described above could have an adverse effect on their marketing and, more generally on the Group's business, financial position, results, development and prospects.

# 5.5.1.4.1.7 Risks related to commercial partnership agreements

The Company has concluded licensing agreements for the marketing of its registered products. Inadequate sales performance by a commercial partner may limit revenue from the Company's products and impact on its growth.

The first two products developed by Onxeo, Loramyc® / Oravig® and Sitavig®, are marketed in Europe and the United States respectively by several partners - Therabel, Midatech, and Cipher Pharmaceuticals in particular. These two products are not part of the strategic orphan products in the oncology portfolio, do not make any significant contribution to either income or results and should not be considered as important elements in its valuation.

An initial product of the orphan oncology portfolio, Beleodaq®, began marketing in the US via the partner Spectrum Pharmaceuticals. The Company could be negatively affected by the inadequate commercial performance of this partner due to insufficient resources deployed, however the impact is not considered significant in the short term.

In general terms, and to prevent risks associated with licensing agreements, the Company benefits from clauses guaranteeing its interests in the various licensing contracts. It also monitors its partners and retains the inhouse expertise needed to coordinate them and monitor their marketing and sales deployment.

## 5.5.1.4.1.8 Risks related to the safety of marketed products

Product liability traditionally represents a significant risk for the pharmaceutical industry. Indeed, all possible side effects of a product cannot be detected during testing prior to receiving its marketing authorization. A



systematic review and regular analysis of data collected through clinical trials and post-marketing surveillance provide additional information (e.g., on the occurrence of rare adverse effects or those affecting a given population), which may lead to changes in the products' composition, limits on its therapeutic indications or even the suspension or withdrawal of the product.

Onxeo took out specific product liability insurance to cover the safety risks associated with the marketing of its products.

In addition, the Company has a pharmacovigilance system that complies with international regulations duly inspected by the health authorities.

#### 5.5.1.4.1.9 Risks related to the Group's exposure to liability

Although the Group has a pharmacovigilance system that complies with international regulations and that has been inspected by the health authorities, it may incur product liability in connection with the testing, manufacturing, and marketing of therapeutic products for humans, particularly due to possible unanticipated side effects following administration of the product during clinical development and marketing.

Criminal complaints or lawsuits could be filed or brought against the Group by patients, regulatory agencies, pharmaceutical companies or any other third party using or marketing its products. These actions may include claims arising from actions of its partners, licensees and subcontractors of the Group, over which it exerts little or no control.

The Group cannot guarantee that the insurance policies subscribed to (please refer to section 5.5.1.5 of the Registration Document) or that indemnification undertakings agreed to by its subcontractors in favor of the Group, contractually capped where applicable, will be sufficient to cover any liability claim that may be brought against the Company.

In the event claims were brought against the Group or its partners, licensees or subcontractors, or if the Group or its partners, licensees or subcontractors were not able to obtain and maintain adequate insurance coverage at an acceptable cost, or if it was unable to protect itself in any manner against liability claims, the Group's marketing of its products would be seriously affected and, more generally, this would harm its business, results, financial position and development prospects.

#### 5.5.1.4.2 Risks related to the Group's organization

#### The Group could lose key employees and not be in a position to attract other qualified personnel.

The Group's success depends largely on the work and expertise of its management team and its Chief Executive Officer. To date, the Group has not subscribed to any so-called "key person" insurance (permanent disability/death insurance policy). The temporary or permanent unavailability of one or more members of its management team could impair the Group's ability to achieve its objectives, in particular by depriving it of their experience and know-how.

In addition, the Group will need to recruit new managers and qualified scientific personnel in order to develop its business as and when the Group expands in areas requiring additional skills, such as manufacturing, regulatory matters and, ultimately, marketing. The Group competes with other companies, research organizations and academic institutions to recruit and retain highly qualified scientific, technical and managerial personnel. As this competition is very intense, the Group may not be able to attract or retain key personnel on financially acceptable terms.

The Group's inability to attract and retain key personnel could prevent it from achieving its overall objectives and have a material adverse effect on its business, results, financial position and prospects.

#### 5.5.1.4.3 Legal risks

#### 5.5.1.4.3.1 Challenges and constraints related to the regulatory environment

One of the Company's major challenges consists in successfully developing products through to their marketing phase, in an ever more restrictive regulatory environment.



Legislative and regulatory provisions defined by the French health product safety agency (ANSM) in France, the European Commission, the EMA in Europe, the FDA in the United States and equivalent regulatory authorities in other countries, govern research and development, preclinical and clinical studies, infrastructure health and safety standards and the manufacture and marketing of drugs (see section 4 of the Registration Document). Throughout the world, the pharmaceutical industry is confronted with a toughening of this regulatory environment. The health authorities – notably the FDA and the EMA – have imposed ever more stringent requirements in terms of volumes of data required to demonstrate a product's efficacy and safety.

Consequently, the regulatory process for approval of new therapeutic products is long and complex and its outcome is uncertain. Moreover, regulatory requirements and procedures vary greatly from one country to another.

For a growth company like Onxeo, whose product portfolio is, for the most part, still in development, the uncertainties associated with both applying for marketing authorization and its phase of examination by the regulatory authorities carry major risks whose financial impacts may be significant.

Authorities in the United States, Europe and other countries may:

- Require additional testing to validate the product's registration;
- Restrict the indications for which the Company would be authorized to market its products;
- Significantly delay the issuance of the market authorization to the Company.

To address such risks which are likely to increase costs and reduce its future revenues, the Company has acquired strong expertise in the clinical and regulatory fields. It also closely coordinates its pharmaceutical and clinical subcontractors to ensure the quality and availability of test data, and maintains active relations with regulatory agencies through the registration procedure.

# 5.5.1.4.3.2 Limits on patent protection and other intellectual property rights: risks that patents issues or granted to the Group under license are contested by a third party or cancelled

Onxeo regularly files patent applications in order to protect its technologies, products, preparation processes and pharmaceutical compositions. Through its patents and other industrial property rights, Onxeo holds exclusive rights to the products it develops by its own research or through acquired licensing. As of the date of this Registration Document, the Company holds the rights to 313 patents or patent applications, including 230 patents granted in several countries or major jurisdictions, notably in the United States, Europe and Japan.

The Company's ability to market its products successfully will therefore depend chiefly on its ability to obtain, maintain and protect its intellectual property rights.

In the pharmaceutical sector, patent law is still evolving and presents uncertainties. In particular, no uniform global policy has so far emerged on the content of patents issued in the fields of biotechnology and the scope of allowed claims. Uncertainties also result from the possible emergence of new precedents.

As regards the extent of protections claimed, some of the Company's patents may cover products derived from compounds protected by patents held by third parties.

Regarding the possible emergence of new precedents, patent applications are never published before a period of eighteen months after their first filing and, in the United States, some applications are not published before the award of the patent. Thus, at the time a patent application is filed, other as-yet unpublished patent applications belonging to third parties may constitute unidentified prior trademarks. The filing of a patent application or issuance of a patent does not therefore guarantee its validity or its applicability, both of which may be challenged by third parties.

If third parties claim a proprietary right over the Company's patents or other intellectual property rights, the Company may have to obtain suitable licenses for those patents, interrupt or modify certain activities or procedures, or even develop or obtain alternative technologies, which is liable to have adverse effects on the development of its products and the generation of future revenues.

It may be necessary to take legal action to enforce intellectual property rights, protect trade secrets and establish the validity and scope of the Company's intellectual property rights. Litigation could involve considerable expense, reduce the Company's potential profits and not provide the protection sought.

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Faced with these risks, the Company has a proactive Industrial Property strategy, directly linked to its research and development projects, both as regards the detection of inventions in order to increase their number and as regards monitoring third-party publications and patent procedures.

# 5.5.1.4.3.3 Risks associated with active patents becoming public domain, or with the expiration of marketing licenses, or with the eventual emergence of generic drugs for market products

At the expiration of their protective property or marketing rights, the products marketed by the Company could be subject to competition by the introduction on the market of comparable drugs, or by the development of generic drugs, which would lead to a reduction in prices and/or sales volumes and could have a negative effect on the Company's business and financial condition.

These risks are currently not significant to Onxeo because, on the one hand, the Company develops most of its product portfolio for niche markets that are not prime targets for generics and, on the other hand, under its Industrial Property strategy, the Company regularly files new patent applications within existing patent families.

#### 5.5.1.4.3.4 Legal Actions

The main pending disputes are described in note 10.4 of the notes to the consolidated accounts set out in section 6.1 of the Registration Document.

#### 5.5.1.4.4 Financial Risks

# 5.5.1.4.4.1 Funding risk

The Company has posted net operating losses since the start of operations. At December 31, 2016, the Company's cumulative losses amounted to €163 million in accordance with French accounting standards. These operating losses are primarily the result of investments in research and development especially for the completion of preclinical studies and clinical trials.

The Group expects further operating losses for the next few years as it continues its research and development activities.

The profitability of the Group will depend primarily on its ability to enter into new partnership agreements for the various products under development in its portfolio. In the event of a significant delay in identifying and negotiating new partnerships, the Group may not break even for several years.

Furthermore, the Company's financing requirements will continue to increase as the Company invests to develop existing and new products. The Company has carried out a specific review of its liquidity risk and considers that it can meet its future payments over the next 12 months. However, the Company may need to raise additional funds ahead of time for reasons such as:

- Higher costs and slower progress than the Company anticipates in developing new products and obtaining crucial marketing authorizations; and
- Opportunities to develop promising new products or to acquire products, technologies or other activities;

#### 5.5.1.4.4.2 Risks related to the research tax credit

To finance its activities, the Group has also opted, via the Company, for the research tax credit (Crédit d'Impôt Recherche – "CIR") pursuant to article 244 quater B of the French general tax code, which provides for a tax incentive mechanism, by way of a tax credit grant to French companies that invest significantly in research and development.

Since the fusion with Danish company Topotarget in 2015, the Group also benefits from the Danish CIR system, on account of its Copenhagen office.

The sums recorded by the Company in respect of the CIR for the fiscal years ended December 31, 2015 and 2016 amount to €3.8 million and €4 million respectively.

Upon request of the French tax authorities, the Company could be required to justify the amount of the CIR claim and the eligibility of the R&D work claimed to benefit from the measure.



The Group cannot exclude the possibility of the tax authorities challenging the methods used by the Group for calculating research and development expenditure or of the CIR being called into question pursuant to a regulatory change, or of it being challenged by the tax authorities even though the Group complies with the requirements in respect of documentation and eligibility of expenditure.

If such a situation arose, it could have an adverse effect on the Group's results, financial position, development and prospects.

#### 5.5.1.4.4.3 Foreign Exchange risk

The Company has signed several licensing agreements with partners located outside the Eurozone. These agreements generally involve payments in US dollars, whether milestone payments for specific goals in terms of development/product approval, sales, or royalties.

Given the uncertainty concerning these triggering elements and the likely dates of payments, the Company has not implemented any currency hedges. It is possible that the €/\$ exchange rate evolves adversely for the Company and that the total amount converted into euros may be significantly less than that initially anticipated. As soon as payment assumptions are confirmed, the Company intends to hedge these flows in US dollars.

Regarding day-to-day operations of the Group, insofar as most revenue and payments are in euros, there are no currency exchange risks.

#### 5.5.1.4.4.4 Dilution risk

As part of its incentive policy towards executive officers and employees and to attract additional expertise, the Company has granted shares freely and issued stock options and other rights giving access to its capital and could, in the future, issue or allot new financial instruments giving the right to subscribe to the Company's capital.

As of the date of the Registration Document, the full exercise of all equity instruments allotted to date would result in the subscription of 2,619,627 new shares (refer to section 7.2.2.2 of the Registration Document), representing a 5,6% dilution on the basis of the existing share capital to date (and result in an identical dilution percentage regarding voting rights).

The exercise of all existing equity instruments as well as the exercise of future grants or allotments would lead to a potentially significant dilution for the current and future shareholders of the Company.

# 5.5.1.4.4.5 Interest rate risk

Since the Group has not incurred any debt, this point does not apply.

# 5.5.1.4.4.6 Risk on equity securities

The Company's cash flow is exclusively invested in money market funds, which involve no equity risk. These investments are immediately available and of very low volatility, so they do not present any liquidity risk. Information on the market value of the investment securities portfolio is included in the annex to the consolidated financial statements.

#### 5.5.1.5 Insurance and risk coverage

The Company has an insurance cover appropriate to its business activities on a worldwide basis, and in particular its clinical trials in France, the United States and all countries concerned.

The Company has taken out a number of insurance policies, the main ones being:

- A civil liability insurance policy covering:
  - Operational liability, which insures the Company against the financial consequences of civil liability that could be incurred because of injury, damage and loss caused to third parties and attributable to the activities of the Company;



- Product liability, which insures the Company against the financial consequences of civil liability that could be incurred because of injury, damage and loss caused to third parties and attributable to the Company's products both before and after delivery; and
- Civil liability for the defense of criminal proceedings and third-party claims".
- A 'directors and officers liability' insurance policy, insuring them against the possibility of incurring liability in the performance of their duties.
- A property damage insurance policy, which covers, in particular, the risks of fire, water damage, theft, equipment breakdown and breakage of glass, and tenants' risks, at the Company's premises in Paris, Châtenay-Malabry and Copenhagen.
- Specific insurance policies for each clinical trial sponsored by the Company. Policy prices and cover amounts depend on the local regulations and legislation applicable to the clinical research center concerned. In France, the Public Health Code specifies that sponsors of clinical trials must carry insurance. In countries where there is no requirement to take out such a policy, the Company nonetheless maintains an insurance policy covering its liability in undertaking clinical trials. The overall amount of the premiums depends on the number of patients included in the trials and their geographic location. The Company considers that it is adequately insured for each of the trials currently in progress.
- Key personnel insurance policy covering the risks of physical accidents that could occur to members of management.
- A 'stock and transit' insurance policy, covering storage and transport of the Company's products.

The insurance program has been defined with a concern for efficiency in both negotiating and managing policies. The risk management policy should be continued in light of the development and internationalization of the Group's business activities and in close coordination with the development of our business activities.

# 5.5.1.6 Supervision of risk management systems

The Risk Committee validates action plans with those responsible and ensures a follow-up.

#### 5.5.1.7 Link between risk management and internal control

Risk management aims to identify and analyze major risks and risk factors which could affect the company's business, processes and objectives and to define ways to keep those risks to an acceptable level, particularly by implementing prevention and control measures that fall within the scope of internal control.

At the same time, the internal control system relies, among other things, on risk management to identify the key risks to be controlled.

## 5.5.2 GENERAL PRINCIPLES OF INTERNAL CONTROL

# 5.5.2.1 Internal control: definitions and objectives

Internal control consists of the means, behaviors, procedures and actions adapted to the particular characteristics of each Company and those of the Group as a whole that:

- Contribute to the control of its activities, its operating effectiveness and the efficient use of its resources; and
- Enable it to take appropriate action to tackle any significant risks it may face, whether they are operational, financial or compliance related.

Internal control is designed to ensure:

- Compliance with legislation and regulations;
- Application of instructions and guidelines laid down by the Board of Directors;
- Proper functioning of the Group's internal processes, including those contributing to asset protection; and
- The reliability of financial information.

However, while supporting Company's objectives, internal control cannot provide an absolute guarantee that they will be met. There are, in fact, inherent limitations to any internal control system, for example,



uncertainties in the external environment, the use of good judgment or the cost-benefit relationship of implementing new controls.

# 5.5.2.2 The reference framework used by the Group

Onxeo continues to develop its internal control system based on AMF terms of reference found in its updated application guide of July 22, 2010. This control system applies on the one hand to concurrent processes in publishing financial and accounting information and on the other hand to the overall organization of operations and risk management procedures implemented by the Company.

Internal control at Group level is conducted by taking into account both the Group's operational and legal structure.

It involves all of the Group's subsidiaries consolidated under the global integration method.

The summary information in this report on the applied internal control procedures focuses on the significant elements that may have an impact on financial and accounting information published by the Company.

# 5.5.2.3 The components of internal control

#### 5.5.2.3.1 Organization

The internal control system is based on a clear organization of responsibilities, standards, resources and implemented procedures.

Since the Company's founding, Onxeo has developed a system of quality assurance. Processes of all fields of activity are described by procedures (Standard Operating Procedures or SOP), operating methods, information notices and forms. These documents describe the conduct of activities, define the resources and responsibilities of those involved, specify the know-how held by the Company and give precise instructions in order to carry out a given operation.

All stakeholders of the Company are involved in the internal control system. Their responsibilities are described below.

### 5.5.2.3.2 Reference framework and standards

The Onxeo Group, established in the health and biotechnology sector, is subject to very specific and detailed regulations that oversee its activities and whose compliance is monitored by the internal control system. Legislative and regulatory provisions, defined by the European Commission and equivalent regulatory authorities in other countries including the Agence nationale de sécurité du médicament (ANSM), the European Medicines Agency (EMA), the Food and Drug Administration (FDA), give relevant guidance for research and development, preclinical studies, clinical studies, the regulation of institutions, as well as the manufacture and marketing of drugs. The main regulatory provisions that apply to the activities of the two companies are as follows: Good Clinical Practices (GCP), Good Manufacturing Practices (GMP), Good Laboratory Practices (GLP), the French and European regulations that apply to the development, sale and marketing of drugs, the regulations regarding GMOs, the disposal of waste, the transportation of hazardous substances, the handling of micro-organisms, health and safety.

#### 5.5.2.3.3 Control activities

Monitoring activities implemented by the Company are based on various tools, including:

- A documentation system;
- A reporting system; and
- Specific controls related to the preparation and processing of accounting and financial information.

These activities are carried out by various actors, particularly an internal unit structured around three instances of decision-making and follow-up with an Executive Committee, a Committee on operations and Groups of projects, with the latter two instances being devoted to the management of R&D projects.

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# 5.5.2.3.3.1 The documentation system

All of the internal control system documentation is stored on a dedicated Intranet that optimizes access to documents and enables them to be continually updated as a result of changes in activity (Records and Information Life Cycle Management). The aim is to improve the quality and processes of the Company and the Group on a continuous basis, whether operational, management or support processes

The internal control system covers in particular the following areas:

- Quality assurance, health and safety, risk management;
- The administrative, legal, social, and financial fields, including financial communication and rules relating to the Company's listing on Euronext;
- Production and pharmaceutical operations;
- Regulatory activities liaising with drug agencies;
- Pharmaceutical research and development, pre-clinical and clinical trials including very specific animal experimentation, an Ethics Committee on animal experimentation whose objectives are the validation of all the testing protocols and the monitoring of compliance with the regulations;
- Pharmacovigilance;
- Information systems: computerized management of the rules on information access, protection and storage;
- Human resources and labor regulations; and
- Services performed for third parties.

#### 5.5.2.3.3.2 Reports

The Executive Committee has implemented specific internal control procedures which consist of regular key information reviews relating to each activity. For each of the areas set out below, information considered to be significant for the corresponding activities has been identified and selected. This information must represent the actual situation in the activity and make it possible to retrace such activity both in terms of quantity and quality, also taking into account compliance with the standards governing the activity concerned. This key information must be verifiable and properly documented. It is to be updated each month by the people carrying out the activity concerned. This system covers the following areas:

- Research and development projects preclinical, clinical, pharmaceutical and regulatory;
- Monitoring of the budget and financial operations;
- Company legal issues and intellectual property;
- External communications;
- Quality and the information system; and
- Human resources.

# 5.5.2.4 Procedures relating to the preparation and processing of accounting and financial information

The reliability of financial information is one of the Company's essential internal control objectives. To this end, control and reporting procedures have been set up in order to guarantee control of the processes of information gathering, preparation and approval of the financial statements, in line with the criteria described in the AMF reference framework. These procedures, related to the general accounting of the Company's operations, also specifically cover budgetary aspects and the approval of expense commitments and payments. Furthermore, with regard to the consolidation process for the Group's financial statements, the finance department controls the proper elimination of intercompany transactions and uniform restatements of the individual accounts according to international standards (IFRS).

In general, all the Company's accounting options are defined by the Chief Financial Officer, discussed with the Executive Committee and the Statutory Auditors and then presented to the Audit Committee and discussed with this committee. This makes it possible to ensure that the Company's practices fully comply with French and international (IFRS) standards and that the financial statements are consistently presented.

At the end of each year, a detailed budget is prepared for the following year by the Chief Financial Officer and approved by the Executive Committee. This budget is presented to the Board of Directors. At the end of each month, the accounting teams carry out a closing of the accounts of the Group companies. Budgetary reviews



are organized with all the line managers, making it possible to validate the cost accounting entries in this respect and to review all expenses, and a financial report is prepared by the Chief Financial Officer for the attention of the Executive Management and the directors. This reporting is presented and discussed regularly at meetings of the Board of Directors.

The Finance Department is responsible for developing and releasing all of the Group's financial communications to the financial markets following validation by the executive management.

Such communication takes place via two main channels:

- The annual report, the Registration Document and the interim financial report; and
- Economic and/or financial news releases.

Preparation of the annual report which has Registration Document status and the half-yearly financial statements are coordinated by the Finance Department. Its preparation involves much collaboration; experts in their field contribute to the variety and quality of the information. The Registration Document is reviewed and adopted by the Board of Directors prior to release.

Press releases relating to yearly and half-yearly results are also validated by the Board of Directors.

# 5.5.2.5 Agents involved in risk management and internal control procedures

Internal control is carried out by management structures and by all Group employees through their daily actions.

<u>In-house operatives of the internal control system include:</u>

- The Board of Directors, which validates the broad guidelines and the strategy of the Group;
- The Audit Committee, mentioned earlier in this report, whose powers are defined by the Board of Directors, plays a key role in monitoring (i) the financial information preparation process, (ii) the effectiveness of the internal control and risk management systems, and (iii) the statutory audit of annual and consolidated accounts by the auditors;
- Executive Committee and department heads, through the various management committees, steer the Group's strategy and allocate the necessary human resources for its implementation by setting and monitoring objectives;
- The Finance Department, Quality Department and Legal Affairs all have a particular role to play in internal control due to their cross-functional expertise;
- The Quality Department plays a key role in the various Company activities through its support in the drafting of procedures and document control, by performing and following up internal and external audits of departments and service providers, and by proposing improvements. It also performs regulatory watch activities and checks all documentation issued by the Company, which is submitted to the regulatory authorities within the context of clinical and preclinical trials.
- The Risk Committee leads risk management, which is deployed across the whole of the Group by the department heads. This committee meets at least twice a year to update risk mapping and to reflect on strategies for reducing the impact of major risks. It reports to the Strategy Committee, which validates their mapping and action plans.
- Lastly, employees are responsible for day-to-day compliance with standards and orientations in their area and also for the reliability and relevance of the information they generate or pass on.

These provisions are supported by the action of external actors, including the Auditors. Within the context of their legal mission, the latter are not part of internal control and risk management. They are informed, rely on the internal audit to get a better understanding and independently form an opinion as to their relevance. Each year, they inspect the Group as part of their legal task of certifying the consolidated accounts and auditing the Group's individual company accounts. Currently, in accordance with French commercial law, certification of Onxeo's consolidated and individual company accounts is carried out by two auditors who carry out a joint review of all accounts, their preparation methods and certain internal control procedures relating to the production of accounting and financial information. The auditors present their comments on the Chairman's report, on the internal control procedures that relate to the preparation and processing of the accounting and financial information, and certify that other information required by law has been produced.



# 5.5.3 MAIN DEVELOPMENTS

The Company is pursuing its policy aimed at improving its internal control systems.

In 2016, the Company continued to roll out the main action plans identified within its different departments to consolidate the management system put in place during the last few years.



# 5.6 STATUTORY AUDITORS' REPORT ON THE REPORT PREPARED BY THE CHAIRMAN OF THE BOARD OF DIRECTORS OF ONXEO

#### **GRANT THORNTON**

# French member of Grant Thornton International 29, rue du Pont 92200 Neuilly-sur-Seine

Statutory Auditor
member of the Regional Association of statutory
auditors of Versailles

S.A. au capital de € 2.297.184

#### **ERNST & YOUNG Audit**

1/2, place des Saisons 92400 Courbevoie - Paris-La Défense 1 S.A.S. à capital variable

Statutory Auditor member of the Regional Association of statutory auditors of Versailles

This is a free translation into English of a report issued in French and it is provided solely for the convenience of English speaking users. This report should be read in conjunction with and construed in accordance with, French law and professional standards applicable in France.

#### Onxeo

Year ended December 31, 2016

Statutory auditors' report, prepared in accordance with article L. 225-235 of the French commercial code (*Code de commerce*), on the report prepared by the chairman of the board of directors of Onxeo

To the Shareholders,

In our capacity as statutory auditors of Onxeo and in accordance with article L. 225-235 of the French commercial code (*Code de commerce*), we hereby report on the report prepared by the chairman of your company in accordance with article L. 225-37 of the French commercial code (Code de commerce) for the year ended December 31, 2016.

It is the chairman's responsibility to prepare and submit for the board of directors' approval a report on the internal control and risk management procedures implemented by the company and to provide the other information required by article L. 225-37 of the French commercial code (*Code de commerce*) relating to matters such as corporate governance.

# Our role is to:

- report on any matters as to the information contained in the chairman's report in respect of the internal control and risk management procedures relating to the preparation and processing of the accounting and financial information,
- confirm that the report also includes the other information required by article L. 225-37 of the French
  commercial code (Code de commerce). It should be noted that our role is not to verify the fairness of this
  other information.

We conducted our work in accordance with professional standards applicable in France.



# Information on the internal control and risk management procedures relating to the preparation and processing of accounting and financial information

The professional standards require that we perform the necessary procedures to assess the fairness of the information provided in the chairman's report in respect of the internal control and risk management procedures relating to the preparation and processing of the accounting and financial information. These procedures consist mainly in:

- obtaining an understanding of the internal control and risk management procedures relating to the preparation and processing of the accounting and financial information on which the information presented in the chairman's report is based and of the existing documentation;
- obtaining an understanding of the work involved in the preparation of this information and of the existing documentation;
- determining if any material weaknesses in the internal control procedures relating to the preparation and processing of the accounting and financial information that we would have noted in the course of our work are properly disclosed in the chairman's report.

On the basis of our work, we have no matters to report on the information relating to the company's internal control and risk management procedures relating to the preparation and processing of the accounting and financial information contained in the report prepared by the chairman of the board of directors in accordance with article L. 225-37 of the French commercial code (*Code de commerce*).

#### Other information

We confirm that the report prepared by the chairman of the board of directors also contains the other information required by article L. 225-37 of the French commercial code (*Code de commerce*).

Neuilly-sur-Seine and Paris-La Défense, 5 April 2017

# **The Statutory Auditors**

(French originals signed by)

# French member of Grant Thornton International

**GRANT THORNTON** 

**ERNST & YOUNG Audit** 

Jean-Pierre Colle Samuel Clochard Franck Sebag



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# **CONSOLIDATED BALANCE SHEET**

ASSETS K€	31/12/2016	31/12/2015	Note
Non-current assets			
Intangible assets	87 213	86 367	6
Tangible assets	713	841	7
Financial assets	306	307	8.1
Deferred tax liabilities	0	24	
Total non-current assets	88 232	87 539	
Current assets			
Stocks and working in progress	184	106	
Trade receivables	1 548	1 036	8.2
Other receivables	5 893	6 762	8.3
Financial Investments	5 302	5 307	8.4
Cash	23 941	28 486	8.4
Total current assets	36 868	41 696	
TOTAL ASSETS	125 100	129 235	

LIABILITIES AND SHAREHOLDER EQUITY K€	31/12/2016	31/12/2015	Note
Shareholders' equity			
Share capital	11 761	10 138	9.1
Less: treasury shares	-97	-157	9.2
Additional paid-in capital	255 960	243 854	9.3
Reserves	-150 864	-131 628	9.3
Earnings	-22 671	-19 409	
Total shareholder equity	94 089	102 798	
Non-current liabilities			
Deferred tax liabilities	11 895	11 381	10.1
Provisions	637	719	10.2
Other liabilities	6 062	3 731	10.3
Total non-current liabilities	18 594	15 832	
Current liabilities			
Short-term debt	106	69	
Trade payables and related accounts	9 246	6 362	11.1
Other liabilities	3 065	4 175	11.2
Total current liabilities	12 417	10 606	
TOTAL LIABILITIES AND SHAREHOLDER EQUITY	125 100	129 235	



# CONSOLIDATED INCOME STATEMENT

in K€	31/12/2016	31/12/2015	Note
Recurrent sales from licensing agreements	3 455	2 733	
Non-recurrent sales from licensing agreements	969	749	
Total sales	4 423	3 481	13.1
Purchases	-655	-337	
Personnel costs	-6 984	-6 887	13.2
External expenses	-17 130	-16 194	13.3
Taxes other than on income	-223	-274	
Depreciation and amortization, net	-1 864	-1 819	13.4
Allowances to provisions, net	-628	106	
Other operating income	122	9	
Other operating expenses	-229	-260	
Operating expenses	-27 591	-25 657	
Ordinary operating income	-23 168	-22 176	
Share of income under the equity method	-43	-29	
Other operating income and expenses		-160	
Operating income after share of income under the equity method	-23 212	-22 365	
Income from cash and cash equivalents	680	1 818	
Other financial income	1 076	32	
Financial expenses	-649	-1 248	
Financial income	1 106	602	14
Pre-tax profit (loss)	-22 106	-21 763	
Income tax	-566	2 353	15
Out of which deferred taxes	-538	2 448	
Net loss	-22 671	-19 409	
Earnings per share	(0,48)	(0,48)	16
Diluted earnings per share	(0,48)	(0,48)	16

in K€	31/12/2016	31/12/2015	Note
Income for the period	-22 671	-19 409	
Other comprehensive income	0	0	
Translation adjustments	-701	-92	
Losses and gains on de-recognition of assets available for sale	0	0	
Cash flow hedges	0	0	
Tax related to elements of the comprehensive income	0	0	
Other recyclable items classified as income	-701	-92	
Actuarial gains and losses	-57	-45	
Other non-recyclable items classified as income	-57	-45	
Other elements of the comprehensive income for the period net of			
taxes	-758	-137	
Total comprehensive income for the period	-23 429	-19 546	
Total comprehensive income attributable to			
Owners of the parent company	-23 429	-19 546	
Minority interests			



# CONSOLIDATED STATEMENT OF CHANGES IN SHAREHOLDERS' EQUITY AT YEAR-END 2016

# Variations of reserves and results

In K€	Capital	Own shares	Issue premiums	Translation reserves	Share- based premiums	Gains and losses recorded as equity	Consolidated results and reserves	Total variations	TOTAL
Equity as at 1/01/2015	10 136	-122	243 741	23	1 782	0	-133 589	-131 784	121 971
Total overall result of the period				-92		0	-19 454	-19 546	-19 546
Capital increase	2		113					0	115
Own shares		-35				0	-55	55	-90
Other movements						-45	6	-38	-38
Share-based payments					385		0	385	385
Dividends								0	0
Equity as at 31/12/2015	10 138	-157	243 854	-69	2 167	-45	-153 091	-151 038	102 798
Total overall result of the period				-701		-57	-22 671	-23 429	-23 429
Capital increase	1 623		12 106					0	13 729
Own shares		60					-31	-31	29
Other movements							538	538	538
Share-based payments					482			482	482
Dividends								0	0
Equity as at 31/12/2016	11 761	-97	255 960	-770	2 648	-102	-175 312	-173 535	94 089



# CONSOLIDATED CASH FLOW STATEMENT

K€	31/12/2016	31/12/2015
Consolidated net loss	-22,671	-19 409
+/- Depreciation, impairment and provisions, net (1)	1 606	2 207
(excluding provisions against working capital)	0	
/+ Unrealized gain and losses associated with changes in fair value	0	-2
+/- Non-cash income and expenses on stock options and similar items	482	385
-/+ Other calculated income and expenses	109	-66
-/+ Capital gains and losses on disposal	0	-141
-/+ Dilution gains and losses	0	
+/- Share of earning associates	43	
- Dividends (non-consolidated investments)	0	
Gross operating cash flow after cost of net debt and taxes	-20 432	-17 027
+ Cost of net debt	-923	-600
+/- Tax expenses (including deferred taxes)	538	-2 448
Gross Operating cash flow before cost of net debt and taxes	-20 817	-20 075
- Taxes paid	0	
+/- Changes in operating WCR (including debt related to employee benefits)	3 208	-3 042
NET CASH FLOW FROM OPERATING ACTIVITIES	-17 609	-23 116
- Expenditures on acquisition of tangible and intangible assets	-316	-410
+ Proceeds of disposal of tangible and intangible assets	-229	161
- Expenditures on acquisition of financial assets	-7	-1
+ Proceeds of disposal of financial assets	-5	16
+/- Effect on changes in scope of consolidation	0	
+ Dividends received (equity accounted investment)	0	
+/- Change in loans and advance granted	0	
+ Capital grants received	0	
+/- Other changes from investment transactions	2 406	
NET CASH FLOW FROM INVESTING ACTIVITITES	1 849	-235
Cash flow resulting from the merger	0	0
+ Net amount received from shareholders on capital increase	-	
. Paid by shareholders of the parent company	12 122	115
Paid by minority interest in consolidated companies	12 122	113
+ Amount received on exercise of stock options		
-/+ Purchase and Sale of treasury shares	60	-35
- Dividends paid in the year	80	-55
- Dividends paid to minority shareholders in consolidated companies		
'- Dividends paid to minority shareholders		
+ Amounts received on issuances of new loans	0	898
- Reimbursements of loans (including finance leases)	-213	-1 417
- Net interest received	0	-18
+/- Others flows related to financing activities	0	509
NET CASH FLOW FROM FINANCING ACTIVITIES	11 968	53
+/- Effects of fluctuations in foreign exchange rates	-758	-136
CHANGE IN CASH AND CASH EQUIVALENTS	-4 549	-23 434
CASH AND CASH EQUIVALENTS at start of year	33 793	57 227
CASH AND CASH EQUIVALENTS at year end	29 243	33 793



# NOTE 1 - COMPANY PRESENTATION

Onxeo ("the Company") is a clinical-stage biotechnology company specialized in developing innovative drugs for treating rare diseases particularly in the field of oncology., responding to high demand for treatment in one of the sectors with the strongest growth in the pharmaceutical industry.

Onxeo aims to be become a world leader and a pioneer in the field of orphan or rare cancers. Onxeo's strategy is based on the development of cutting-edge safe and effective treatments, designed to improve the life of patients suffering from rare or resistant cancers by providing a real difference in relation to current treatments.

The Onxeo portfolio in rare cancers includes 3 major projects in several pre-clinical and clinical programs in progress, alone or in combination for multiple indications of cancer.

The Company is based in Paris, France, with offices in Copenhagen and in New York and has about 60 employees. Onxeo is listed on Euronext in Paris, France, and on Nasdaq Copenhagen, Denmark.

The consolidated financial statements of Onxeo as at December 31, 2016 were prepared under the responsibility of the CEO and were approved by the Board of directors on March 7 2017.

# NOTE 2 - SIGNIFICANT EVENTS AND TRANSACTIONS

# 2.1. ACQUISITIONS OF DNA THERAPEUTICS

On March 25, 2016 the Group announced the completion of the acquisition of 100% of the shares of DNA Therapeutics for an initial amount of €1.7 million in Onxeo ordinary shares, leading to the creation of 553,819 new shares. The accounting treatment of the acquisition in the consolidated financial statements is described in Note 4 below.

This acquisition reinforces the Group's portfolio of orphan products in oncology and positions it on a new domain in the forefront of scientific and clinical progress in oncology, that of breaking down DNA, through the siDNA (signal interfering DNA) technology developed by DNA Therapeutics and an initial "first-in-class" product arising from this technology, AsiDNA.

Additional milestone payments would be made, namely €1 million in shares or cash at Onxeo's discretion, when AsiDNA enters Phase II in a selected indication. Also anticipated is the payment of royalties on sales if the product goes to market, worth up to €25 million per indication.

In parallel to this acquisition, some historic shareholders of DNA Therapeutics subscribed to a reserved capital increase at the beginning of April 2016, of an amount of €1 million which led to the creation of 364,958 new shares.

# 2.2. R&D PROGRAMS

## 2.2.1. LIVATAG®

In the financial year 2016, the Company increased the recruitment of patients in the study of "ReLive" phase III aiming to evaluate the effectiveness of Livatag in the treatment of 2<sup>nd</sup> line advanced hepatocellular carcinoma. The end of the recruitment of the planned 390 patients was announced on January 31, 2017, allowing for confirming the publication of the preliminary results of the study in mid-2017.

In parallel, the Company has actively pursued its Livatag pre-clinical development program in combination with other anti-cancer agents, for future applications in other indications and in particular published encouraging results in various types of tumors.

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#### 2.2.2. ASIDNA™

Since March 2016 and the acquisition of DNA Therapeutics, the Group continued the development of AsiDNA, particularly the optimization of the manufacturing processes, in parallel to a pre-clinical program which should allow for the entry of the product into a phase I clinical trial at the end of 2017.

# 2.2.3. BELEODAQ (BELINOSTAT)®

Just as Livatag, belinostat is the object of a development program in association with other anti-cancer agents in a product life cycle management approach. In 2016, the Company announced encouraging results of preclinical trials of belinostat in association with control point inhibitors as a possible treatment option for new indications.

In 2016, the Company also announced the development of an oral formulation of belinostat, which would constitute a net competitive advantage for the product.

#### 2.3. LICENCE AGREEMENT WITH PINT PHARMA

In July 2016, the Company signed an exclusive licensing agreement with Pint Pharma for the commercialization of Beleodaq in the field of peripheral T-cell lymphoma for seven key South American countries. An initial payment of \$3 million has been received by Onxeo and has been deferred to operating income until the estimated date of marketing authorization. The agreement also provides payments based on regulatory milestones and turnover levels as well as royalties on Beleodaq® net sales, for a total value in excess of \$20 million.

#### 2.4. FINANCING

At the end of September 2016, the Company announced a capital increase by the issue of new ordinary shares with cancellation of the preferential subscription right, reserved for a category of investors defined in the 17th Resolution adopted by the General Meeting of April 6 2016, namely: "companies and investment funds investing on a regular basis in small-cap growth companies, i.e. their market capitalization does not exceed €1 billion, including, without limitation, all private equity venture capital funds working in the area of health or biotechnology and participating in the capital increase for a unit amount of over €100,000 including premium, within the limit of a maximum of 25 subscribers".

This capital increase resulted in the issuance of 5,434,783 new common shares on September 30, 2016 for an amount of €12.5 million. The funds raised reinforced the cash flow and gives the Company additional resources to continue its R&D programs in the field of orphan diseases in oncology.

# 2.5. EVENTS TAKING PLACE AFTER 31 DECEMBER 2016

There are no post-balance sheet events likely to have a material effect on the accounts.

# NOTE 3 - ACCOUNTING PRINCIPLES, RULES AND METHODES

#### 3.1. BASIS OF PREPARATION OF THE FINANCIAL STATEMENTS

The consolidated financial statements at December 31, 2016 were prepared in accordance with international accounting standards issued by the IASB (International Accounting Standards Board), as published by the IASB on December 31 2016, and with international standards as adopted by the European Union at December 31, 2016.

The standards adopted by the European Commission may be consulted on the following website: <a href="http://ec.europa.eu/internal market/accounting/ias/index fr.htm">http://ec.europa.eu/internal market/accounting/ias/index fr.htm</a>.

The accounting principles and methods applied to the consolidated financial statements at December 31, 2016 are identical to those used in the consolidated financial statements at December 31, 2015, and with the international financial reporting standards (IFRS) as adopted by the European Union and the IASB, which are



compulsory for financial years beginning on or after January 1st 2016 (and which had not been applied early by the Group), namely:

#### New texts applied as at December 31, 2016 and subsequent implementing texts

Standard	Name			
Amendments to IFRS 11	Acquisition of interests in joint ventures			
Amendments to IAS 16 and 38	Acceptable amortization methods			
Annual improvement to IFRS (cycle 2012-2014)				
IFRS 5	Assets held in view of sale and discontinued operations			
IFRS 7	Financial instruments - disclosures			
IAS 19	Personnel benefits - discount rate			
IAS 34	Interim financial reporting			
Amendments to IAS 1	Disclosure			
Amendments IFRS 10, IFRS 12 and IAS 28	Investment entities - consolidation exception			

Applying these standards, amendments and interpretations had no significant effect on the consolidated financial statements of the Group.

In addition, the other standards, amendments or interpretations published respectively by the IASB and the IFRIC (International Financial Reporting Interpretations Committee) at December 31, 2016 were not applied early by the Group:

- Adopted by the European Union but whose mandatory application is subsequent to the financial year started January 1st, 2016: IFRS 9 (financial instruments), IFRS 15 (revenue from contracts with customers).
- Not yet adopted by the European Union as at December 31 2016: clarifications on IFRS 15, IFRS 16 (leasing agreements), amendments to IAS 12 (deferred taxes), amendments to IAS 7 (disclosure initiative), amendments to IFRS 2 (payments on shares), amendments to IFRS 4 (inter-relation IFRS 4 insurance agreements with IFRS 9 financial instruments), annual improvements to IFRS (cycle 2014-2016), amendments to IFRS 12 (scope of the standard), amendments to IAS 28 (related companies exemptions to evaluation methods), IFRIC 22 (transactions in foreign currencies), amendments to IAS 40 (investment properties).

## **Judgments and estimates of Group Management**

Preparing the financial statements requires the management to make a judgment, make estimates and make assumptions which have an impact on the application of the accounting policies and on the amounts of the assets and liabilities, income and expenditure. Real values may differ from estimated values.

The estimates and underlying assumptions are continuously re-examined. The impact of accounting estimate changes is recognized over the period of the change and all affected subsequent periods.

Information on the main sources of uncertainty relating to the estimates and assumptions and the judgments made to apply the accounting policies, which have the most significant impact on the amounts recognized in the consolidated financial statements, concern the following items:

The market value of the R&D programs acquired within the context of business combinations (mergers and acquisitions) – see Note 6,

- Share-based payments see Note 9.4,
- Provisions see Note 10.2,



- The recognition within sales of amounts received within the context of licensing agreements see Note 13.1
- 4<sup>th</sup> quarter royalties from partner Spectrum Pharmaceuticals calculated on the basis of actual quantities sold valued with historical unit prices

The information provided in respect of assets and liabilities existing at the date of preparation of consolidated financial statements also uses estimates (see Note 16).

Financial statements have been established on a going concern basis. This principle has been elected by the board of directors as a result of the following elements: the consolidated net cash of €29.2 million allows the Company to fund its activities until early 2018 based on its finance plan. Moreover, the Company has identified potential additional funding allowing to extend its cash runway until at least mid-2018.

#### 3.2. SCOPE OF CONSOLIDATION

The Group's companies close their accounts on December 31 of each year.

The scope of consolidation includes the following companies as at December 31, 2016:

#### Onxeo

- Topotarget UK
- Topotarget Switzerland
- BioAlliance Pharma Switzerland
- SpeBio
- Onxeo US (created in 2016)

During FY 2016, BioAlliance Pharma and DNA Therapeutics both had their assets transferred 100% to Onxeo SA and were indeed dissolved. Furthermore, Topotarget Germany, a 100% non-active subsidiary of Onxeo SA, was liquidated in 2016.

All subsidiaries are 100% owned and fully consolidated, except SpeBio, which is a joint-venture 50% owned and is consolidated under the equity method since January 1st, 2014. Inter-company transactions and balances arising from transactions between group companies have been eliminated. When the accounting methods used by the subsidiaries differ from those of the Group, they are restated for preparing the consolidated financial statements.

The subsidiary Topotarget UK Limited, with Company Registration No. 02899713, is exempted from the requirements of the law relating to the auditing of accounts pursuant to Section 479A of the UK Companies Act 2006.

# 3.3. SEGMENT REPORTING (IFRS 8)

The Group constitutes a single business segment. In accordance with the IFRS standard 8.32 and 33, information regarding the breakdown of sales by geographical zone and product portfolio ("orphan products in oncology" and "other products") is provided in Note 13.1. In reference to this standard it is also specified that the noncurrent assets of the group are mainly located in France, Denmark and the United Kingdom.

Main Group customers representing more than 10% of consolidated revenues are Spectrum Pharmaceuticals, Pint Pharma International and Cipher Pharmaceuticals.

# 3.4. THE EFFECTS OF CHANGES IN FOREGIN RATES (IAS 21)

# 3.4.1. CONVERSION OF THE FINANCIAL STATEMENTS PREPARED IN A CURRENCY OTHER THAN THE EURO

The presentation currency of the consolidated financial statements is the euro, which is also the functional currency of the parent company.

The assets and liabilities of the subsidiaries having a functional currency other than the euro are converted into euros at the exchange rates prevailing at the balance sheet date. Their profit and loss accounts are translated at the average exchange rates for the year.



The differences arising from these conversion methods of the balance sheet and profit and loss account are recognized on the balance sheet in shareholders' equity in the item "Translation adjustments". When the foreign entity is sold, these translation adjustments are recognized in the profit and loss account as part of the gain or loss on disposal.

#### 3.4.2. REPORTING ON FOREIGN CURRENCY TRANSACTIONS

Transactions denominated in foreign currencies are translated into euros using the exchange rates prevailing at the dates of the transactions. At the balance sheet date, cash and cash equivalents and operating receivables and payables denominated in foreign currencies are translated into Euros on the basis of the closing exchange rate for the year. Any foreign exchange gains or losses resulting from this translation are recognized in the profit and loss account for the year.

#### 3.5. INTANGIBLE ASSETS

#### 3.5.1. PATENTS

Patents created by Onxeo are recognized in expenses or capitalized in line with the accounting treatment for research and development costs set out below.

The patents acquired for consideration by Onxeo are recognized as fixed assets and are amortized. The amortization period generally applied by Onxeo is ten years, which corresponds to the estimated useful life of the patents.

#### 3.5.2. RESEARCH AND DEVELOPMENT COSTS

Research costs are always expensed. Development costs are capitalized once the conditions set out in IAS 38 are satisfied. The Company considers that the six criteria set out in IAS 38 are not satisfied until such time as a marketing authorization is obtained.

The research and development projects which were acquired (or contributed) are recognized as intangible assets at their acquisition value even in the absence of marketing authorization.

Pursuant to IAS 38, intangible assets are classified in two categories:

- Assets with a defined useful life, whose initial value is recognized on the balance sheet, minus, as appropriate the residual value, are depreciated over the useful life expected by the Company, from their activation (start of marketing). They are subjected to impairment tests as soon as an indication of impairment is identified. In case these assets would not yet be in use and therefore not yet depreciated, they would also be subjected to impairment tests.
- Assets with a non-defined useful life, which are not depreciated but subjected to annual impairment tests as soon as an indication of impairment is identified.

#### 3.5.3. GOODWILL

In the case of business combinations, mergers and acquisitions, the goodwill corresponds to the difference between the amount of the transaction and the market value of the acquired assets and liabilities.

The goodwill is not amortized but is subjected to impairment tests on an annual basis as soon as an indication of impairment is identified.

### 3.5.4. IMPAIRMENT TEST

Pursuant to IAS 36 «Impairment of assets»

- Cash generating units (CGU) are subjected to impairments tests at least once a year provided they comprise
  a goodwill; Onxeo performs this test at closing date;
  - R&D assets relating to products in development or not yet commercialized (and thus not depreciated)
     subjected to impairment tests on an annual basis; Onxeo performs this test at closing date;

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- R&D assets relating to commercialized (and thus amortized) products are subjected to impairment tests, when circumstances indicate that these assets might have incurred value losses. This would be the case may commercialization be slower than expected.

The Group considers that it is a single CGU, insofar as the projects it develops belong to the same family of products, have overlapping economic models and are therefore inter-dependent. This single CGU includes goodwill and R&D assets acquired within the framework of the acquisition of Topotarget (comprising Beleodaq in its indication in 1st and 2<sup>nd</sup> line PTCL, as well as potential future indications for this product).

These impairment tests consist of comparing the recoverable value of the single CGU as well as of the acquired R&D assets (the higher value between the net fair value of the sale costs and the utility value) to their tested base. Depreciation is recognized when the recoverable value is lower than their tested base. In addition, sensitivity analyses are performed on the key parameters of the financial model used to determine the value in use and help identify potential risks of impairment.

#### 3.6. TANGIBLE ASSETS

In accordance with IAS 16, tangible fixed assets are recognized at acquisition cost less accumulated depreciation and impairment losses. Amortization of tangible assets is calculated on a straight-line basis.

The most common depreciation periods are as follows:

	Plant & equipment	5 years	
-		Specialized equipment	5 years
-		Fixtures and fittings	10 years
-	Office	and computer equipment	4 years
-		Furniture	5 years

Tangible assets are subjected to a depreciation test as soon as an indication of impairment is identified.

#### 3.7. FINANCIAL ASSETS AND INVENTORIES

Financial assets included in the scope of IAS 39 are classified either in financial assets at fair value through profit or loss, in loans and receivables, in investments held to maturity, or in available-for-sale financial assets. On initial recognition, financial assets are measured at fair value, increased, in the case of investments that are not recognized at fair value through profit or loss, by directly attributable transaction costs.

The Group determines the classification of its financial assets at the date of initial recognition and, in cases where it is authorized and appropriate to do so, revises this classification at each year-end.

Non-current financial assets include long-term investments, in particular:

- pledged cash mutual funds;
  - deposits and guarantees mainly corresponding to deposits required when entering lease agreements;
  - and the 'cash' portion of the liquidity contract related to the purchase of treasury shares (Note 8.1).

Current financial assets include trade receivables, other current assets, and cash and cash equivalents:

- other current assets include research tax credit receivables;
  - cash includes available balances in bank current accounts;
  - cash equivalents include cash funds and mutual investment funds, which can be mobilized or transferred in the very short term into a known cash amount and subject to a negligible risk of change in value.

These assets are recognized, depending on their nature, on the basis of the following policies:

# 3.7.1. ASSETS AT FAIR VALUE THROUGH PROFIT OR LOSS

Financial assets at fair value through profit or loss account include financial instruments designated as being measured at fair value through profit or loss account as from the date of their initial recognition, in accordance with the conditions of application of the fair value option which can apply to items that are managed, and whose performance is measured, on the basis of fair value.



This item includes bank current accounts and cash mutual funds that can be converted to cash, or sold in the very short term, and which do not present significant risks of loss of value if interest rates were to change.

These assets are classified in the balance sheet under 'Cash and cash equivalents'. They are recognized at fair value, without deducting any transaction costs which could be incurred on their sale. Realized and unrealized gains and losses associated with a change in the fair value of the assets are recognized in profit and loss as Cash and cash equivalents.

#### 3.7.2. LOANS AND RECEIVABLES

Loans and receivables are non-derivative financial assets with fixed or determinable payments that are not quoted on an active market. After initial recognition, loans and receivables are measured in accordance with the amortized cost method, applying the effective interest rate, net of any impairment.

This category includes deposits and guarantees recognized in non-current assets and operating receivables (trade receivables and other current assets) recognized in current assets.

Trade receivables and related accounts are initially recognized at fair value. They are discounted when their due date for settlement is more than one year. They are then recognized at the depreciated cost and the interest is recognized as financial income on the profit and loss account.

These assets may be subject to a provision for impairment if objective indications of impairment exist. The amount of the impairment is equal to the difference between the carrying amount of the asset and the present value of the estimated future cash flows (excluding future credit losses which have not yet been incurred), discounted at the original effective interest rate (i.e. at the effective interest rate calculated at the date of initial recognition).

As regards trade receivables, an impairment loss is recognized when the expected cash flows at the balance sheet date are less than the carrying amount. The analysis of the risk is carried out case by case, taking account of criteria such as the client's financial situation (probability of bankruptcy or significant financial difficulties), the age of the receivable or the existence of a dispute.

# 3.7.3. AVAILABLE FINANCIAL ASSETS

Available-for-sale financial assets are those non-derivative financial assets that are designated as available for sale or are not classified in one of the three previous categories. After initial recognition, available-for-sale financial assets are measured at fair value and gains and losses arising in relation to them are recognized through equity. When an available for sale financial asset is derecognized or impaired, the cumulative profit or loss previously recognized through equity is taken to the profit and loss account.

#### 3.7.4. Inventories

Inventories are stated at the lower of cost or net realizable value. Cost is calculated in accordance with the average weighted cost method. The cost of finished goods and work in progress incorporates the cost of raw materials, direct costs and general production overheads.

Impairment is calculated by comparing the value of the inventories at the balance sheet date with cost.

# 3.8. SHARED-BASED PAYMENTS (IFRS 2)

Share-based payments granted by the Company such as stock options, free shares and share subscription warrants are valued on the allocation date in accordance with the IFRS 2 standard in order to recognize an expense in profit and loss. The valuation is made using the Black-Scholes and binomial / trinomial methods. The application of these methods requires in particular assumptions to be made regarding the underlying Onxeo share price, as well as its volatility. The cost is generally staggered over the acquisition period.

The definitive vesting of stock options allocated to Group employees is subject to their presence within the company on the vesting date. Should an employee leave the company prior to this date, the condition is no longer met and the employee loses the benefit of their rights. In this situation, the Group applies the so-called 'forfeiture' method under which all previously-recognized expenses are credited in profit and loss.

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#### 3.9. NON-CURRENT LIABILITIES

# 3.9.1. EMPLOYEE BENEFIT OBLIGATIONS (IAS 19)

#### Post-employment benefits

Post-employment obligations are recognized in provisions. In accordance with IAS 19, the actuarial valuation method used is the Projected Unit Credit Method with Service Prorate, which is based on financial (discount rate, inflation rate) and demographic (rate of increase in salaries, employee turnover rate) assumptions. This method enables the present value of the benefit obligation to be determined on the basis of services rendered by the employee at the valuation date. The actuarial gains and losses are recognized as "other items of the total profit (loss)".

#### 3.9.2. Provisions for Litigation

A provision is recognized where the Group has a current legal or constructive obligation to a third party, as a result of a past event, which it is probable will lead to an outflow of resources to the third party without receipt of equivalent consideration, where such future cash outflows can be estimated reliably.

#### 3.9.3. REFUNDABLE ADVANCES

In application of IAS 20 on the recognition of public grants and information to be provided on public aid, the advantages pertaining to loans at zero or low interest over market ones are taken into account and therefore recognized as grants. Refundable advances minus the amount of the grant are recognized as financial liabilities. The interest charges are calculated based on the market interest rate.

Refundable advances without a preferential rate are recognized pursuant to IAS 39 according to the "amortized cost" rule; the financial costs are calculated at the actual interest rate.

Refundable advances are recorded under "Other liabilities" They are initially stated at fair value, which in most cases corresponds to their nominal value, then at amortized cost.

# 3.10. FINANCIAL LIABILITES

Bank borrowings and debt instruments are initially recognized at fair value less directly attributable transaction costs. Subsequent to initial recognition, they are measured at amortized cost using the effective interest rate method.

Gains and losses are recorded in the profit and loss account when the debt is derecognized, as well as through the amortized cost mechanism. The amortization expense as calculated in application of the effective interest rate method is recognized under 'Financial income/expense, Cost of debt'.

# 3.11. OTHER CURRENT LIABILITES

Current liabilities are stated at fair value.

#### 3.12. OPERATING REVENUES

The Group's net sales include income from the sale of pharmaceutical products, income generated under licensing agreements, the proceeds collected on sales, and income from services rendered.

Sales of goods are recognized under net sales at the date of transfer to the client of the risks and rewards inherent in ownership. They are measured on the basis of the price stipulated in the contract of sale.

Agreements under which the Group issues a license to a third party providing it with rights to market one or more products in its portfolio generally involve an initial upfront payment at the date of signature, various other additional payments which are subject to the achievement of regulatory and sales objectives and royalties on sales.

In accordance with IAS 18:



- initial payments received under the signing of a licensing agreement, representing the contracting party's share of R&D investments incurred by the Company, are initially recorded as deferred revenue and subsequently spread over the period leading up to the estimated date of obtaining the marketing authorization.
- Subsequent payments related to the achievement of a contractually defined milestone are recognized as income on the date when the contractual condition is met.

Royalties earned are recognized in net sales on the basis of the sales figures achieved by the partners in the period and in application of the contractual royalty rates. Should a partner be unable to forward net sales data, the basis for royalties, prior to the date of publication of the accounts, a valuation would be made by valuing actual quantities for the period with historical net unit sales achieved for the product concerned.

#### 3.13. OPERATING GRANTS

In accordance with IAS 20, public grants whose amounts are related to the pattern of corresponding costs are classified as a deduction from the corresponding expenses.

#### 3.14. OTHER OPERATING INCOME AND EXPENSES

This item includes non-recurrent, non-operational and significant events.

#### 3.15. DEFERRED TAXES

A deferred tax asset is recognized for tax loss carry forwards and unused tax credits where it is probable that future taxable profits against which these items can be offset will be available.

A deferred tax liability is recognized for all taxable temporary differences and for the acquired R&D fixed assets.

#### 3.16. RESEARCH TAX CREDIT

Research tax credits are granted to companies by the French State in order to encourage them to carry out technical and scientific research. Companies which prove expenditure meeting the criteria required to benefit from the research tax credit may use it to pay the corporation tax of the financial year during which the expenditure was incurred, and also in the next three years. If the amount of the tax is not sufficient to cover the total amount of the tax credit at the end of the three-year period, the difference is reimbursed by the State in cash to the entity. If the company meets certain criteria in terms of sales, workforce or assets in order to be eligible for the SME category, it may request the immediate reimbursement of the research tax credit. Onxeo meets these criteria. Onxeo benefits from a similar mechanism in Denmark.

The Group uses the research tax credits for the research costs incurred in each financial year and recognizes the amount to be received as a reduction of these costs in the same financial year.

# NOTE 4 - TREATMENT OF THE ACQUISITION OF DNA THERAPEUTICS

DNA Therapeutics was acquired on March 25 2016, the effective date of taking control of it. Onxeo acquired 100% of the shares of DNA Therapeutics in exchange for 553,819 Onxeo shares evaluated at €3.13 per share (spot price on 24 March 2016), i.e. a total amount of €1,733,000. This acquisition enabled to add to Onxeo's R&D portfolio the unique DNA Therapeutics project, namely the signal interfering DNA AsiDNA.

This acquisition has been booked according to IFRS 3 revised. Following the allocation of the purchase price to the assets and liabilities of the company, at their fair value for a net negative amount of €739,000, a R&D asset has been booked for an amount of €2,472,000. No goodwill has been recognized as a result of the purchase price allocation.

The initial valuation of acquired R&D assets is based on information in existence as of the acquisition date regarding the development plan of the project and takes into account certain assumptions deemed to be reasonable by the company's management. However, such assumptions may be inaccurate and in the event of any delay or failure, the value of the R&D assets acquired may not be recoverable and could negatively impact the operating result. In this respect, a value test was implemented on December 31, 2016 (see methodology

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explained in Note 6 - Intangible Assets) which was able to conclude as to the absence of loss of value of the R&D assets related to the AsiDNA project.

Given the impact, considered to be not significant, of this acquisition in the financial statements of the Group, no pro forma profit and loss account is presented.

# NOTE 5 - MANAGEMENT OF RISKS RELATED TO FINANCIAL INSTRUMENTS (IFRS 7)

The Group's operational and financial activities expose it to the following main risks linked to the financial instruments employed:

### 5.1. LIQUIDITY RISK

Liquidity risk is essentially linked with the Company's financial profile, as long as it does not generate significant revenues in proportion of its expenses, notably in research and development. Cash reserves at year-end provides a cash runway until early 2018. Ahead of this timeline, the Company might need new fund-raising or non-dilutive financing to secure its operations in case additional revenues from new licensing agreements would not suffice.

Besides, the Company is not structurally a borrower. The only financial liabilities are advances from public organizations (including from BPI France) as part of R&D programs, which are repayable only in the event of commercial or technical success. There is no short-term risk and repayment is dependent on revenue being generated by the financed projects.

### 5.2. MARKET RISK

Only available-for-sale financial assets (see Note 11) are subject to market risk. They correspond to the portion invested in Onxeo shares of the liquidity contract implemented by the company with CM-CIC Securities. The value of these shares depends on the share price on the NYSE Euronext Paris market.

### 5.3. COUNTERPARTY RISK

The counterparty risk is limited to investments made by the Company. These investments are in leading establishments, and the Company monitors its exposure to counterparty risk on a continual basis.

### 5.4. FOREIGN EXCHANGE RISK

Because the Company has implemented no foreign exchange hedging instruments, this point is not applicable.

### 5.5. INTEREST RATE RISK

Since the Company has not incurred debt, this point does not apply.

### NOTE 6 - INTANGIBLE ASSETS

Les Intangible assets of a net amount of €87,213,000 at December 31, 2016 consist primarily of:

- R&D assets acquired within the context of the merger with Topotarget amounting to €64,650,000
- R&D assets acquired within the context of the acquisition of DNA Therapeutics amounting to €2,472,000
- Goodwill recorded from the Topotarget merger of €20,059,000

The R&D assets linked with Beleodaq were depreciated by a total amount of €1,650,000 over the year in counterparty of the revenues generated by the commercialization of the product by partner Spectrum Pharmaceuticals in second-line peripheral T-cell lymphoma. These assets are depreciated over the duration of the product's anticipated commercialization for this indication (17 years).

R&D assets and the single CGU comprising the goodwill were subject to a value test at December 31, 2016.



### 6.1. R&D ASSETS

R&D assets acquired within the framework of the Topotarget acquisition, namely Beleodaq in its current PTCL indication as well as in its potential future indications, have all been tested no matter whether they are commercialized or not. Indications in 1st and 2nd line PTCL have been have been tested together, the Group considering that they concern the same pathology and have a common development plan. The value in use if these R&D assets has been determined using the provisional cash flow method. A discount rate of 16.45% has been applied to the cash flow, taking account of the market risk and the specific risks related to Onxeo. Since the fair value obtained is higher than the tested base, both for Beleodaq in 1st and 2nd line PTCL and for potential future indications of the product, no depreciation of the acquired R&D assets of an amount of €64.7 million has been recognized.

These tests have been performed taking into account Beleodaq current operating conditions. However, the Group does not exclude a potentially greater loss of value in case operating conditions pertaining to Beleodaq would change in the future.

### 6.2. SENSITIVITY TESTS

Further, the Group performed sensitivity tests on the key parameters of the model which enabled it to determine that a 0.5% increase of the discount rate would entail a limited loss of value of the assets concerned, amounting to €0.7 million. The 5% reduction of other parameters such as the probabilities of success of indications not yet registered or the revenue expected from the different indications planned would entail a loss of value of between €1.4 million and €2.6 million. The impact of a combined decrease of these parameters would entail a loss of value of around €8.5 million.

### 6.3. GOODWILL

The Group determined the recoverable value of the single CGU comprising the goodwill as being the higher value between the fair value and the value in use. Given that the Onxeo share market can be considered an active market within the meaning of IFRS 13.38.a, in view of the volumes of shares traded characterizing major liquidity, the fair value of the single CGU has been assessed in reference to its stock market capitalization as at December 31, 2016. The value in use for its part has been determined based on provisional cash flow, incorporating all income and expenditure relating to the indications currently in portfolio, including the potential developments on the products developed by the Group. A discount rate of 16.45% has been applied to the cash flow, taking account of the market risk and the specific risks related to Onxeo. Since the recoverable value thus determined is significantly higher than the tested base (net book assets consolidated on that date), no goodwill depreciation of an amount of €20 million has been recognized.

Research and development costs incurred in financial year 2016 were recognized as a cost in the amount of €18,075,000, including €3,536,000 for personnel expenses, €36,000 for regulatory taxes and fees, and €14,397,000 for external expenses.

No new significant development costs were incurred on the Company's registered products. Consequently, there were no capital development costs over the year.

### NOTE 7 - TANGIBLE ASSETS

In thousands of €	31/12/2015	Increase	Decrease	31/12/2016
Gross value	7 276	479	-3 350	4 405
Depreciation	-6 418	-451	3 121	-3 748
Capital grants	-80		37	-43
Original value of lease	163	67	-58	171
Accumulated amortization of lease	-100	-31	58	-74
Net value of tangible assets	841	64	-192	713

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The increase in tangible assets is due mainly to acquisitions of sundry laboratory and research equipment and computer equipment. The reductions correspond to an updating of the file with recognition of the exit of fully amortized old fixed assets.

### **NOTE 8 - OTHER ASSETS**

### 8.1. FINANCIAL ASSETS

In thousands of €	31/12/2015	Increase	Decrease	Discounting	31/12/2016
Receivable from investments	1				1
Deposits and guarantees	201	7	12		196
Liquidity contract (cash)	105	4			109
Net value of financial assets	307	11	12	0	306

### 8.2. TRADE RECEIVABLES

In thousands of €	31/12/2016	< 1 year	> 1 year	31/12/2015
Trade receivables, net	1 548	1 548		1 036

Trade receivables essentially correspond to receivables in respect of the partner Spectrum Pharmaceuticals corresponding to re-invoicing of R&D costs and to royalties on sales due by this partner. This amount is depreciated up to €972,000.

### 8.3. OTHER RECEIVABLES

In thousands of €	31/12/2016	< 1 year	> 1 year	31/12/2015
Personnel	8	8		2
Research tax credit	3 955	3 955		3 814
Other tax receivables	705	705		2 202
Other receivables	283	283		104
Prepaid expenses	941	941		640
Net amount of other receivables	5 893	5 893	0	6 762

The change in the 'research tax credit' item is due to the collection of the receivable recognized at December 31, 2015 corresponding to the 2015 research tax credit, and the recognition of the research tax credit for 2016 in the amount of €3,955,000. This item also includes the Danish research tax credit of €186,000. These receivables were recovered early and were therefore all classified as less than one year.

In accordance with the IAS 20 standard, the research tax credit for FY 2016 reduced expense and income items according to their nature, as follows:

In thousands of €	31/12/2016	31/12/2015
Reduction in personnel costs	613	749
Reduction in external expenses	3275	3 014
Reduction in depreciation and amortization	67	51
Total research tax credit	3 955	3 814



Other tax receivables essentially correspond to sundry VAT credits.

### 8.4. CASH AND CASH EQUIVALENTS

In thousands of €	Net at 31/12/2016	Net at 31/12/2015	Change in cash and cash equivalents
Cash	23 941	28 486	-4 545
Financial investments	5 302	5 307	-4
Total net cash	29 243	33 793	-4 549

The change in net cash is a decrease of €4.5 million. It mostly comes from the operating costs of the company, particularly in terms of research and development, for an amount of €16.2 million, partly offset by the raising of funds finalized at the end of September for a net amount of €11 million and the signing payment of \$3 million for the new partner Pint Pharma.

Bank current accounts are Euro and US dollar accounts opened with Neuflize-OBC and Crédit du Nord. Investments mainly consist of:

- Marketable medium-term warrants, available at any time and having low volatility with a very low risk of changes in value linked to changes in interest rates.
- Short-term deposits of less than three months with a capital guarantee (current bank accounts), acquired from the banks Neuflize-OBC and Crédit du Nord, capable of boosting performance and that meet the definition of cash equivalents in accordance with IAS 7.6 and IAS 7.7.

### NOTE 9 - SHAREHOLDER'S EQUITY

### 9.1. SHARE CAPITAL

### 9.1.1. CHANGES IN SHARE CAPITAL

At 31 December 2016, the share capital amounted to €11,760,851, divided into 47,043,404 ordinary shares with a nominal value of €0.25 each, all of the same class and fully paid up.

During the financial year, the company's share capital changed as follows:

		Nominal	Number of shares	€
Shares fully paid at 31/12/2015		0,25	40 552 083	10 138 021
Capital increase - DNA acquisition	(1)	0,25	553 819	138 454,75
Capital increase - reserved to DNA shareholders	(2)	0,25	364 958	91 239,50
Capital increase private investment	(3)	0,25	5 434 783	1 358 695,75
AGA capital increase acquired	(4)	0,25	137 761	34 440,25
Shares fully paid at 30/06/2016		0,25	47.043.404	11 760 851,00

- (1) Capital increase due to the acquisition of 100% of DNA Therapeutics shares on March 25, 2016: issuance of 553,819 new ordinary shares at the unit price of €3.13, with par value of €0.25 each, corresponding to a capital increase of €138,000 along with an issue premium of €1,595,000.
- (2) Capital increase reserved for certain historical shareholders of DNA Therapeutics on April 1, 2016: issuance of 364,958 new ordinary shares at the unit price of €2.74, with par value of €0.25 each, corresponding to a capital increase of €91,000 along with an issue premium of €909,000.

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(3) Reserve capital increase on 30 September 2016: issuance of 5,434,783 new ordinary shares at the unit price of €2.30, with a par value of €0.25 each, corresponding to an increase in share capital of €1,359,000 along with an issue premium of €11,141,000.

(4)

The item Issue Premium increased from €243,854,000 to €255,960,000 euros as a result of the following main events:

- Capital increases described above, for a total amount over the year 2016 of €13,578,000
- Share subscription warrants newly allocated for €88,000
- Charging of the 2016 capital increase costs for an amount of €1,519,000
- Minus the withdrawal related to the free shares allocated in 2016 for an amount of €41,000

### 9.2. TREASURY SHARES

In accordance with the IAS 32 standard, paragraph 33, treasury shares acquired in the context of the liquidity contract signed with CM-CIC Securities were deducted from shareholders' equity for an amount of €97,000. Losses on share buybacks as of December 31, 2016 amounting to €31,000 were deducted from income pursuant to the standard.

### 9.3. RESERVES

Reserves, amounting to (€150,864,000), are made up mainly of a retained earnings deficit of (€150,200,000).

### 9.4. SHARE-BASED PAYMENTS

All disclosures concerning the BSAs, stock options and free shares granted by the Group are set out in Note 18 helow

The 2016 expense related to share-based payments amounts to €482,000.

### 9.4.1. BSA: French share purchase warrants

The valuation of these BSAs was made using the Black & Scholes method, supported by the binomial / trinomial method to reflect different possible exercise dates.

The Board of Directors made two allocations of share purchase warrants (BSA 2016 and BSA 16-3) to non-executive or non-salaried employees of the company and an allocation to key consultants (BSA 2016-2), as follows:

	Warrants 2016	Warrants 2016-2	Warrants 2016-3
Date of grant	23/01/2016	28/07/2016	21/12/2016
Number of warrants granted	90 000	260 000	70 000
Number of warrants subscribed	90 000	190 000	40 000
Vesting	15 months	18 months	18 months
Exercise price (€)	3,33	2.61	2.43

The expense corresponding to the financial year is €61,000.

### 9.4.2. STOCK OPTIONS (SO)

The valuation of these SOs was made using the Black & Scholes method, value supported by the binomial / trinomial method to reflect different possible exercise dates.

On July 28, 2016, the board of directors made two allocations of stock options to the benefit of employees ("Employee SO 2016" plan) and executives ("Executive SO 2016" plan), as follows:



	Employee SO 2016	<b>Executive SO 2016</b>
Allocation date	28/07/2016	28/07/2016
Number of warrants allocated	333 500	70 000
Vesting	4 year	4 year
Subscription price	3,16	3,16

The expense corresponding to the financial year is €35,000.

The Board of Directors meeting of 22 January and 28 July 2016 have noted the cancellation, due to the departure of employees, of 19,500 SO 2012, 1,800 SO 2013, 12,261 SO 2014, 26,500 SO 2015, 33,700 SO SAL 2016.

The consequence of the cancellations is a decrease in liability of €58,000.

### 9.4.3. AGAs (FREE SHARES)

On July 28, 2016, the board of directors made two free share allocations to the benefit of employees ("Employee AGA 2016" plan) and executives ("Executive AGA 2016" plan), as follows:

	<b>Employee AGA 2016</b>	<b>Executive AGA 2016</b>
Date of grant	28/07/2016	28/07/2016
Number of warrants granted	134 750	30 000
final acquisition	28/07/17	28/07/17
Exercise price (€)	3,16	3,16

The expense corresponding to the financial year is €197,000.

On January 22 and July 28 2016, the Board of Directors recorded the automatic cancellation due to employee departures of 17,154 AGA 2014 and 16,700 AGA 2016.

The impact of these cancellations is a decrease in the total cost of €47,000.

### NOTE 10 - NON-CURRENT LIABILITES

### 10.1. NON-CURRENT DEFERRED TAX

This item of €11,895,000 relates to research and development assets acquired within the context of the Topotarget merger in June 2014. The increase of the differed tax liability over the year results from the variation of the Danish tax value of the underlying assets.

### 10.2. PROVISIONS

In thousands of €	31/12/2015	Allowances	Rev	ersals	31/12/2016
			Used	Unused	
Post-employment benefits	489	109			598
Provision for litigation	230			191	39
Total non-current provisions	719	109	0	191	637

### 10.2.1. Pension Liabilities (IAS 19 Revised)

The provision for pension commitments amounts to €598,000 compared to €489,000 in 2015, i.e. reducing income by €42,000. The actuarial gap of €67000 was recognized directly as a reserve according to the standard.

The actuarial assumptions are as follows:



	31/12/2016	31/12/2015
Collective bargaining agreement	Medical industry	Medical industry
Retirement age	Between 65 and 67 years, under the Pension Reform Act of November 10 2010	Between 65 and 67 years, under the Pension Reform Act of November 10 2010
Calculation date	30/06/2016	31/12/2015
Mortality table	INSEE 2015	INSEE 2015
Discount rate	1.63%	2.26% (AA rate Reuters)
Rate of salary increase	2%	3%
Employee turnover rate	By age category: - 0% from 16 to 24 - 4.09 % from 25 to 34 - 5.26 % from 35 to 44 - 1.75 % from 45 to 54 - 0.00 % above 55	By age category: - 0% from 16 to 24 - 2.30 % from 25 to 34 - 8.05 % from 35 to 44 - 2.30 % from 45 to 54 - 0.57 % above 55
Social charges	46% for Onxeo FR	46% for Onxeo FR

### 10.2.2. Provisions for Litigation

Provisions for contingencies and charges represented an amount of €73.000 corresponding to provisions for contingencies with ex-employees.

### Litigation with SpeBio/SpePharm

Just as on December 31, 2015, the possible litigation risks under way with SpePharm and SpeBio cannot be reliably measured. As the Company considers itself to be within its rights, no provision has been made as of December 31, 2016.

On February 27, 2009, Onxeo broke off collaboration with SpePharm and reacquired the rights to market Loramyc® in Europe from the SpeBio joint venture. Onxeo has taken SpePharm and SpeBio to the International Court of Arbitration of the International Chamber of Commerce to obtain damages for the losses suffered on account of breaches of contract committed by these companies under the partnership that had been agreed for the commercial launch of Loramyc®. This process is part of the ongoing law suit filed by Onxeo on SpeBio before the Commercial Court of Paris on February 27, 2009 and which has not been placed by Onxeo. SpeBio itself referred the suit to the Clerk of the Commercial Court while being aware of Onxeo's referral to the Arbitral Tribunal.

SpePharm and SpeBio issued counterclaims for damages before the Arbitral Tribunal and the Commercial Court respectively.

In a partial arbitral decision as to the question of its jurisdiction, the Court of Arbitration affirmed its jurisdiction in respect to the one framework contract and only against SpePharm.

Having stayed the proceedings on its own jurisdiction, the Paris Commercial Court assumed jurisdiction. In pursuing its strategy to bring the dispute under a single proceeding, Onxeo filed an objection before the Paris Court of Appeals. This objection was rejected and the procedure has now resumed before the Commercial Court.

Onxeo requested the Commercial Court to force the intervention of SpePharm. By a May 3, 2016 ruling, the Paris Commercial Court upheld Onxeo's request pronouncing the forced intervention of SpePharm and the joinder of the Onxeo v. SpeBio and Onxeo v. SpePharm proceedings.

SpePharm filed contradicts against the ruling of May 3, 2016.

SpePharm filed conclusions for severance in order to obtain severance of the proceedings and alternative claims requesting that the Paris Commercial Court decline jurisdiction in favor of the ICC. On July 5, 2016, the Commercial Court stayed the proceedings pending the decision of the Court of Appeal brought by SpePharm



and dismissed the claims of SpePharm and SpeBio believing that there was no need to separate the two proceedings.

On September 20, 2016, the Paris Court of Appeals declared inadmissible the contradiction formed by SpePharm. Therefore, the proceedings before the Commercial Court of Paris were resumed.

At the February 6, 2017 hearing, SpePharm made conclusions in which it requested that the Tribunal decline jurisdiction in its respect and made various appeals.

### 10.3. OTHER NON-CURRENT LIABILITIES

This item mainly includes:

- An advance from BPI France paid under the Livatag program (NICE consortium), repayable in case of commercial success. An amount of €256,000 was received during the financial year in consideration of the crossing of contractual milestones at the clinical and industrial development of the product and the balance of the advance at 31 December 2016 is €4,516,938, of which €625,567 remain to be received in the coming years according to the funding schedule specified in the contract.
- An advance from BPI France paid under the ASIDNA program, repayable in case of commercial success. An amount of €550,000 was already collected in 2009 by DNA Therapeutics, €269,500 of which still have to be repaid over the financial years 2017 and 2018.
- An advance from BPI France paid under the ASIDNA program, repayable in case of commercial success. An
  amount of €562,000 was already collected in 2010 by DNA Therapeutics. The repayment schedule of this
  advance is scheduled as of September 2018.
- Deferred licensing revenues over one year for an amount of €1,136,000 (see Note 11.2)

### NOTE 11 - CURRENT LIABILITIES

### 11.1. TRADE PAYABLES

Trade payables have not been discounted to present value as none are payable more than one year after the balance sheet date.

In thousands of €	31/12/2016	31/12/2015
Trade payables	9 246	6 362

The increase in the Trade Payables item is mostly explained by the increase in clinical and pharmaceutical expenses related to the R&D programs.

### 11.2. OTHER LIABILITIES

In thousands of €	31/12/2016	31/12/2015
Social security and similar liabilities	1 536	2 177
Tax liabilities	123	1 637
Other liabilities	1 405	362
Total	3 064	4 175

Tax debts significantly decreased due to the repayment during the financial year of withholding tax amounting to €1,379,000.

Other liabilities at December 31, 2016 essentially consist of license revenues deferred to less than a year amounting to €1,188,000. This license revenue, collected on the signature of the agreements, is staggered according to an estimated date of obtaining the marketing authorization. The amount of short-term deferred license revenues transferred to revenue on the 2016 profit and loss account is detailed below:

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In thousands of €	Balance at 31/12/2015	Increase	Reversal through profit and loss	Balance at 31/12/2016	Less than 1 year	More than 1 year
Novamed	36		18	18	18	
Sosei	90		45	45	45	
PINT Pharma	0	2 730	469	2 261	1 125	1 136
Total	126	2 730	530	2 324	1 188	1 136

### NOTE 12 - INSTRUMENTS FINANCIERS

The carrying amount of financial instruments by category under IAS 39 is detailed as follows:

	Category in Not at	Notes	Balance sheet amounts as per IAS 39			Fair value	
In thousands of €	accordance with IAS 39		Net at Net at 31/12/2015 31/12/2016	Amortized cost	Fair value in equity	Fair value in income	as per IFRS7
Loans	P&C	0	0	0	0	0	0
Derivatives at fair value	AJVPR	0	0	0	0	0	0
Trade receivables and related accounts	P&C	1 036	1 548	1 548	0	0	1 548
Other receivables	P&C	6 762	5 579	5 579	0	0	5 579
Security deposits	P&C	201	164	164	0	0	164
Other assets available for sale	ADV	106	110	0	0	110	110
Cash and equivalents	AJVPR	33 793	29 243	23 941	0	5 302	29 243
Total Assets		41 897	36 645	31 232	0	5 412	36 645
Debenture loans	DACA	0	0	0	0	0	0
Loans debts/ credit inst.	DACA	69	106	106	0	0	106
Derivatives at fair value	PJVPR	0	0	0	0	0	0
BPI advances	DACA	3 545	4 454	4 454	0	0	4 454
Trade payables	DACA	6 362	9 030	9 030	0	0	9 030
Other debts/other liabilities	DACA	4 362	4 995	4 995	0	0	4 995
Total Liabilities		14 337	18 585	18 585	0	0	18 585

### Breakdown of fair values of financial assets and liabilities:

The table below shows financial instruments at fair value broken down by level:

- Level 1: financial instruments listed on an active market
- Level 2: financial instruments whose fair value is determined by comparison with observable market transactions in similar instruments, or based on a valuation whose variables include only observable market data
- Level 3: financial instruments whose fair value is determined entirely or in part using a valuation based on an estimation not based on market transaction prices in similar instruments.



	Level 1	Level 2	Level 3
Derivatives at fair value by income			
Derivatives at fair value by equity	0	0	0
Financial assets available for sale	0	110	0
Money market securities available for sale	0	5 302	0
Total Financial Assets	0	5 412	0
Derivatives at fair value by income	0	0	0
Derivatives at fair value by equity	0	0	0
Total Financial Liabilities	0	0	0

### NOTE 13 - OPERATING INCOME AND EXPENSES

### **13.1.** SALES

In thousands of €	31/12/2016	31/12/2015
Recurring sales from licensing agreements	3 455	2 733
Non-recurring sales from licensing agreements	969	749
Total sales	4 423	3 481

Recurring sales come from product sales and sales-based royalties related to license agreements established by the Company. The increase on 2015 comes from the roll-out of the business activity of the partners, mainly Spectrum Pharmaceuticals which sells Beleodaq in the United States.

Non-recurring sales from license agreements include a portion of sums received when signing some agreements entered into during the financial year or previous financial years and transferred over time to revenue on the profit and loss account in accordance with IAS 18 (see above §11.2) It particularly includes a portion representing €481,000 of the amount upon signature of \$3M paid by the new partner Pint Pharma.

In accordance with IFRS 8.32 and 33, the table below shows the provenance of sales by geographic area and in comparison with two Company product portfolios:

Breakdown of revenue In thousands of €	31/12/2016	31/12/2015
Orphan Products in Oncology	1 940	1 466
Other Products	2 483	2 015
Total	4 423	3 481
Europe	791	846
Rest of the world	3 632	2 636
Total	4 423	3 481

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### 13.2. PERSONNEL COSTS

Personnel costs are broken down as follows:

In thousands of €	31/12/2016	31/12/2015
Salaries	4 946	5 233
Expenses	2 171	2 068
Employee benefits (IFRS 2)	482	385
Deduction of research tax credit	-613	-749
Deduction of government grants	0	-51
Total personnel costs	6 984	6 887
Headcount (employees and officers)	53	53

The reduction in salaries is mainly due to a decrease in objective-linked bonuses due to personnel for 2016.

### 13.3. EXTERNAL EXPENSES

External expenses include mainly the following items:

In thousands of €	31/12/2016	31/12/2015
R&D expenses	14 067	12 676
Deduction of government grants	0	-9
Deduction of research tax credit	-3 275	-3 014
General and administrative expenses	6 338	6 541
Total	17 130	16 194

The increase in R&D expenses is explained by the mobilization of R&D programs with Livatag and AsiDNA.

### 13.4. AMORTIZATION

As explained in Note 6, amortization of part of the research and development programs acquired under the merger has been recognized in the accounts in the amount of €1,650,000. Other amortization charges (€264,000) relate essentially to the Company's tangible assets.

## NOTE 14 - NET FINANCIAL INCOME (EXPENSE)

In thousands of €	Cash	Non-Cash	31/12/2016	31/12/2015
Income from cash and cash equivalents	1 258	285	1543	1 805
Cost of gross debt	-437	0	-437	-1 205
Cost of net debt	821	285	1 106	600
Other financial income and expenses	0	0	0	2
Financial income	821	285	1 106	602

Cash income basically corresponds to a currency gain in the amount of €680,000, as well as interest in short-term investments.

The financial costs primarily include foreign exchange losses amounting to €235,000, and interest costs relating to the BPI France refundable advance for the Livatag program, calculated based on the actual interest rate according to IAS 39.



### NOTE 15 - TAXES

Deferred tax liabilities relating to research and development assets acquired within the context of the merger have increased by €541,000 in 2016, as a result of Danish tax rules. At 31 December 2016, the Onxeo Group had French tax loss carry-forwards of €208 million.

A request for tax ruling has been submitted to the French tax administration to allow transfer of DNA deficit to Onxeo.

No deferred tax asset was recognized insofar as the Company is unable to recover these tax losses in the short term.

### NOTE 16 - EARNINGS PER SHARE

### 16.1. NET EARNINGS PER SHASRE

In thousands of €	31/12/2016	31/12/2015
Net income/(loss) attributable to ordinary shareholders	-22 671	-19 409
Number of ordinary shares	47 043 404	40 544 204
Number of treasury shares	32 907	36 774
Earnings per share	(0,48)	(0,48)

Basic earnings per share is calculated by dividing the net profit (or loss) attributable to common shareholders (the numerator) by the weighted average number of outstanding ordinary shares (the denominator) for the period.

### 16.2. DILUTED EARNINGS PER SHARE

In thousands of €	31/12/2016	30/06/2015
Net income/(loss) attributable to ordinary shareholders	-22 671	-11 347
Number of ordinary shares	47 043 404	40 544 204
Effect of dilution (1)	-	-
Number of shares adjusted for diluted earnings	47 043 404	40 544 204
Diluted earnings	(0,48)	(0,48)

(1) Taking into account the conversion into shares of all of the stock-options, free shares and share purchase warrants attributed as of the balance sheet date, 2,619,627 extra shares would be created; the impact of dilution is not presented due to the accretive effect resulting from negative earnings.

To calculate diluted earnings per share, the average number of outstanding shares is adjusted to take into account the conversion of all ordinary shares that may be issued in the future, notably due to stock options and bonus shares during the vesting period.

The dilution effect is calculated using the treasury stock method. The number thus calculated is added to the average number of outstanding shares to obtain the denominator. To calculate diluted earnings, the net profit (or loss) attributable to holders of ordinary BioAlliance shares is adjusted by:

- any dividends or other items related to dilutive potential ordinary shares deducted in arriving at the profit (or loss) attributable to ordinary-share holders
- interest recognized in the period in respect of the dilutive potential ordinary shares
- any other changes in income or expense that would result from the conversion of the dilutive potential ordinary shares.

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### NOTE 17 - OFF-BALANCE-SHEET COMMITMENTS

# 17.1. OFF-BALANCE-SHEET COMMITMENTS RELATED TO THE COMPANY'S OPERATIONAL ACTIVITIES

### Operating leases (IAS 17)

The company has concluded real estate lease contracts for its head offices at 49, Boulevard du général Martial Valin, Paris, and for the registered offices of its establishment in Denmark, plus a company vehicle leasing contract. The future minimum lease expense is as follows:

< 1 year	Between 1 and 5 year	> 5 years
835	2 595	3 168

### 17.2. OFF-BALANCE-SHEET COMMITMENTS RELATED TO THE COMPANY'S FINANCING

### **Refundable Advances**

If the project is successful, these advances shall be refunded based on forecast operating income arising from the project, repayment equal to 3.0% of turnover over a maximum period of 15 years. In case the project is a failure, the justified, due and paid advances will not result in any repayment.

# 17.3. OTHER COMMITMENTS LINKED TO COMPANIES INCLUDED IN THE SCOPE OF CONSOLIDATION

None.



# NOTE 18 - SUMMARY OF BSA (SHARE PURCHASE WARRANTS), BCES (SPECIAL FOUNDER'S WARRANTS) AND STOCK OPTIONS AT 31 DECEMBER 2016

### Summary of the share purchase warrants (BSA) as at 31 December 2016

Туре	Authorization date	Authorized BSA	Allocation date	BSA allocated	Beneficiaries	BSA in circulation on 31/12/2016 adjusted (1)	BSA exercisable on 31/12/2016 adjusted (1)	Subscription price per share in euros adjusted (1)	Expiry date
BSA 2011	29/06/2011 Resolution 18	100 000	21/09/2011	70 000	Non-employee and non-executive Board Members	41 864	41 864	3,63	21/09/2017
BSA 2012	31/05/2012 Resolution 15	100 000	13/09/2012	85 000	Non-employee and non-executive Board Members	41 857	41 857	3,75	13/09/2018
BSA 2013	26/06/2013 Resolution 17	100 000	19/09/2013	85 000	Non-employee and non-executive Board Members	88 490	88 490	3,85	19/09/2023
	30/06/2014		22/09/2014	107 500	Non-employee and non-executive Board Members	85 886	85 886	6,17	22/09/2024
BSA 2014	Resolution 19	314 800	04/03/2015	35 500	Non-employee and non-executive Board Members	19 000	19 000	6,26	04/03/2025
BSA 2015	20/05/2015	405.000	27/10/2015	80 000	Non-employee and non-executive Board Members	65 000	45 000	3,61	27/10/2025
BSA 2015-2	Resolution 18	405 000	23/01/2016	90 000	Non-employee and non-executive Board Members	90 000	80 000	3,33	23/01/2026
BSA 2016			28/07/2016	260 000	Non-employee and non-executive Board Members	190 000	0	3,16	28/07/2026
BSA 2016-2	06/04/2016 Resolution 23	405 520	25/10/2016	30 000	Non-employee and non-executive Board Members	30 000	0	2,61	25/10/2026
BSA 2016-3			21/12/2016	70 000	Non-employee and non-executive Board Members	70 000	0	2,43	21/12/2026
TOTAL						722 097	402 097		

<sup>1)</sup> Adjustment of the number and of the subscription price of the warrants following the capital increases of July 2011, July 2013 and December 2014, pursuant to Article L. 228-99 of the French Commercial Code (Board Meeting of 28 July 2011, of 14 November 2013 and of 22 January 2015)



### Summary of the share subscription options (SO) as at 31 December 2016

Name of the Plan	Authorization Date	Number of options authorized	Allocation Date	Number of options allocated	Beneficiaries	Options in circulation as at 31/12/2016 adjusted (1)	Options exercisable as at 31/12/2016 adjusted (1)	Adjusted subscription price in euros (1)	Expiry Date
Employee SO 2010 (1)	22/04/2010	150 500	25/08/2010	120 800	employees	49 700	49 700	5,28	25/08/2020
Employee SO 2010 (2)	Resolutions 20 and	130 300	16/12/2010	16 000	employees	17 491	17 491	5,23	16/12/2020
Executive SO 2010	21	25 000	25/08/2010	25 000	executives	10 791	10 791	5,28	25/08/2020
TOTAL SO 2010		175 500		161 800		77 982	77 982		
Employee SO 2011 (1)	29/06/2011	300 000		218 500	employees	143 398	143 398	3,63	21/09/2021
Executive SO 2011	Resolutions 16 and 17	210 000	21/09/2011	210 000	executives	219 782	219 782	3,63	21/09/2021
TOTAL SO 2011		510 000		428 500		363 180	363 180		
Employee SO 2012	31/05/2012	333 000		268 000	employees	211 919	211 919	3,75	13/09/2022
Executive SO 2012	Resolutions 13 and 14	110 000	13/09/2012	110 000	executives	103 597	103 597	3,75	13/09/2022
TOTAL SO 2012		443 000		378 000		315 516	315 516		
Employee SO 2013	26/06/2013 Resolution 15	283 000	19/09/2013	195 500	employees	158 773	119 070	3,85	19/09/2023
TOTAL SO 2013		283 000		195 500		158 773	119 070		
Employee SO 2014	30/06/2014	314 800	22/09/2014	138 700	employees	107 242	53 631	6,17	22/09/2024
Executive SO 2014	Resolution 17	314 800	22/09/2014	40 000	executives	34 487	25 052	6,17	22/09/2024
TOTAL SO 2014		314 800		178 700		141 729	78 683		
Employee SO 2015	20/05/2015	405 000	27/10/2015	290 000	employees	262 500	82 625	3,61	27/10/2025
Executive SO 2015	Resolution 16	403 000	27/10/2013	60 000	executives	60 000	15 000	3,61	27/10/2025
TOTAL SO 2015		405 000		350 000		322 500	97 625		
Employee SO 2016	4/06/2016	405 520	28/07/2016	333 500	employees	299 800	0	3,16	
Executive SO 2016	Resolution 22	403 320	20/07/2010	70 000	executives	70 000	0	3,16	
TOTAL SO 2016		405 520		403 500		369 800	0		
TOTAL SO						1 749 480	1 052 056		

<sup>1)</sup> Adjustment of the number and of the subscription price of the warrants following the capital increases of July 2011, July 2013 and December 2014, pursuant to Article L. 228-99 of the French Commercial Code (Board Meeting of 28 July 2011, of 14 November 2013 and of 22 January 2015).



### Summary of rights to free shares (AGA) as at 31 December 2016

Name of the Plan	Authorization Date	Number of free shares authorized	Allocation date	Number of shares allocated	Beneficiaries	Rights to free shares in circulation as at 31/12/2016	Shares permanently acquired as at 31/12/2016
Employee AGA 2016	6/04/2016	405 520	28/07/2016	134 750	Employees	118 050	0
Executive AGA 2016	Resolution 24	403 320	103 320 28/07/2010	30 000	Executives	30 000	0
TOTAL AGA 2016		405 520		164 750		148 050	0
TOTAL AGA						148 050	0

<sup>1)</sup> Adjustment of the number and of the subscription price of the warrants following the capital increases of July 2011, July 2013 and December 2014, pursuant to Article L. 228-99 of the French Commercial Code (Board Meeting of 28 July 2011, of 14 November 2013 and of 22 January 2015)



### NOTE 19 - REMUNERATIONS OF CORPORATE OFFICERS

The table below summarizes the remuneration accounted for at December 31, 2016 for Judith Greciet (Managing Director), a non-salaried corporate officer as well as for members of the Board of Directors.

In thousands of €	31/12/2016	31/12/2015
Executives and corporate officers		
Short-term benefits (fixed/variable/except.)	381	502
Post-employment benefits	73	76
Long-term benefits	0	0
Share-based payment	127	218
Benefits in kind	3	7
Contract termination indemnities	0	311
Directors' fees	216	125
Fees (regulated agreement))	2	24
Total	802	1 262

Onxeo has established a method of remuneration of its directors through fees. The Annual General Meeting of April 6 2016 set the overall annual amount of directors' fees to be paid and divided among the members of the Board of Directors, at €220,000.

Corporate officers' retirement benefits amount to €73,184.

### NOTE 20 - RELATED PARTIES

With regard to paragraph 9 of IAS 24, Onxeo SA's related parties are as follows:

- Financière de la Montagne which, in its capacity as the largest shareholder of the company with 12.03% of the capital and as a board member, is considered to exert a significant influence on the company.
   No transactions were made in the year 2016 with Financière de la Montagne.
- The Chairman of the Board of Directors, as one of the main executives presenting the financial statements.

PJL Conseil, headed up by Patrick Langlois who held the position of Chairman of the Board of Directors until his resignation on January 22, 2016, collected fees under the consulting contract authorized by the Board of Directors on July 17 2013 for an amount of €2,000.

### NOTE 21 - INTRA-GROUP TRANSACTIONS

The transactions which took place between the parent company and the other companies of the group are summarized in gross values in the following table:

In thousands of €	31/12/2016	31/12/2015
Assets	77 698	104 875
Liabilities	2 904	2 836
Income	56	1 131
Expenses	176	74



### NOTE 22 - STATUTORY AUDITORS' FEES

The fees paid by Onxeo to its external auditors in 2016 and 2015 are as follows:

	Grant Thornton					Ernst & Young			
In thousands of €	Amo	ount	9	6		Amo	unt	%	ó
	2016	2015	2016	2015		2016	2015	2016	2015
Audit, statuto	ory audit, c	ertification,	review of	financial st	atei	ments und	er French	GAAP and I	FRS
Issuer	91	73	100%	88%		81	94	92%	100%
Fully consolidated subsidiary		9	0%	10%				0%	0%
Other procedures and services directly related to the statutory audit assignment	10	2	0%	2%		43		8%	0%
Sub-total	101	84	100%	100%		124	94	100%	100%
Other services rendered by the networks to the fully consolidated subsidiary						13			
Sub-total									
Total	101	84	100%	100%		137	94	100%	100%



# 6.2 STATUTORY AUDITOR'S REPORT ON THE CONSOLIDATED FINANCIAL STATEMENTS

GRANT THORNTON

French Member of Grant Thornton International
29, rue du Pont
92200 Neuilly-sur-Seine
S.A. au capital de € 2.297.184

ERNST & YOUNG Audit 1/2, place des Saisons 92400 Courbevoie - Paris-La Défense 1 S.A.S. à capital variable

Statutory Auditor Member of the Regional Company of Versailles Statutory Auditor Member of the Regional Company of Versailles

This is a free translation into English of the statutory auditors' report on the consolidated financial statements issued in French and it is provided solely for the convenience of English speaking users.

The statutory auditors' report includes information specifically required by French law in such reports, whether modified or not. This information is presented below the audit opinion on the consolidated financial statements and includes an explanatory paragraph discussing the auditors' assessments of certain significant accounting and auditing matters. These assessments were considered for the purpose of issuing an audit opinion on the consolidated financial statements taken as a whole and not to provide separate assurance on individual account balances, transactions or disclosures.

This report also includes information relating to the specific verification of information given in the Group's management report.

This report should be read in conjunction with, and construed in accordance with, French law and professional auditing standards applicable in France.

### Onxeo

Year ended December 31 2016

# Statutory auditors' report on the consolidated financial statements

To the Shareholders,

In compliance with the assignment entrusted to us by your annual general meetings, we hereby report to you, for the financial year ended December 31, 2016, on:

- the audit of the accompanying consolidated financial statements of Onxeo;
- the justification of our assessments;
- the specific verification required by law.

The consolidated financial statements have been approved by the Board of Directors. Our role is to express an opinion on these consolidated financial statements based on our audit.

### I. Opinion on the consolidated financial statements



We conducted our audit in accordance with professional standards applicable in France; these standards require that we plan and perform the audit to obtain reasonable assurance as to whether the consolidated financial statements are free of material misstatement. An audit involves performing procedures, using sampling techniques or other methods of selection, to obtain audit evidence about the amounts and disclosures in the consolidated financial statements. An audit also includes evaluating the appropriateness of accounting policies used and the reasonableness of accounting estimates made, as well as the overall presentation of the consolidated financial statements. We believe that the audit we have obtained is sufficient and appropriate to provide a basis for our audit opinion.

In our opinion, the consolidated financial statements give a true and fair view of the assets and liabilities and of the financial position of the group as at December 31, 2016 and of the results of its operations for the year then ended, in accordance with the IFRS standards as adopted by the European Union.

Without qualifying our opinion, we draw your attention to paragraph "Judgements and estimates of Group Management" of notes 3.1 and 5.1 "Liquidity risk" to the consolidated financial statements that exposes elements used by management to justify the application of the going concern principle for the preparation of the financial statements for the year ended December 31, 2016.

#### II. Justification of our assessments

In accordance with the requirements of article L. 823-9 of the French commercial code (Code de commerce) relating to the justification of our assessments, we bring to your attention the following matters:

- Paragraph 3.5 « Intangible assets » within note 3 « Accounting principles, rules and methods » to the consolidated accounts sets out the accounting rules and methods relating to the valuation of goodwill and research and development intangible assets. Our procedures consisted in examining implementation methods of these assets impairment tests as exposed in note 6 « Intangible Assets » to the consolidated financial statements, in examining data and assumptions on which are based actualized free cash flow forecasts as well as reviewing the calculations performed by your group. In the context of our assessments, we also ensured the reasonableness of estimates and assumptions used as well as verified that the notes mentioned above provide appropriate information.
- Paragraph 3.12 "Sales" within note 3 « Accounting principles, rules and methods » to the consolidated financial statements sets out the accounting rules and methods relating to the revenue recognition including the method of accounting for payments due to the signing of license agreements. We assessed the appropriateness of this method and its correct implementation. Our procedures consisted in examining the reasonableness of the estimates and assumptions on which is based the revenue recognition related to these agreements.

These assessments were made as part of our audit of the consolidated financial statements taken as a whole, and therefore contributed to the opinion we formed which is expressed in the first part of this report.

### III. Specific Verification

We have also performed, in accordance with professional standards applicable in France, the specific verifications required under the law regarding information relating to the Group, as provided in the management report.

We have no matters to report as to its fair presentation and its consistency with the consolidated financial statements.

128 2016 Registration Document



Neuilly-sur-Seine and Paris-La Défense, on 5 April 2017

# **The Statutory Auditors** (French Original signed by)

**GRANT THORNTON** 

**ERNST & YOUNG Audit** 

French member of Grant Thornton International

Jean-Pierre Colle Samuel Clochard

Franck Sebag



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## **BALANCE SHEET**

### 1. ASSETS

Categories	Gross	Amortization /	Net 2016	Net 2015
1	0.000	Depreciation	11012010	11012013
SUBSCRIBED UNCALLED SHARE CAPITAL				
NTANGIBLE FIXED ASSETS				
Incorporation expenses				
Development costs	65 089 350	3 679 888	61 409 462	59 590 000
Concessions, patents and similar rights	180 956	180 871	85	2 130
Goodwill	4 449 952		4 449 952	4 449 952
Other intangible assets	511 802	510 466	1 335	6 402
Advances and prepayments on intangible				
assets				
Total intangible fixed assets	70 232 060	4 371 225	65 860 835	64 048 483
TANGIBLE FIXED ASSETS				
Land				
Buildings				
Plant & equipment	1 220 944	986 735	234 209	20 261
Other tangible assets	3 182 668	2 760 758	421 910	611 613
Tangible assets in progress	1 724		1 724	226 740
Advances and prepayments				
Total tangible fixed assets	4 405 336	3 747 493	657 843	858 614
LONG-TERM INVESTMENTS				
Holdings valued by the equity method				
Other equity holdings	48 629 858	38 863 428	9 766 431	10 245 383
Receivables from investments				
Other long-term securities	97 060		97 060	157 057
Loans				
Other long-term investments	297 966		297 966	307 939
Total long-term investments	49 024 884	38 863 428	10 161 456	10 710 379
NON-CURRENT ASSETS	123 662 280	46 982 146	76 680 134	75 617 476
STOCKS				
Raw materials and supplies				
Work in progress - goods				
Work in progress - goods  Work in progress - services				
Semi-finished and finished goods				
Goods held for resale	102 022		102 022	106 106
	183 823		183 823	106 198
Total stocks	183 823		183 823	106 198
RECEIVABLES				
Prepayments to suppliers  Trade receivables	2 270 207	072 244	1 405 063	1 101 220
	2 378 207	972 244	1 405 963	1 181 229
Other receivables	34 353 949	25 613 186	8 740 763	9 721 085
Subscribed, called, unpaid share capital	26 722 457	26 505 420	10 146 726	10 002 21
Total receivables	36 732 157	26 585 430	10 146 726	10 902 314
LIQUID ASSETS	F 202 407		5 202 407	<b>5</b> 205 504
Securities including treasury shares:	5 302 407		5 302 407	5 306 681
Cash	23 681 068		23 681 068	28 225 576
Prepaid expenses	914 323		914 323	629 203
Total liquid assets	29 897 798		29 897 798	34 161 459
ACTIF CIRCULANT	66 813 778	26 585 430	40 228 348	45 169 971
leguing costs to be enveed ever several ves				
Issuing costs to be spread over several years				
Loan redemption premiums Translation adjustment - assets				201 02
Translation aujustinent - assets				281 027
TOTAL GENERAL				



### 2. LIABILITIES

Category			Net 2016	Net 2015
NET EQUITY				
Share capital	Of which paid:	11 760 851	11 760 851	10 138 021
Issue, merger and acquisition prem	iums		242 660 592	230 554 853
Excess of restated assets over histo	orical cost			
Legal reserve				
Reserves required by the articles of	of incorporation or	by contract		
Regulated reserves				
Other reserves			43 872	37 125
Retained earnings			(141 544 626)	(116 381 346)
NET INCOME for the period (profit	or loss)		(21 236 246)	(25 163 280)
Total net equity			91 684 444	99 185 373
Capital grants			42 820	79 520
Regulated provisions				
SHAREHOLDERS' EQUITY			91 727 264	99 264 892
Proceeds from issue of preference	shares			
Advances with specific conditions a			5 348 438	4 426 567
OTHER SHAREHOLDERS' EQUITY			5 348 438	4 426 567
·				
Contingency provisions			73 000	594 807
Loss provisions				
PROVISIONS FOR CONTINGENCIES AND LOS	SSES		73 000	594 807
FINANCIAL LIABILITIES				
Convertible bonds				
Other bonds				
Bank debts			7 737	8 791
Other debts			204 663	204 663
Total financial liabilities			212 401	213 454
OPERATING LIABILITIES				
Customer prepayments				49 200
Trade payables			9 116 052	6 309 953
Accrued taxes and personnel costs			1 659 193	2 415 902
Total operating liabilities			10 775 245	8 775 056
· · ·				
OTHER LIABILITIES				
Payables on fixed assets and relate	d accounts			116 450
Other liabilities			3 283 740	4 672 513
Total other financial liabili	ties		3 283 740	4 788 963
ACCRUALS				
Deferred revenue			2 319 813	343 346
LIABILITIES			16 591 198	14 120 819
Translation adjustment - liabilities			3 168 582	2 661 389
TOTAL GENERAL			116 908 482	121 068 474
		******		



## PROFIT AND LOSS ACCOUNT

## 1. PROFIT AND LOSS ACCOUNT (PART 1)

Categories	France	Export	Net 2016	Net 2015
Sale of goods held for resale		530 505	530 505	435 537
Production goods sold				
Production services sold		26 350	26 350	374 805
NET SALES		556 854	556 854	810 343
Production left in stock				
Capitalized production				
Operating grants			105	59 586
Excess depreciation and recovery on pro years	ovisions charge	ed in prior	76 906	63 794
Royalties from licensing and other incom	ne		3 484 930	2 898 437
TOTAL OPERATING INCOME			4 118 796	3 832 159
EXTERNAL EXPENSES				
Purchases of goods for resale (including	customs dutie	es)	344 201	298 028
Change in inventories			(77 625)	(41 027)
Purchases of raw materials and supplies			125 403	80 010
Change in inventories				
Other purchases and external expenses			20 009 247	19 106 108
Total external expenses			20 401 227	19 443 119
TAXES OTHER THAN ON INCOME			218 874	293 454
CHARGES DE PERSONNEL				
Wages and salaries			4 613 673	5 447 799
Payroll charges			2 070 805	2 063 410
Total personnel costs			6 684 478	7 511 210
OPERATING ALLOWANCES				
Amortization on fixed assets			1 735 470	1 712 880
Provisions on fixed assets				
Provisions on current assets			246 736	29 260
Provisions for contingencies and losses				
Total operating allowances			1 982 206	1 742 140
OTHER OPERATING EXPENSES			225 503	241 032
TOTAL ODERATING EVERNICES			20 542 207	20 220 055
TOTAL OPERATING EXPENSES			29 512 287	29 230 955
OPERATING INCOME/(LOSS)			(25 393 492)	(25 398 796)



## 2. PROFIT AND LOSS ACCOUNT (PART 2)

Categories	Net 2016	Net 2015
OPERATING INCOME/(LOSS)	(25 393 492)	(25 398 796)
JOINT TRANSACTIONS		
Allocated gain or transferred loss		
Sustained loss or transferred gain		
FINANCIAL INCOME		
Financial income from investments	61 301	99 718
Financial income from other securities and from fixed asset securities	51 610	234 555
Other interest and similar income	36 201	27 274
Provision reversals and expense transfers	21 936 065	74 395
Foreign exchange gains	680 018	1 571 397
Net gains on sales of marketable securities		
TOTAL FINANCIAL INCOME	22 765 195	2 007 339
FINANCIAL EXPENSES		
Amortization, depreciation and provisions	290 834	3 687 720
Interest and similar expenses	267 375	572 234
Foreign exchange losses	535 513	733 065
Net losses on sales of marketable securities		
TOTAL FINANCIAL EXPENSES	1 093 723	4 993 019
FINANCIAL INCOME	21 671 472	(2 985 679)
LOSS BEFORE EXCEPTIONAL ITEMS AND TAX	(3 722 020)	(28 384 475)
EXCEPTIONAL INCOME		
Exceptional income on operating transactions	4 379	250
Exceptional income on capital transactions	33 025	57 100
Provision reversals and expense transfers	240 780	2 962
Exceptional income	278 184	60 312
EXCEPTIONAL EXPENSES		
Exceptional expenses on operating transactions	5 009	120 880
Exceptional expenses on capital transactions	21 742 275	123 770
Exceptional provisions and expense transfers		312 536
Exceptional expenses	21 747 283	557 186
EXCEPTIONAL ITEMS	(21 469 099)	(496 873
Employee profit sharing		
Corporate income tax	(3 954 873)	(3 718 068
TOTAL INCOME	27 162 174	5 899 811
	40.000	04.000.00
TOTAL EXPENSES	48 398 420	31 063 091
PROFIT/(LOSS) FOR THE YEAR	(21 236 246)	(25 163 280)



### ACCOUNTING RULES AND METHODS

Onxeo ("the Company") is a clinical-stage biotechnology company specialized in developing innovative drugs for treating rare diseases particularly in the field of oncology. , responding to high demand for treatment in one of the sectors with the strongest growth in the pharmaceutical industry.

Onxeo's accounts at 31 December 2016 were made under the supervision of the Chief Executive Officer and were validated by the Board of Directors meeting on 7 March 2017.

### ACCOUNTING POLICIES

The annual financial statements for the year ended December 31, 2016 have been prepared and presented in accordance with the provisions of the Commercial Code and the French General Accounting Plan, in conformity with the prudence principle and the accruals basis of accounting.

The financial statements were prepared on a going concern basis based on the Company's cash flow forecasts. This principle has been elected by the board of directors as a result of the following elements: the consolidated net cash of €29.2 million allows the Company to fund its activities until early 2018 based on its finance plan. Moreover, the Company has identified potential additional funding allowing to extend its cash runway until at least mid-2018.

Items are recognized in the financial statements on a historical cost basis. The valuation methods applied for this year are unchanged from the previous financial year.

### 1.1. INTANGIBLE ASSETS

Intangible assets are recognized at acquisition cost or contribution value less accumulated depreciation and impairment losses.

Research and development costs are expensed directly to the profit and loss account. They may be capitalized in fixed assets when the following criteria are satisfied simultaneously:

- The projects in question are specific, well-defined projects,
- Each project must be technically feasible and have a realistic chance of commercial success at the balance sheet date,
- The cost of each project can be clearly identified.

These criteria are considered to be satisfied only once the Company has obtained marketing authorization.

Acquired research and development projects are recognized as intangible assets at transfer value even in the absence of marketing authorization.

Where a finite useful life has been defined the cost of intangible assets less any residual value is depreciated over the useful life as estimated by the Company. This period is determined on a case-by-case basis depending on the nature and characteristics of the elements included within the category. In particular, concessions and patents are amortized over a 10-year period on a straight-line basis, software is amortized over a 12-month period using a straight-line method, and R&D assets with finite useful lives in the marketing phase are amortized over their useful life expected by the Company.

When their useful life is indefinite, intangible assets are not amortized but are subject to annual impairment tests.

### 1.2. TANGIBLE ASSETS

The gross cost of tangible assets corresponds to their initial carrying value in the balance sheet including costs to bring such assets into condition for use, but excluding ancillary expenses related to their acquisition.



Depreciation of tangible assets is calculated on a straight-line basis. Depreciable lives and depreciation methods are generally as follows:

-	Plant and equipment	5 years
-	Specialized equipment	5 years
-	Fixtures and fittings	10 years
-	Office and computer equipment	4 years
-	Furniture	5 years

### 1.3. FINANCIAL ASSETS

- Investments and other long-term securities are measured at cost, excluding acquisition-related expenses.
- A provision for impairment is recorded at the balance sheet date if the actual value is less than their net book value.
- The amounts invested in the context of the liquidity contract managed by an investment services provider are recognized:
- under 'Other long-term securities' for treasury shares (being the portion invested in the Company's shares),
- under 'Other financial assets' for the portion kept in cash.

### 1.4. INVENTORIES

Inventories are measured at purchase cost using the weighted average cost method.

A provision for impairment is recorded if the actual value is less than the net book value.

### 1.5. RECEIVABLES AND PAYABLES

Receivables and payables are measured at their face value. A provision for impairment is recorded at the balance sheet date if the actual value of thee receivables is less than their net book value.

Receivables and payables denominated in foreign currencies are recognized at the exchange rate prevailing on the transaction date and are restated at the closing rate at each period end. Foreign exchange differences arising on such restatements are recognized in balance sheet assets and liabilities. A provision for losses is recognized in the event of unrealized foreign exchange losses.

Receivables are examined on a case-by-case basis and a provision for depreciation is established in line with the incurred risk.

### 1.6. MARKETABLE SECURITIES

Marketable securities are measured at cost, excluding acquisition-related expenses.

In the event of the sale of a number of similar securities granting the same rights, the carrying value of the securities sold is estimated using the FIFO method.

### 1.7. CASH

All liquid assets held in cash or banks are valued at their nominal value.

### 1.8. PROVISIONS FOR CONTINGENCIES AND LOSSES

Provisions correspond to obligations resulting from various disputes and risks, whose timing and amount is uncertain, to which the Group may be exposed in the context of its operations. A provision is recognized where the Company has a legal or constructive obligation to a third party, as a result of a past event, which it is probable or certain will lead to an outflow of resources to the third party without receipt of equivalent consideration, where such future cash outflows can be estimated reliably.

### 1.9. LICENSING AGREEMENTS

### Licenses granted to third parties



Agreements under which the Company licenses rights to third parties for marketing one or more products in its portfolio generally involve an upfront payment at the date of signature, as well as future milestone payments and the payment of royalties on net sales.

Upfront payments due on signature of a licensing agreement, representing the contracting party's share of R&D investments incurred by the Company, are initially recognized in deferred revenue and are subsequently taken to the profit and loss account over the period of the agreement or over a shorter period, depending on the Company's involvement and the specific conditions of the agreement.

In general, the future payments are conditional and depend on the achievement of certain objectives: registration of products, marketing authorization for products, obtaining a price and/or achievement of sales thresholds (sales performance). They are immediately recognized in other income in the year in which they are received by the Company.

### **1.10. GRANTS**

Operating grants are taken to profit and loss as the costs are incurred.

Refundable advances are recorded under "Other equity". Where the project is successful, these advances are refundable based on forecast operating income (loss) arising from the project. In case the project is a failure, the justified, due and paid advances will not result in any repayment.

### 2. SIGNIFICANT EVENTS DURING THE FINANCIAL YEAR

### 2.1. ACQUISITION OF DNA THERAPEUTICS

The Group announced on March 25, 2016 the final completion of the acquisition of 100% of the shares of DNA Therapeutics for an initial amount of €1.7 million in common shares of Onxeo giving rise to the creation of 553,819 new shares.

This acquisition strengthens the Group's portfolio of orphan oncology products and positions it in a new field at the forefront of scientific and clinical progress in oncology - repairing DNA using siDNA technology to signal interfering DNA, developed by DNA Therapeutics, and also AsiDNA a first-in-class product from this technology.

Additional milestone payments would be made, namely €1 million in shares or cash at Onxeo's discretion, if AsiDNA enters Phase II trial in a selected indication. Also anticipated is the payment of royalties on sales if the product goes to market, worth up to €25 million per indication.

Along with this acquisition, some longstanding shareholders of DNA Therapeutics subscribed to a reserved capital increase in early April 2016 for an amount of €1 million that led to the creation of 364,958 new shares.

On November 2, 2016, all assets and liabilities of DNA Therapeutics were part of a universal asset transfer to Onxeo, resulting in the dissolution of that company. As a result of this transaction, goodwill representing the value of the R&D assets acquired was recorded under "Development costs" for €3.26 million.

### 2.2. R&D PROGRAMS

During the financial year of 2016, the Company accelerated the recruitment of patients into the Phase III study "ReLive" to assess the effectiveness of Livatag in the 2nd line of advanced hepatocellular carcinoma treatment. The end of the planned recruitment of 390 patients was announced on January 31, 2017, enabling the release of preliminary results from the study by mid-2017.

In parallel, the Company has actively continued its preclinical development program for Livatag in combination with other anti-cancer agents for future applications in other indications, and has published some very encouraging results in various types of tumors

### 2.2.1. **ASIDNA**

Since March 2016 and the acquisition of the company DNA Therapeutics, the Group pursued the development of AsiDNA, focusing on the optimization of manufacturing processes, in parallel with a pre-clinical program that should enable entering the product in a Phase I clinical trial by the end of 2017.



### 2.2.2. BELEODAQ (BELINOSTAT)

As with Livatag, belinostat is being developed in combination with other anti-cancer agents, using a product life cycle management approach. In 2016, the Company announced encouraging preclinical study results for belinostat in association with control point inhibitors as a possible treatment option for new indications.

In 2016, the Company also announced the development of an oral delivery formula for belinostat that would be a net competitive advantage for patients and doctors.

### 2.3. LICENSE AGREEMENT WITH PINT PHARMA

In July 2016, the Company signed an exclusive licensing agreement with Pint Pharma to market Beleodaq (belinostat) in the field of peripheral T cell lymphoma in seven key countries in South America. An initial \$3 million payment at the signing was received by Onxeo that was spread as revenue over several months until the estimated market approval date. The agreement also calls for payments based on regulatory milestones and revenue levels as well as extensive royalties on net sales of Beleodaq®, for a total value greater than \$20 million.

### 2.4. FINANCING

At the end of September 2016, the Company announced a capital increase through the issuance of new common shares without preferential subscription rights., Pursuant to Article L.225-138 of the Commercial Code, this capital increase was reserved for a category of investors defined in the 17th Resolution adopted by the Company's General Meeting of April 6, 2016, namely: "companies and investment funds investing on a regular basis in small-cap growth companies, i.e. their market capitalization does not exceed €1 billion, including, without limitation, all private equity venture capital funds working in the area of health or biotechnology and participating in the capital increase for a unit amount of over €100,000 including premium, within the limit of a maximum of 25 subscribers.

This capital increase resulted in the issuance of 5,434,783 new common shares on September 30, 2016 for an amount of €12.5 million. The funds raised increased the Company's cash position to €34.9 million at the end of the settlement and delivery of the capital increase, providing the Company with the additional resources to continue its R&D programs in the field of orphan diseases in oncology.

### 2.5. UNIVERSAL ASSET TRANSFER OF BIOALLIANCE PHARMA LABORATORIES

On 2 November 2016, the totality of the assets and liabilities of the subsidiary Laboratoires BioAlliance Pharma were universally transferred to Onxeo, leading to the dissolution of the subsidiary. This transaction had no significant effect on the accounts.

### 2.6. POST-BALANCE SHEET EVENTS AT 31 DECEMBER 2016

There are no post-balance sheet events likely to have a material effect on the accounts.

### 3. NOTES TO THE BALANCE SHEET

### **3.1.** INTANGIBLE ASSETS

- Gross intangible assets amounted to € 70 232 060 on December 31, 2016, and consist mainly of:
- €61,830,000 in development costs, corresponding to the acquisition cost of Beleodaq® (belinostat) in connection with the merger-absorption transaction of Topotarget in 2014.
- Goodwill of €4,450,000 represents the difference between the acquisition value of Topotarget and the net assets contributed.
- Technical loss due to merger of €3.259.350 represents the difference between the acquisition value of DNA Therapeutics and the net assets contributed.

Intangible assets also include patents, brands, and software acquired by the Company for a gross total amount of €693,000.

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Depreciation amounted to €4 371 225, of which €3 679 888 resulted from the depreciation of assets associated with the product Beleodaq® for its second-line indication in peripheral T-cell lymphoma, generating income through the marketing efforts of Spectrum Pharmaceuticals, a partner company. These assets are depreciated over the duration of the product's anticipated commercialization for this indication (17 years).

The intangible assets from the merger with Topotarget including R&D assets and goodwill, were the subject of a value test at December 31, 2016, as follow:

### - Recoverable amount of intangible assets

Every year, goodwill is subjected to an impairment test. This test is performed once per year at the closing date, and if a change in the value is observed during the year. R&D assets, which are depreciable, were also tested. An impairment is recorded if the recoverable amount of the intangible assets is lower than its book value, i.e. the higher value between the net fair value at the disposal cost and the value in use.

#### - Goodwill

On December 31, 2016, the Group determined the recoverable value of the goodwill as the higher value between the fair value and value in use. The fair value was assessed by reference to Onxeo's market capitalization at December 31, 2016. As for the value in use, it was determined based on projected cash flow, including all income and expenses related to the indications currently in the portfolio, as well as potential advances on products developed by the Group. As the recoverable amount thus obtained, net of disposal costs, was higher than the book value of the goodwill, no depreciation appeared necessary.

### - R&D assets

On December 31, 2016, the Group estimated the fair value of the R&D assets based on projected cash flow, including income and expenses related to Beleodaq's PTCL indication, as well as the product's other potential indications that may be developed in the future. A discount rate of 16.45% was applied to the cash flow to take into account market risk and other specific risks associated with Onxeo. As a result, the fair value of the R&D assets, net of disposal costs, were higher than their book value thus there is no cause to depreciate them.

### **3.2.** TANGIBLE ASSETS

Tangible assets are made up mainly of laboratory and research equipment, computer equipment and other fittings and equipment purchased by the Company.

During the year 2016, acquisitions amounted to €479 034. Capital depreciation was €3 029 781, fully amortized, corresponding to an asset update made by Onxeo.

### 3.3. FINANCIAL ASSETS

Financial assets correspond primarily to equity securities held by Onxeo in its subsidiaries in France and abroad.

Changes to this item correspond mainly to depreciation in 2016 of €635,000, resulting from losses at subsidiaries.

The merger of Laboratoire Biolliance Pharma has no impact on this item, due to the depreciations of the assets.

The amount of treasury shares held within the context of the liquidity contract at December 31, 2016, was €59,500 corresponding to 23,800 shares recognized in "Other long-term securities" and non-invested cash increased to €109,241.

### 3.4. TRADE RECEIVABLES

Net trade receivables amounted to €1 405 963 at December 31, 2016, corresponding to deliveries of products made by the Company and royalties on sales due by these partners.

The amount is mainly consisting of receivables from the partner Spectrum Pharmaceuticals and covered by a provision of doubtful debt amounting to €972,244.38.

### 3.5. OTHER RECEIVABLES



Other net receivables amount to €8 740 763 at December 31, 2016, and mainly consist of the following:

- Research Tax Credit, France and Denmark 2016: €3,954,873
- Net current accounts of subsidiaries: €3,220,105
- Grants to be received: €625,567VAT refund requested: €588,975
- VAT deductible on purchases and on unreceived invoices: €177,414

The decrease of € 980,322 corresponds mainly to the clearance of the 2015 foreign tax receivable of € 1,379,534 in 2016.

### 3.6. CASH

On December 31, 2016, cash totaled €28,983,475 including €5 302 407 of marketable securities (negotiable medium term certificates) and cash totaling €23 681 068 invested in money markets for €11,000,000 and \$2,000,000.

The change in the net cash position was a decrease of €4.5 million. This essentially stems from the Company's operating costs, including research and development, offset in part by fundraising finalized at the end of September for a net amount of €11 million and the payment at the signing of the new Pint Pharma partnership for \$3 million.

### 3.7. PREPAYMENTS

Prepaid expenses at December 31, 2016, rose to €914 323 and mainly correspond to subcontracted services and fees.

### 3.8. SHAREHOLDERS' EQUITY

At December 31, 2016, share capital amounted to €11 760 851, divided into 47,043,404 common shares with a nominal value of €0.25 each, all of the same class and fully paid up.

During the year 2016, share capital went from €10,138,020.75 to €11,760,851, as follows:

- Capital increase due to the acquisition of 100% of DNA Therapeutics shares on March 25, 2016: issuance of 553,819 new common shares at a unit price of €3.13, with a par value of €0.25 each, corresponding to an increase in the share capital of €138,000 and an issue premium of €1,595,000.
- Increase in the reserved capital subscribed by certain longstanding DNA Therapeutics shareholders on April 1, 2016: issuance of 364,958 new common shares at a price of €2.74, with a par value of €0.25 each, corresponding to an increase in the share capital of €91,000 with an issue premium of €909,000.
- Increase of the reserved capital on September 30, 2016: issuance of 5,434,783 new common shares at a price of €2.30, with a par value of €0.25 each, corresponding to an increase in the share capital of €1,359,000 with an issue premium of €11,141,000.
- Issuance of 137,761 vested bonus shares of a par value of €0.25 each, for an amount of €34,440.25.

The issue premium increased from €230,554,852.99 to €242,660,592.32 mainly as a result of the following events:

- The capital increases described above, for a total amount in 2016 of €13,578,591.01
- Subscription of warrants newly awarded for €88,100
- Cost of capital amounted to €1,519,764.18 in 2016
- Reduction corresponding to the collection of €41,187.50 is related to the allocation of bonus shares in 2016

### 3.9. OTHER SHAREHOLDERS' EQUITY

Other equity capital corresponds to:

- An advance from BPI France paid under the Livatag program (NICE consortium), repayable in case of commercial success. An amount of €256 000 was taken in during the year in payment for contractual milestones for clinical and industrial developments to the product. The balance of the advance at December



31, 2016 is €4,516,938, including €625,567 to be received over the next few years according to the schedule of funding provided in the agreement.

- An advance from BPI France paid under the AsiDNA program is repayable in case of commercial success. The balance of the advance at December 31, 2016 is €269,500 and will be repaid in 2017 and 2018.
- An advance from BPI France paid under the AsiDNA program is repayable in case of commercial success. The balance of the advance at December 31, 2016 is €562,000 and repayment is scheduled from September 2018.

### 3.10. CAPITAL GRANTS

The capital grant of €367,000 corresponds to the landlord's contribution to some of the work on the new registered office which started in 2008. The amount of depreciation at December 31, 2016 amounted to 324,180.13 euros.

### 3.11. PROVISIONS FOR RISKS AND LOSSES

Provisions for risks and losses amounted to €73 000 mainly corresponding to litigation provisions.

### Litigation with SpeBio/SpePharm

Just as on December 31, 2015, the possible litigation risks under way with SpePharm and SpeBio cannot be reliably measured. As the Company considers itself to be within its rights, no provision has been made as of December 31, 2016.

On 27 February 2009, Onxeo broke off collaboration with SpePharm and reacquired the rights to market Loramyc® in Europe from the SpeBio joint venture. Onxeo has taken SpePharm and SpeBio to the International Court of Arbitration of the International Chamber of Commerce to obtain damages for the losses suffered on account of breaches of contract committed by these companies under the partnership that had been agreed for the commercial launch of Loramyc®. This process is part of the ongoing law suit filed by Onxeo on SpeBio before the Commercial Court of Paris on February 27, 2009. SpeBio itself referred the suit to the Clerk of the Commercial Court while being aware of Onxeo's referral to the Arbitral Tribunal.

SpePharm and SpeBio issued counterclaims for damages before the Arbitral Tribunal and the Commercial Court respectively.

In a partial arbitral decision as to the question of its jurisdiction, the Court of Arbitration affirmed its jurisdiction in respect to the one framework contract and only against SpePharm.

Having stayed the proceedings on its own jurisdiction, the Paris Commercial Court assumed jurisdiction. In pursuing its strategy to bring the dispute under a single proceeding, Onxeo filed an objection before the Paris Court of Appeals. This objection was rejected and the procedure has now resumed before the Commercial Court

Onxeo requested the Commercial Court to force the intervention of SpePharm. By a May 3, 2016 ruling, the Paris Commercial Court upheld Onxeo's request pronouncing the forced intervention of SpePharm and the joinder of the Onxeo v. SpeBio and Onxeo v. SpePharm proceedings.

SpePharm filed contradicts against the ruling of May 3, 2016.

SpePharm filed conclusions for severance in order to obtain severance of the proceedings and alternative claims requesting that the Paris Commercial Court decline jurisdiction in favor of the ICC. On July 5, 2016, the Commercial Court stayed the proceedings pending the decision of the Court of Appeal brought by SpePharm and dismissed the claims of SpePharm and SpeBio believing that there was no need to separate the two proceedings.

On September 20, 2016, the Paris Court of Appeals declared inadmissible the contradiction formed by SpePharm. Therefore, the proceedings before the Commercial Court of Paris were resumed.

At the February 6, 2017 hearing, SpePharm made conclusions in which it requested that the Tribunal decline jurisdiction in its respect and made various appeals.



### 3.12. LOANS AND FINANCIAL DEBTS

This item includes primarily a COFACE indemnity collected as part of the export development of non-strategic products in the amount of €204,663.15.

### 3.13. TRADE PAYABLES

Trade payables went from €6 309 953 on December 31, 2015 to €9 116 052 on December 31, 2016 due to increases in R&D activity.

### 3.14. ACCRUED TAXES AND PERSONNEL COSTS

The decrease of €485,000 comes mainly from a reduction in premiums for assigned personnel of €396,000 in 2016.

### 3.15. OTHER LIABILITIES

This item of €3 283 740 corresponds to the current account of the subsidiary Topotarget UK.

### 3.16. DEFERRED REVENUE

Deferred income consists mainly of payments received on signing of the Beleodaq licensing agreements with Pint Pharma and Loramyc with Sosei and NovaMed, which are recognized in the profit or loss over several financial years and the balance at December 31, 2016 is €2,319,813.

### 3.17. TRANSLATION ADJUSTMENT - LIABILITIES

This amount of €3,168,582 mainly corresponds to unrealized exchange loss related to subsidiaries.

### 4. NOTES ON THE PROFIT AND LOSS ACCOUNT

### 4.1. REVENUE

Revenue for the year 2016 amounting to €556 854 came from sales of products to license partners for €530 505 as well as from various services for €26 350.

### 4.2. ROYALTIES FROM LICENSING AND OTHER INCOME

This item in the amount of €3 484 930 includes a proportion of the amounts received at the signing of the marketing licensing agreements for €734,909 spread over time, as well as the royalties on partner sales for €2,732,201. The increase over 2015 is related to the growth of royalties for Onxeo as well as the impact of the payment at the signing of the agreement with Pint Pharma during the year.

### 4.3. OPERATING EXPENSES

Operating expenses changed from €29 230 955 in 2015 to €29 512 287 in 2016.

The major changes of the year are:

- An increase of €0.9 million in external charges came mainly from an increase of scientific outsourcing expenditures as a result of the continuation of Livatag developments and research work on the AsiDNA project following the acquisition of DNA Therapeutics.
- A reduction of €0.8 million in personnel costs was mainly related to the lower bonuses attributed during 2016 as well as changes in the number of staff.

The costs of research and development in 2016 amounted to €13.9 million.

The competitiveness employment tax credit (CICE) for FY 2016 came to €20,501.41 and was recorded as a reduction of operating expenses. It was assigned exclusively to the Company's research and development effort.

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### 4.4. FINANCIAL INCOME

Financial income mainly includes reversals of financial provisions in the amount of €21 936 065 from the liquidation of the German subsidiary Topotarget Germany, foreign exchange gains for €680 018, interest on the Group's current accounts for €61 301, and income generated by short-term investments for €87,811.

Financial expenses include interest relating to current account advances for a total amount of €176,567, an amount of €9,371 corresponding to interest on the repayable BPI advance calculated at the effective interest rate. Currency losses totaling €535 513 and provisions on investment holdings in the amount of €290,834.

### 4.5. EXCEPTIONAL ITEMS

The negative extraordinary result of € (21 469 099) corresponds mainly to the technical loss on the liquidation of the German subsidiary Topotarget Germany.

### 4.6. CORPORATE INCOME TAX

Corporate income tax is an income of €3 954 873 corresponding to French and Danish research tax credits.

Onxeo had a tax loss carry forward of €208 million at December 31, 2016.

### OFF-BALANCE SHEET COMMITMENTS

### **5.1.** POST-EMPLOYMENT BENEFITS

The actuarial valuation method used is the retrospective valuation method. This method enables the present value of the benefit obligation to be determined on the basis of services rendered by the employee at the valuation date. The plan is a defined benefit plan.

The actuarial assumptions applied are as follows:

	31/12/2016	31/12/2015
Collective bargaining agreement	Medical industry	Medical industry
Retirement age	Between 65 and 67 years, under the Pension Reform Act of November 10 2010	Between 65 and 67 years, under the Pension Reform Act of November 10 2010
Calculation date	30/06/2016	31/12/2015
Mortality table	INSEE 2015	INSEE 2015
Discount rate	1.63%	2.26% (AA rate Reuters)
Rate of salary increase	2%	3%
Employee turnover rate	By age category: - 0% from 16 to 24 - 4.09 % from 25 to 34 - 5.26 % from 35 to 44 - 1.75 % from 45 to 54 - 0.00 % above 55	By age category: - 0% from 16 to 24 - 2.30 % from 25 to 34 - 8.05 % from 35 to 44 - 2.30 % from 45 to 54 - 0.57 % above 55
Social charges	46% for Onxeo FR	46% for Onxeo FR

On December 31, 2016, pension commitments amounted to €598,000.

### **5.2.** LEASING COMMITMENTS

Leasing commitments amounted to €146,386 on December 31, 2016.



### REMUNERATION OF CORPORATE OFFICERS

Remuneration of corporate officers came to €802,000, including the CEO's retirement benefits in an amount of €73,000.

### 7. RELATED PARTIES

Onxeo SA's related parties are as follows:

- Financière de la Montagne which, in its capacity as the largest shareholder of the company with 12.03% of the capital and as a board member, is considered to exert a significant influence on the company.

No transactions were made in the year 2016 with Financière de la Montagne.

- The Chairman of the Board of Directors, as one of the main executives presenting the financial statements.

PJL Conseil, headed up by Patrick Langlois who held the position of Chairman of the Board of Directors until his resignation on January 22, 2016, collected fees under the consulting contract authorized by the Board of Directors on July 17 2013 for an amount of €2,000.

### 8. INTRA-GROUP TRANSACTIONS

Transactions with other companies related to the Group concern only those companies included in the scope of consolidation. These essentially involve sales of finished goods and services, billings of marketing license fees, and intercompany loans and borrowings as part of cash management agreements.

The table below shows the impact of intra-group transactions on December 31, 2016:

In €	31/12/2016	31/12/2015
Assets	77 697 757	104 875 776
Liabilities	2 903 802	2 836 014
Income	56 367	1 130 987
Expenses	176 567	73 926

The amount of the assets mainly corresponds to the current account of the subsidiary Topotarget Switzerland and to the equity securities.



# **ANNEXES**

# **ASSETS**

	Amount at start of 2016	Increases	Decreases	Amount at end of 2016
Formation costs and research and development costs	61 830 000	3 259 350		65 089 350
Other intangible assets	5 192 707	2 663	52 660	5 142 710
TOTAL INTANGIBLE FIXED ASSETS	67 022 707	3 262 013	52 660	70 232 060
Land				
Construction on own land				
Leaseholds				
Facilities, fixtures and fittings				
Plant & equipment, and manufacturing tools	821 844	405 382	6 281	1 220 944
Facilities, fixtures and fittings	3 631 163	31 714	1 381 933	2 280 944
Transport equipment				
Office and computer equipment, furniture	2 276 337	40 214	1 414 827	901 724
Recoverable packaging & other				
Property, plant and equipment in progress	226 740	1 724	226 740	1 724
Advances and prepayments				
TOTAL TANGIBLE FIXED ASSETS	6 956 084	479 034	3 029 781	4 405 336
Holdings valued by the equity method				
Other equity holdings	86 284 012	884	37 655 038	48 629 858
Other long-term securities	157 057	206 840	266 838	97 060
Loans and other financial assets	307 939	417 454	427 428	297 966
TOTAL LONG-TERM INVESTMENTS	86 749 009	625 178	38 349 303	49 024 884
GRAND TOTAL	160 727 799	4 366 225	41 431 744	123 662 280



## **DEPRECIATION TABLE**

	Amount at start of 2016	Increases	Decreases	Amount at end of 2016
Formation costs and research and development costs	2 240 000	1 453 221	13 333	3 679 888
Other intangible assets	734 224	9 773	52 660	691 337
TOTAL INTANGIBLE FIXED ASSETS	2 974 224	1 462 994	65 993	4 371 225
Land				
Construction on own land				
Leaseholds				
Facilities, fixtures and fittings				
Plant & equipment	801 583	191 433	6 281	986 735
Fixtures and fittings	3 105 462	210 778	1 381 933	1 934 307
Transport equipment				
Office and computer equipment, furniture	2 190 424	48 801	1 412 774	826 451
Recoverable packaging & other				
TOTAL TANGIBLE FIXED ASSETS	6 097 470	451 012	2 800 989	3 747 493
GRAND TOTAL	9 071 694	1 914 007	2 866 982	8 118 718



# **ALLOWANCE TABLE**

	Amount at start	Increases: in	Decreases :			Amount at end of 2016
Type of provisions	of 2016	allowances in the year	Used during the period	Unused during the period	Reversals during the year	01 2010
			'	•	<u> </u>	
Regulated provisions						
Provisions for replenishing sources (mines, oil).						
Provisions for investment						
Provisions for price rises						
Special depreciation allowances						
Additional depreciation for tax purposes of which exceptional increases of 30%						
Tax provisions for foreign establ. (av.1.1.92)						
Tax provisions for foreign establ. (ap.1.1.92)						
TOTAL REGULATED PROVISIONS						
Provisions for contingencies and losses						
Provisions for litigation Provisions for customer warranties						
Provisions for losses on futures markets						
Provisions for fines and penalties						
Provisions for foreign exchange losses	281 027				281 027	
Provisions for pensions and similar obligations						
Provisions for taxes						
Provisions for capital renewal						
Provisions for major repairs and major overhauls						
Prov. for tax and soc. chgs on holiday pay						
Other provisions for contingencies and losses	313 780				240 780	73 000
TOTAL PROV. FOR CONTINGENCIES AND LOSSES	594 807				521 807	73 000
Provisions for impairment						
On intangible fixed assets						
On tangible fixed assets						
On long-term investments in equity securities						
On long-term investments in equity capital	76 038 630	287 688			37 462 890	38 863 42
On other long-term investments On stocks and work in progress						
On trade receivables	957 623	14 621				972 24
Other provisions for impairment	25 407 851				29 260	25 613 180
TOTAL PROVISIONS FOR IMPAIRMENT	102 404 104				37 492 150	65 448 858
GRAND TOTAL	102 998 911	536 905			38 013 957	65 521 858
0, 1, 1						
Of which operating allowances an			246 736			26 779
Of which financial allowances and	reversals		290 834			21 936 065



# **INVENTORY**

	Gross value	Provision for depreciation of inventory	Net value
Raw materials and supplies			
Work in progress - goods			
Work in progress - services			
Semi-finished and finished goods			
Goods held for resale	183 823		183 823
Total stocks	183 823		183 823

# **RECEIVABLES**

RECEIVABLES	Gross amount	Less than 1 year	More than 1 year
Receivables from investments			
Loans (1) (2)			
Other long-term investments	297 966	138 136	159 830
Total fixed assets	297 966	138 136	159 830
Doubtful or contentious receivables	960 292	960 292	
Other trade receivables	1 417 915	1 417 915	
Receivables representing loaned securities			
Personnel	59 665	59 665	
Social security and other employee benefit charges	2 752	2 752	
Corporate income tax	3 954 873	3 954 873	
Value added tax	783 035	783 035	
Taxes other than on income			
Other	83 342	83 342	
Group and shareholders (2)	28 833 291	28 833 291	
Miscellaneous receivables	636 991	636 991	
Total current assets	36 732 157	36 732 157	
Prepaid expenses	914 323	914 323	
TOTAL RECEIVABLES	37 944 445	37 784 616	159 830

(1) Amount of loans granted during the period	
(1) Amount of repayments obtained during the period	
(2) Shareholders' loans and advances (natural persons)	



## **PAYABLES**

PAYABLES	Gross amount	Less than 1 year	Between 1 and 5 years	More than 5 years
Convertible bonds (1)				
Other bonds (1)				
Bank debts < 1 year	7 737	7 737		
Bank debts > 1 year				
Other debt (1) (2)	204 663	204 663		
Trade payables	9 116 052	9 116 052		
Personnel	863 324	863 324		
Social security and other employee benefit charges	672 554	672 554		
Corporate income tax				
Value added tax	2 767	2 767		
Secured obligations				
Taxes other than on income	120 548	120 548		
Payables on fixed assets and related accounts				
Group and shareholders (2)				
Other liabilities	4 721 713	4 721 713		
Debt representing borrowed securities				
Deferred revenue	2 319 813	1 183 647	1 136 166	
PAYABLES	14 120 819	14 102 450	1 136 166	

(1) Loans contracted during the year

- (1) Loans repaid during the year
- (2) Amount of loans and debts payable to shareholders

# TRANSLATION ADJUSTMENTS

		LIABILITIES			
RELATED ITEMS	Gross amount	Offset by currency hedging	Allowance	Net amount	Amount
Payments on fixed assets					
Loans					
Other current receivables					
Operating receivables					
Other receivables					
Financial liabilities					
Operating liabilities					
Debts on fixed assets					
Other					
Translation adjustment					3 168 582
current account					
TOTAL					3 168 582



# **ACCRUED INCOME**

Accrued income	2016	2015
Financial assets		
Receivables from investments		
Other long-term investments		
Total long-term investments		
Receivables		
Trade receivables	757 419	749 273
Other receivables	97 518	153 455
Total receivables	854 937	902 728
Liquid assets		
Marketable securities	2 407	6 681
Cash	2 004	3 810
Total liquid assets	4 411	10 491
Other		
Total other		
TOTAL	859 348	913 219

## **ACCRUED EXPENSES**

Nature of expenses	2016	2015
Financial liabilities		
Convertible bonds		
Other bonds		
Bank debts		6 678
Other debt		
Customer prepayments		49 200
Total financial liabilities		55 878
Operating liabilities		
Trade payables	5 107 074	3 128 472
Accrued taxes and personnel costs	1 237 703	1 711 373
Total operating liabilities	6 344 777	4 839 845
Other payables		
Payables on fixed assets and related accounts		116 450
Other liabilities		
Total operating liabilities		116 450
Other		
Total other liabilities		
TOTAL	6 344 777	5 012 173

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## **DEFERRED REVENUE AND PREPAID EXPENSES**

Nature of expenses	2016	2015
Operating expenses		
PREPAID EXPENSES	914 323	629 203
	044000	500,000
Total	914 323	629 203
Expenses, financial:		
Total		
Expenses, Exceptional:		
Total		
TOTAL PREPAID EXPENSES	914 323	629 203
Comparative BALANCE (Balance Sheet Assets: 2050 rubrique CH)	914 323	629 203

Nature of income	2016	2015
Income from operations:		
DEFERRED INCOME	2 319 813	343 346
Total	2 319 813	343 346
Income, financial:		
Tatal		
Total		
Income, exceptional:		
Total		
TOTAL DEFERRED INCOME	2 319 813	343 346
Comparative BALANCE (Balance Sheet Liabilities: 2051 heading EB)	2 319 813	343 346

TOTAL DEFERRED REVENUE AND PREPAID EXPENSES	(1 405 490)	285 857



# SHARE CAPITAL COMPOSITION

Classes of securities	١	Number of securitie	Total	Nominal Value	
	Closing N-1	Created during	Redeemed		
		period N	during period N		
Common shares	40 552 083	6 491 321		47 043 404	0.25
Shares redeemed					
Priority dividend					
shares					
Preference shares					
Shares					
Investment					
certificates					
Total	40 552 083	6 491 321		47 043 404	

# TABLE OF CHANGES IN SHAREHOLDERS' EQUITY

	01/01/2016	Capital increase	Capital reduction	Appropriation of income N-1	Other changes	Net profit (loss) for yr N	31/12/2016
Share capital in number of shares							
Nominal value							
Share capital	10 138 021	1 622 830					11 760 851
Issue, merger and acquisition premiums	230 554 853	13 666 691			(1 560 952)		242 660 592
Excess of restated assets over historical cost							
Legal reserve							
Reserves required by the articles of incorporation or by contract							
Regulated reserves							
Other reserves	37 125	41 187	34 400				43 872
Retained earnings	(116 381 346)				(25 163 280)		(141 544 626)
Net profit (loss) for the year	(25 163 280)			25 163 280		(21 236 246)	(21 236 246)
Capital grants	79 520				(36 700)		42 820
Regulated							
provisions							
Dividends paid							
T-t-1	00.264.802	4F 220 <del>700</del>	24.400	25 462 200	/26 760 022	/24 226 246	04 727 264
Total shareholders' equity	99 264 892	15 330 709	34 400	25 163 280	(26 760 932)	(21 236 246)	91 727 264

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## **BREAKDOWN OF TURNOVER**

Breakdown of			2016			2015
turnover	France	Export	Total	France	Export	Total
Sales of goods		530 505	530 505		435 537	435 537
Products from additional activities		26 350	26 350		374 805	374 805
Services						
TOTAL		556 854	556 854		810 342	810 342

# **EXCEPTIONAL INCOME EXCLUDING EXPENSES AND AMORTIZATION**

Nature of expenses	2016	2015
Exceptional expenses on operating transactions		
Contract penalties	5 000	98 309
Tax and criminal penalties and fines	9	21 413
Gifts, donations		
Uncollectable receivables in the financial year		
Grants		
Tax reminders		
Other exceptional expenses on management operations		12
Total	5 009	119 734
Expenses over previous financial years		1 146
Book value of assets sold		
Intangible assets		
Tangible assets		19 637
Financial assets	21 655 359	
Other assets (excluding inventories and securities)		
Total	21 655 359	19 637
Other operating expenses		
Penalties deriving from indexation clauses		
Lots		
Penalties deriving from the repurchase of own shares	86 916	104 133
Miscellaneous exceptional expenses		
Total	86 916	104 133
TOTAL	21 747 283	244 650

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## **EXCEPTIONAL INCOME EXCLUSING PROVISIONS AND AMORTIZATION**

Nature of income	2016	2015
Exceptional income on operating transactions		
Forfeits and penalties levied on purchases and sales		
Donations received		
Proceeds from debt written off		
Balancing grants		
Tax reductions (other than income taxes)		
Other exceptional income on management operations	4 379	250
Total	4 379	250
Income over previous financial years		
Proceeds from sale of assets		
Intangible assets		
Tangible assets	2 002	7 687
Financial assets		
Other assets (excluding inventories and securities)		
Total	2 002	7 687
Share of investment subsidies transferred to income		
Other exceptional income		
Bonuses from indexation clauses		
Lots		
Bonuses from the repurchase of own shares	31 024	49 413
Miscellaneous exceptional income:		
Total	31 024	49 413
TOTAL	37 404	57 350

## **LEASING**

LEASED ASSETS Initial cost		Amortisation ar	Net Value	
LEASED ASSETS	LEASED ASSETS INITIAL COST		Cumulative	ivet value
Land				
Buildings				
Plant & equipment	45 000	9 000	15 750	29 250
Other tangible assets	184 827	22 434	116 168	68 659
Tangible assets in				
progress				
TOTAL	229 827	31 434	131 918	97 909

LEASE	Amount paid		Amounts outstanding				Residual
COMMITMENTS	For the period	Cumulative	< 1 year	From 1 to 5 years	> 5 years	Total	purchase price
Land							
Buildings							
Technical installations	10 576	18 508	10 576	31 727		42 303	881
Other tang. fixed assets	37 726	144 967	40 390	63 693		104 083	
Tangible assets in							
progress							
TOTAL	48 302	163 475	50 966	95 420		146 386	881



# **AVERAGE HEADCOUNT**

Category	Average h	neadcount		available count	Total	
	2016	2015	2016	2015	2016	2015
Executives	41	42			41	42
Supervisors						
Staff and	11	11			11	11
Technicians						
Other:						
Total	52	53			52	53



# **RELATED COMPANIES AND HOLDINGS**

	Amount co	ncerning
Item	related companies	with which the Company has an equity interest
Financial assets		
Advances and prepayments on intangible assets		
Investments	48 629 958	
Receivables from investments		
Loans		
Total long-term investments	48 629 958	
Receivables		
Prepayments to suppliers		
Trade receivables	234 508	
Other receivables	28 833 291	
Subscribed, called, unpaid share capital		
Total receivables	29 067 799	
Liabilities		
Convertible bonds		
Other bonds		
Bank debts		
Other debst		
Customer prepayments		
Trade payables	26 876	
Other liabilities		
Total payables	26 876	
Financial income		
Income from investments		
Other financial income	56 368	
Financial expenses	176 567	
Total financial income	232 935	
Other		
Total other		
Grand total	77 957 568	

# TABLE OF SUBSIDIARIES AND HOLDINGS

Shan		Share Percentage		of the shares	Loans and advances granted	Result (profit or
Companies	Capital	owned	Gross	Net	by the Company not yet repaid	loss at last FY)
BIOALLIANCE PHARMA SWITZERLAND	81 460	100	31 918		238 544	(8 597)
SPEBIO	40 000	50	20 000		1 475 000	(86 887)
TOPOTARGET SWITZERLAND	559 949	100	9 917 835		26 804 455	92 562
TOPOTARGET UK LTD	1 636 474	100	38 659 221	9 765 546		349 977
ONXEO US	884	100	884	884	315 291	(211 066)

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# FIVE YEAR SUMMARY OF PROFIT/LOSS

Type of indicator	2012	2013	2014	2015	2016
Share capital at year end					
Share capital	4 414 929	5 170 748	10 136 051	10 138 021	11 760 851
Number of common shares outstanding	17 659 715	20 682 992	40 544 204	40 552 083	47 043 404
Number of preference shares outstanding					
Maximum no. of future shares to be issued:					
By conversion of bonds					
By exercise of subscription rights					
Operations and results					
Net sales, excluding VAT	911 214	643 656	456 774	810 343	556 854
Net loss before tax, profit-sharing, depreciation, amortization and provisions	-11 778 599	-17 162 260	8 842 926	-23 266 312	-45 158 403
Corporate income tax	-1 978 587	-2 389 161	878 352	-3 718 068	-3 954 873
Employee profit sharing for the period					
Net loss after tax, profit-sharing, depreciation, amortization and provisions	-10 417 994	-15 022 175	8 521 759	-25 163 280	-21 236 246
Distributions					
Earnings per share					
Net loss after tax, profit-sharing, depreciation, amortization and provisions	-0.55	-0.71	0.20	-0.48	-0.88
Net loss after tax, profit-sharing, depreciation, amortization and provisions	-0.59	-0.73	0.21	-0.62	-0.45
Dividend per share					
<u>Personnel</u>					
	_	_	_	_	_
Average headcount during the period	53	51	59	53	52
Gross payroll for the period	3 698 761	3 945 900	8 023 027	5 447 799	4 613 673
Amounts paid for employee benefits	1 850 493	1 944 581	2 392 857	2 063 410	2 070 805



#### 6.4 STATUTORY AUDITOR'S REPORT ON THE FINANCIAL STATEMENTS

#### **GRANT THORNTON**

French member of Grant Thornton International 29, rue du Pont 92200 Neuilly-sur-Seine S.A. au capital de € 2.297.184

Statutory Auditor Member of the Regional Company of Versailles

#### **ERNST & YOUNG Audit**

1/2, place des Saisons 92400 Courbevoie - Paris-La Défense 1 S.A.S. à capital variable

> Statutory Auditor Member of the Regional Company of Versailles

This is a free translation into English of the statutory auditors' report on the consolidated financial statements issued in French and it is provided solely for the convenience of English speaking users.

The statutory auditors' report includes information specifically required by French law in such reports, whether modified or not. This information is presented below the audit opinion on the consolidated financial statements and includes an explanatory paragraph discussing the auditors' assessments of certain significant accounting and auditing matters. These assessments were considered for the purpose of issuing an audit opinion on the consolidated financial statements taken as a whole and not to provide separate assurance on individual account balances, transactions or disclosures.

This report also includes information relating to the specific verification of information given in the Group's management report.

This report should be read in conjunction with, and construed in accordance with, French law and professional auditing standards applicable in France.

#### Onxeo

Year ended December 31, 2016

Statutory auditors' reports on the financial statements

To the Shareholders,

In compliance with the assignment entrusted to us by your Annual General Meetings, we hereby report to you, for the year ended December 31, 2016, on:

- the audit of the accompanying financial statements of Onxeo,
- the justification of our assessments,
- the specific verifications and information required by law.

These financial statements have been approved by the Board of Directors. Our role is to express an opinion on these financial statements based on our audit.



#### I. Opinion on the financial statements

We conducted our audit in accordance with professional standards applicable in France; these standards require that we plan and perform the audit to obtain reasonable assurance as to whether the financial statements are free of material misstatement. An audit involves performing procedures, using sampling techniques or other methods of selection, to obtain audit evidence about the amounts and disclosures in the financial statements. An audit also includes evaluating the appropriateness of accounting policies used and the reasonableness of accounting estimates made, as well as the overall presentation of the financial statements. We believe that the audit we have obtained is sufficient and appropriate to provide a basis for our audit opinion.

In our opinion, the financial statements give a true and fair view of the assets and liabilities and of the financial position of the Company as at December 31, 2016 and of the results of its operations for the year then ended, in accordance with French accounting principles.

Without qualifying our opinion, we draw your attention to note 1 "Accounting principles and methods" to the financial statements that exposes elements used by management to justify the application of the going concern principle for the preparation of the financial statements for the year ended December 31, 2016.

#### II. Justification of our assessments

In accordance with the requirements of Article L. 823-9 of the French Commercial Code (Code de commerce) relating to the justification of our assessments, we draw to your attention to the following matters:

- Note 1.1 "Intangible assets" to the annual financial statements describes the accounting rules and methods relating to the valuation of goodwill and development costs. Our procedures consisted in examining implementation methods of these assets impairment tests as exposed in note 3.1 "Intangible assets" of the annual financial statements, in examining data and assumptions on which are based actualized free cash flow forecasts as well as reviewing the calculations performed by your company. In the context of our assessments, we also ensured the reasonableness of estimates and assumptions used as well as verified that the notes mentioned above provide appropriate information.
- Note 1.9.1 "License Agreement" to the annual financial statements describes the method used to account for the recognition of signing of license agreements. We verified the appropriateness of this method and have verified the correct implementation. Our procedures consisted in verifying the reasonableness of significant estimates and assumptions on which is based the revenue recognition related to these agreements.

These assessments were made as part of our audit of the financial statements taken as a whole, and therefore contributed to the opinion we formed which is expressed in the first part of this report.

#### III. Specific verifications and information

We have also performed, in accordance with professional standards applicable in France, the specific verifications required by French law.

We have nothing further to report as to the fair presentation and the consistency with the financial statements of the information given in the management report of the Board of Directors and in the documents addressed to the shareholders with respect to the financial position and the financial statements.

Concerning the information given in accordance with the requirements of Article L. 225-102-1 of the French Commercial Code (Code de commerce) relating to remunerations and benefits received by the directors and any other commitments made in their favor, we have verified its consistency with the financial statements, or with the underlying information used to prepare these financial statements and, where applicable, with the information obtained by your Company from companies controlling your Company or controlled by it. Based on this work, we attest the accuracy and fair presentation of this information.

In accordance with French law, we have verified that the required information concerning the purchase of investments and controlling interests and the identity of the shareholders or holders of the voting rights has been properly disclosed in the management report.



Neuilly-sur-Seine and Paris-La Défense, 5 April 2017

## **The Statutory Auditors**

(French original signed by)

**GRANT THORNTON** 

**ERNST & YOUNG Audit** 

French member of Grant Thornton International

Jean-Pierre Colle

Samuel Clochard

Franck Sebag



#### 6.5 OTHER FINANCIAL INFORMATION

#### Date of latest financial data

7 March 2017: Publication of the press release on the audited 2016 consolidated annual financial statements approved by the Board of Directors on 7 March 2017.

#### Interim and other financial data

None.

#### Dividend distribution policy

Because of its losses, Onxeo has never distributed any dividends.

In its shareholders' interests, the Company intends to dedicate all of its financial resources to increasing its enterprise value. Any distributable profits as may be earned during the business development phase will be kept by the Company and used in developing its activities.

Subsequently, depending on the level of distributable reserves, the Company intends to adopt a dividend distribution policy reflecting increases in profits and cash generated by the business. The Company does not, however, project any dividend distributions in the near future.

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# 6.6 STATUTORY AUDITOR'S REPORT ON THE REGULATED AGREEMENT AND COMMITMENTS

#### **GRANT THORNTON**

French Member of Grant Thornton International 29, rue du Pont 92200 Neuilly-sur-Seine S.A. au capital de € 2.297.184

> External Auditor Member of the Regional Company of Versailles

#### **ERNST & YOUNG Audit**

1/2, place des Saisons 92400 Courbevoie - Paris-La Défense 1 S.A.S. à capital variable

> External Auditor Member of the Regional Company of Versailles

This is a free translation into English of a report issued in French and it is provided solely for the convenience of English speaking users.

This report should be read in conjunction with and construed in accordance with French law and professional standards applicable in France

#### Onxeo

Annual General Meeting to approve the financial statements for the year ended December 31, 2016

Statutory auditors' report on related party agreements and commitments

To the Shareholders,

In our capacity as statutory auditors of your company, we hereby report on certain related party agreements and commitments.

We are required to inform you, on the basis of the information provided to us, of the terms and conditions of those agreements and commitments indicated to us, or that we may have identified in the performance of our engagement, as well as the reasons why they benefit the company. We are not required to comment as to whether they are beneficial or appropriate or to ascertain the existence of any such agreements and commitments. It is your responsibility, in accordance with article R. 225-31 of the French Commercial Code (Code de commerce), to evaluate the benefits resulting from these agreements and commitments prior to their approval.

In addition, we are required, where applicable, to inform you in accordance with article R. 225-31 of the French Commercial Code (Code de commerce) concerning the implementation, during the year, of the agreements and commitments already approved by the Annual General Meeting.

We performed those procedures which we considered necessary to comply with professional guidance issued by the national auditing body (Compagnie nationale des commissaires aux comptes) relating to this type of engagement. These procedures consisted in verifying that the information provided to us is consistent with the documentation from which it has been extracted.

#### Agreements and commitments submitted for approval by the Annual General Meeting

We hereby inform you that we have not been advised of any agreement or commitment authorized during the year to be submitted to the approval of the Annual General Meeting pursuant to Article L. 225-28 of the French Commercial Code (Code de commerce).



#### Agreements and commitments already approved by the Annual General Meeting

In accordance with Article R. 225-30 of the French Commercial Code (Code de commerce), we have been advised that the implementation of the following agreements and commitments which were approved by the Annual General Meeting in prior years continued during the year.

#### With PJL Conseil EURL

#### Person concerned

Mr. Patrick Langlois, Chairman of Onxeo's Board of Directors until January 22, 2016 and Managing Partner of PJL E.U.R.L. Councils.

#### Nature and purpose

Consulting contract between your Company and the company PJL Conseils E.U.R.L. authorized by the board of directors on July 17, 2012.

This agreement covers the benefits of strategic advice and communication within the development strategy and the creation of value for your Company.

Under this agreement, your Company recognized as expenses in the amount of € 2,000 excluding taxes as at December 31, 2016.

This agreement ended on January 22, 2016, when Mr. Patrick Langlois resigned from his position of Administrator and Chairman of your Company's board of directors.

Neuilly-sur-Seine and Paris-La Défense, 5 April 2017

The Statutory Auditors (French original signed by)

GRANT THORNTON
French Member of Grant Thornton International

**ERNST & YOUNG Audit** 

Jean-Pierre Colle Samuel Clochard Franck Sebag

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# 6.7 INDEPENDENT VERIFIER'S REPORT ON CONSOLIDATED SOCIAL, ENVIRONMENTAL AND SOCIETAL INFORMATION PRESENTED IN THE MANAGEMENT REPORT

This is a free translation into English of the original report issued in the French language and it is provided solely for the convenience of English speaking users. This report should be read in conjunction with, and construed in accordance with, French law and professional standards applicable in France.

#### Onxeo

Year ended the 31/12/2016

Independent verifier's report on consolidated social, environmental and societal information presented in the management report

To the shareholders,

In our quality as an independent verifier accredited by the COFRAC<sup>33</sup>, under the number n° 3-1050, and as a member of the network of one of the statutory auditors of the company Onxeo, we present our report on the consolidated social, environmental and societal information established for the year ended on the 31/12/2016, presented in chapter 10 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 of which a summary is included in introduction to chapter XX of the management report 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);

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<sup>33</sup> Scope available at : www.cofrac.fr



- to express a limited assurance conclusion, that the CSR Information, overall, is fairly presented, in all material aspects, in according with the Criteria; and
- to express, at the request of the company, a reasonable assurance conclusion that the information selected by the company and identified by the symbol xx in chapter xxx of the management report, has been established, in all material aspects, in accordance with the Criteria.

Our verification work mobilized the skills of 4 people in February 2017 for an estimated duration of two 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 and the reasonable assurance report, in accordance with the international standard ISAE 3000<sup>34</sup>.

#### 1. Attestation of presence of CSR Information

#### Nature and scope of the work

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 programs.

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 consolidated 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).

We verified that the information covers the consolidated perimeter, namely the entity and its subsidiaries, as aligned with the meaning of the Article L.233-1 and the entities which it controls, as aligned with the meaning of the Article L.233-3 of the French Commercial code (Code de commerce) with the limitations specified in the Methodological Note in chapter 10.1 of the management report, notably that social indicators (without arrivals and leaves) relates only to France.

#### Conclusion

Based on this work, and given the limitations mentioned above 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 interviews with the people responsible for the preparation of the CSR Information in the different 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.

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<sup>&</sup>lt;sup>34</sup> ISAE 3000 – Assurance engagements other than audits or reviews of historical information



For the CSR Information which we considered the most important<sup>35</sup>:

- At the level of the consolidated entity, we consulted documentary sources and conducted interviews to corroborate the qualitative information (organization, 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;
- At the level of the representative selection of divisions that we selected<sup>36</sup>, based on their activity, their contribution to the consolidated indicators, their location and a risk analysis, we undertook interviews to verify the correct application of the procedures and undertook detailed tests on the basis of samples, consisting in verifying the calculations made and linking them with supporting documentation. The sample selected therefore represented on average 100% of the total workforce for the indicator "total workforce" and 93% of the total workforce for all other indicators.

For the other consolidated CSR information, 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.

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, 6 March 2017

(French originals signed by)

#### Independent Verifier ERNST & YOUNG et Associés

Eric Duvaud Associé Développement durable Bruno Perrin Associé

<sup>&</sup>lt;sup>35</sup> Environmental and Societal information: training and information delivered to the employees, resources dedicated to the prevention of risks and pollutions, pollution and waste management (preventative measures, reduction of and compensation for discharges into the air, water and soil, preventative measures, recycling and waste management, consideration of environmental and social issues in purchasing policies and relations with suppliers and subcontractors.

Social information: employment (total headcount and breakdown, hiring and terminations, remunerations and their evolution), absenteeism, health and safety at the work place, work accidents, notably their frequency and their severity, as well as occupational diseases, training policies, number of days of training.

<sup>&</sup>lt;sup>36</sup> Perimeter for total workforce: France, Denmark, for others indicators: France only.



# FURTHER ECONOMIC AND LEGAL INFORMATION

#### 7.1 CAPITAL AND THE STOCK MARKET

#### 7.1.1 ONXEO AND ITS SHAREHOLDERS

All shareholders have access to full, transparent and clear information that is adapted to the needs of the individual and can be used to make an objective assessment of Onxeo's growth strategy and results. This financial communication policy aims to ensure that all shareholders have access to information that complies with usual market practice.

A very diverse array of public documents including regulatory information covers the company's business activities, strategy and financial position: Registration Document, annual report, interim financial statements, shareholder communiqués, the Company's articles of association and the rules of procedure of the board. All these documents are readily accessible via the company's website at www.onxeo.com under the Investors section in both French and English and on request by contacting the company's general management. Email us at contact@onxeo.com to directly receive annual reports, institutional brochures, and press releases.

Onxeo circulates and publishes in the BALO legal announcements publication the regulatory information required of a listed company in the form of various annual and other periodic information. Financial information is complemented by press releases aimed at the financial community and the wider public, concerning subjects of significant importance to better understand the company's business activities and strategy. The company holds periodic meetings with financial analysts and economic journalists in order to explain in interactive mode the company's challenges, products, plans and results.

In 2016, Onxeo ensured a number of meetings with institutional investors, mainly in France but also in Europe and the USA, and with retail investors in France and Denmark.

The annual report presented and submitted as a Registration Document with the AMF (Autorité des Marchés Financiers) and the report on the interim accounts are widely distributed amongst the financial community.

#### CALENDAR 2016

- 7 March 2017: Consolidated financial statements 2016
- 26 April 2017: General Meeting of Shareholders
- 27 April 2017: Sales number for Q1 2017
- 28 July 2017: Consolidated financial statements for Q1 2017
- 26 October 2017: Sales numbers for Q3 2017

#### 7.1.2 ONXEO'S CAPITAL

At the date of the Registration Document, the Company's share capital consisted of 86.52% bearer shares and 13.48% registered shares.

The table below references the shareholders with shareholding in excess of the 5% threshold, namely those possessing more than a twentieth, tenth, three twentieths, one fifth, one quarter, one half, two thirds or nineteen twentieths of the share capital or voting rights as the date of the Registration Document:

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Shareholder	Sha	res	Voting Rights		
	Number of Shares	% of Share Capital	Number of Voting Rights	% of Voting Rights	
Jean-Nicolas Trebouta	40 500	0,09%	40 500	0,09%	
Lise Besançon	104 240	0,22%	104 240	0,22%	
Louis Trebouta	17 990	0,04%	17 990	0,04%	
Financière de la Montagne	6 403 379	13,61%	6 403 379	13,62%	
Concert	6 566 109	13,96%	6 566 109	13,97%	
Others	40 477 295	86,04%	40 442 408	86,03%	
Total	47 043 404	100,00%	47 008 517	100,00%	

The shareholder structure remained stable during FY 2016, with the percentage of holdings by institutional investors accounting for 40% of the base shareholding. As of December 31, 2016, the Company's share capital consisted of 47,043,404 shares.

The Company has not been notified of the existence of a shareholders' agreement.

During the financial year 2016, the Company has not received any notification of threshold crossing.

# 7.1.3 CHANGES IN ONXEO'S SHARE PRICE AND OTHER INFORMATION CONCERNING THE SHARE CAPITAL

The Company's shares have been listed on Compartment C of the Euronext Paris regulated market since 27 January 2017. According to NYSE Euronext regulations, market segment changes are made annually based on market cap of the final 60 days of the year. Compartment C includes listed companies with a market cap below €150 million.

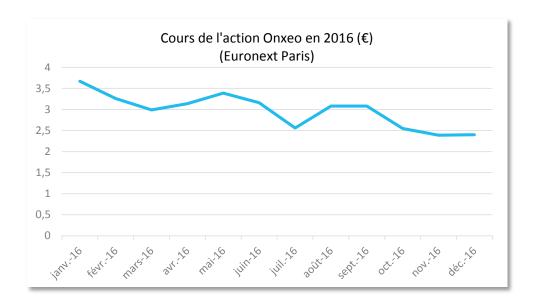
During FY 2016, the share price hit its lowest level of €2.29 on 8 November 2016 and closed at €2.50 on 31 December 2016. A high of €3.72 was reached on 5 July 2016.

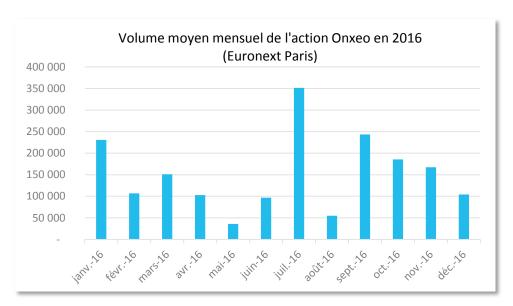
Furthermore, the share has had a secondary listing on NASDAQ in Copenhagen since 1 August 2014. Between 1 January 2016 and 31 December 2016, the share price hit its lowest level of DKK 17.0 on 8 November 2016, closing at DKK 18.6 on 31 December 2016. A high of DKK 28.2 was reached on 5 July 2016.

#### 7.1.3.1 Changes in share price and trading volume

The graphs below show the changes in the share price and trading volume of the share for the period from 2 January 2016 to 31 December 2016 for the Euronext Paris market.







# 7.1.3.2 Stock Exchange Data

	31/12/2016
Market capitalization at the end of the period (millions of Euros)	117.61
Share price (in euros)	
Highest (at closing)	3.72
Lowest (at closing)	2.29
At end of period (at closing)	2.50



#### 7.1.3.3 Dividends

#### **Actions ONXEO**

Financial Year	Number of shares	Dividend paid for the period
2010	13 536 072	-
2011	17 659 715	-
2012	17 659 715	-
2013	20 682 992	-
2014	40 544 204	-
2015	40 552 083	-
2016	47 043 404	-

#### 7.2 SUPPLEMENTARY INFORMATION ABOUT THE GROUP

#### 7.2.1 HISTORY

1997. Founding of the company on 5 March 1997.

**1999-2005.** The Company financed the development of its first projects, notably its first clinical trials of products based on two patented technologies - the Lauriad™ mucoadhesive oral technology and the Transdrug™ nanoparticle technology - by means of a number of financing rounds with venture capital investors. In 2005, this enabled it to complete and submit a registration application in France for Loramyc®, the first product entirely developed by the Group.

**2005**. Listing of Onxeo on Euronext Paris on 7 December 2005.

**2006-2008.** MA issued for Loramyc® in France (October 2006) and in eleven countries across Europe (2008). Launch of Loramyc® in late 2007 on the French market. Agreement signed with PAR Pharmaceutical for the marketing of Oravig® in the USA (2007) and completion of a pivotal phase III clinical trial with the product in the same country (2008).

**2009.** Three new products entered clinical phase: two emanating from the Lauriad® technology: fentanyl Lauriad® (phase I) for severe and chronic cancer pain and clonidine Lauriad® (phase II) in the treatment of oral mucositis, and a new chemical entity, the anti-invasive biotherapy AMEP® (phase I), designed for the treatment of invasive melanoma. Positive phase III results obtained in December 2009.

**2010.** MA issued for Loramyc® in the USA in April, under the brand name Oravig®. Marketing launch of Oravig® in the USA at the end of August 2010 by Strativa Pharmaceuticals, the "support care product" division of Par Pharmaceutical. Issue of 13 new MAs for Loramyc® in Europe, bringing the number of European countries in which it is registered to twenty-six.

Agreement with the Therabel Pharma group to market Loramyc® and Setofilm® in Europe, and transfer of commercial operations. Two other partnership agreements were concluded for the marketing of the product, with Handok and NovaMed in Asia.

In parallel, the Group conducted a pivotal international phase III trial for Sitavig® in the treatment of labial herpes.

**2011.** A year marked by the departure of Dominique Costantini, CEO and co-founder of the company, and the appointment of a new CEO, Judith Gréciet, and a new chairman, Patrick Langlois, incorporating the restructuring of the board of directors. 16 million euro financing round for the Livatag® development program and to strengthen the Group's orphan drugs portfolio.

**2012**. Clinical programs start of the Livatag® phase III trial, widening in Europe of the phase II Validive® trial and ANSM approval for the AMEP® phase I/II clinical trial protocol.

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Signature of licensing agreements: with the Pharmaceutical Industries Limited for the marketing in Israel of Sitavig®; with Vestiq Pharmaceuticals for the marketing of Oravig® in the USA; and with Shafayab Gostar for the distribution of Loramyc® in Iran.

**2013**. Continuation of the ReLive phase III trial with Livatag® in France and authorization from the regulatory authorities to conduct the trial in the USA and in 7 other countries in Europe. Continuation of the phase II trial with Validive® in the USA and Europe. Issue of MA for Sitavig® in the USA. Capital increase of 8.7 million euros, notably intended for the acceleration and completion of the Validive® Phase II trial.

**2014.** In the summer of 2014, BioAlliance Pharma merged with Danish biopharmaceutical company Topotarget to create Onxeo (August) with a double-listing on Euronext Paris regulated market and NASDAQ Copenhagen market. With the merger came anti-cancer drug belinostat (Beleodaq®), which received FDA approval for PTCL in the US. For Validive, positive preliminary phase II results were presented and the product was granted Fast Track status by the FDA. In that same year, Livatag® also received Fast Track status by the FDA for second-line treatment of HCC. In December, a capital increase of 40.7 million euros was completed to finance the research and development of the Group's key products.

**2015.** Livatag®: Progression of the ReLive Phase III trial in primary liver cancer with the opening of 4 new centers. Filing of a new patent based on a specific composition of Livatag® nanoparticles, which if granted, would extend industrial protection of Livatag until 2036. Launch of a preclinical research program of Livatag® and Beleodaq® with other cancer agents. Beleodaq®: Publication in December 2015 of the positive results of the Beleodaq® (belinostat) Phase I study in association with the CHOP chemotherapy protocol (BelCHOP study) as 1st line treatment for PTCL. Validive®: Presentation of the final results of the Phase II trial of Validive® in oral mucositis in several international meetings.

2016. Livatag® and Beleodaq®: partnership with Univerity of Navarra (CIMA) as part of the preclinical development combination program. Acquisition of DNA Therapeutics and its lead compound: AsiDNA. Strategic decisions to continue the development of Validive® (Phase III) in partnership. Evolution of Company Board of Directors. Opening of a US subsidiary (Onxeo US) in New York. Development of a new oral formula for Beleodq®. Presentation of the AsiDNA™ development plan. Notice by the American Patent Office of receipt of a key patent for AsiDNA™, maintaining its protection until 2031 in the United States. Partnership with the Irish Royal College of Surgeons on a research program for alternate applications of Beleodaq®. Exclusive license agreement with Pint Pharma for the marketing and sales of Beleodaq® in Latin American in the PTCL domain. AsiDNA™ demonstrates a synergistic effect in combination with PARP inhibitors notwithstanding the tumor's genetic profile. First preclinical results from the Livatag® trial beyond PTCL. Onxeo raises €12.5M with American and European investors. Promising results of the preclinical program for Beleodaq® in combination with control point inhibitors. Promising preclinical results for Livatag® in uses against pancreatic cancer. Ninth positive recommendation from the DSMB for the continuance of its Phase III trial of Livatag® "ReLive" in primary liver cancer.

#### 7.2.2 LEGAL INFORMATION ABOUT THE COMPANY

#### 7.2.2.1 General information

#### Company name and address

Company name: Onxeo

Registered office: 49 boulevard Valin – 75015 Paris – France

Telephone: +33 (0)1 45 58 76 00 Fax: +33 (0)1 45 58 08 81

www.onxeo.com

### **Company legal status**

Onxeo is a French Société Anonyme whose securities are traded on Euronext Paris and also have a secondary listing on Nasdaq Copenhagen regulated market and is governed by the French Commercial Code and its implementation legislation; it complies with the rules of corporate governance generally applicable in France and notably with the MiddleNext code.



Onxeo applies the statutory and regulatory standards governing the corporate bodies of listed companies and reports within this Registration Document on its implementation of the recommendations set out in the aforementioned code.

#### **Statutory Auditors**

The company's accounts are audited by two statutory auditors appointed in accordance with Article L. 225-228 of the Commercial Code.

#### Date of incorporation and duration

Date of incorporation of the Company: 5 March 1997. Incorporation expiry date: 05 March 2096.

#### Registration

The company is registered in the Paris commercial and companies register under number: 410 910 095. APE/NAF code: 7219Z. This corresponds to the activity of research and development in the physical and natural sciences.

#### **Document consultation**

The following corporate documents may be consulted at the Company's registered office (where a copy can be obtained):

- The memorandum and articles of incorporation, the minutes of shareholders' meetings and other corporate documents of the Company;
- All reports, letters and other documents, historical financial information, valuations and declarations prepared by an expert at the Company's request, some of which are included or referred to in this Registration Document; and
- The historical financial information on the Company for each of the two financial years prior to the publication of this Registration Document.

The regulated financial information is available on the Company's website: www.onxeo.com.

#### Corporate purpose

Under the terms of Article 2 of the Articles of Association, the corporate purpose of the Company is as follows:

- The design, research and development of healthcare products from creation until marketing authorizations are obtained, and all operations related thereto;
- The acquisition, filing, award, assignment and licensing of all patents, trademarks, licenses and utilization processes;
- The acquisition of shareholdings or interests in all companies or enterprises created or to be created, both French and foreign, with or without a purpose similar to that of the Company;
- The provision of services, advice, research, development and marketing in the health sector;
- And, more generally, all industrial, commercial, financial, civil, securities or property operations, which may be related directly or indirectly to one of the aforementioned objects or any similar and related purposes, and which may be useful for the performance and development of the Company's business.

#### **Financial year**

The financial year lasting 12 months begins on 1 January and ends on 31 December.

#### **Distribution of profits**

Each share entitles with ownership of the Company's assets, profit sharing, and liquidation surplus in proportion to the number and nominal value of the existing shares.

Whenever it is necessary to own several shares, whether or not preferred shares or securities to exercise any right, shareholders or holders of securities are personally responsible for gathering the number of shares or securities necessary.



On the profit for the financial year, reduced by any prior losses as the case may be, it is mandatory to draw at least five percent (5%) to be assigned to the formation of a reserve fund called "legal reserve". This ceases to be mandatory when the amount of the legal reserve reaches one tenth of the share capital.

Distributable income consists of earnings of the fiscal year minus prior losses and the deduction provided in the previous paragraph plus any retained earnings.

If there is in the financial statements, as approved by the shareholders' meeting, a distributable profit, the shareholders' meeting decided (i) to enroll it in one or more reserve funds for which it regulates the assignment, (ii) to carry it forward or (iii) to distribute it as dividends.

However, except in case of capital reduction, no distribution may be made to shareholders when equity is, or would be after this distribution, below the amount of the share capital plus reserves that the law or the by-laws do not allow to distribute.

The shareholders' meeting may decide to distribute amounts deducted from the optional reserves either to provide or supplement a dividend or as an exceptional distribution.

After acknowledging the existence of reserves at its disposal, the shareholders' meeting may decide to distribute amounts drawn from these reserves. In this case, the decision expressly indicates the reserve items from which these withdrawals were taken. However, dividends are drawn in priority from the distributable profit for the fiscal year.

The modalities of the dividend payment shall be determined by the shareholders' meeting or, failing to do so, by the Board of directors.

However, the dividend payment shall take place within a maximum period of nine months after the closing of the fiscal year.

The shareholders' meeting approving the financial statements for the fiscal year may grant each shareholder, for all or part of the dividend distributed, an option between payment of the dividend in cash or in shares.

Similarly, the ordinary shareholders' meeting, acting in accordance with Article L. 232-12 of the French Commercial Code, may grant shareholders an interim dividend and for all or part of interim dividend, a option of payment of the interim dividend in cash or in shares.

#### **Dividend limitation period**

The dividend limitation period is five years from their date of issue, subsequent to which they are paid to the Treasury.

#### **Amendment to Shareholder rights in Articles of Association**

The rights of shareholders granted by the Articles of Association can only be amended by an extraordinary general meeting of the shareholders of the Company.

#### Establishment providing the company's financial services

Coupon payment and transfer services are provided at the branches of Société Générale, SOCIETE GENERALE Securities Services, 32 rue du Champ de Tir - BP 81236 - 44312 NANTES CEDEX 3.

#### **Onxeo Share Listing**

Onxeo's shares are listed in Segment B on Euronext Paris regulated market and have also had a secondary listing on Nasdaq Copenhagen since 1 August 2014: ISIN Code: FR0010095596.

#### Shareholders' general meetings

Shareholders' meetings are convened and meet under the conditions set by law. Meetings take place at the registered office or at any other location stated in the notice of meeting.

All shareholders have the right to attend shareholders' meetings and to participate in their deliberations either personally or by proxy, regardless of the number of shares that they hold, if an entry is made in respect of the shares held, under the conditions provided for by law, either in the shareholder's own name or in the name of the intermediary registered on such shareholder's behalf, on the third business day before the date of the



shareholders' meeting at zero hours, Paris time, either in the registered share accounts kept by the Company or in the bearer share accounts kept by the duly authorized intermediary.

Shareholders who participate in the meeting via video conferencing or via telecommunications methods that allow identification as required by the regulations then in force, are also deemed to be present for determination of a quorum and majority, if the Board of Directors so decides when the meeting is convened.

Onxeo's website maintains an up-to-date financial events diary for the Group, notably including the date of the general meeting.

#### Voting rights

There is only one class of shares, which conveys to all shareholders the same rights.

Each share conveys rights to the profits and corporate assets in a share proportional to the amount of capital it represents and conveys the right to one vote. The articles of incorporation do not contain any provisions stipulating double voting rights for shareholders or limiting the voting rights attached to shares.

#### Existence of statutory thresholds to be declared to the company (Article 7 – Articles of Association)

In accordance with the provisions of the French Commercial Code, any natural person or legal entity, acting alone or in concert with any other person, who holds bearer shares entered in an account with an authorized intermediary and who comes to own a number of company shares representing more than one-twentieth, one-tenth, three-twentieths, one-fifth, one-quarter, one-third, one-half, two-thirds, eighteen-twentieths or nineteen-twentieths of the capital or voting rights must inform the Company and the AMF, within four trading days of the date when the ownership threshold is crossed, of the total number of shares or voting rights which said person owns. This information must also be transmitted, within the same periods and under the same conditions, when the interest in the capital or voting rights drops below the aforementioned thresholds.

The company's articles of association do not set out any additional thresholds.

Over the course of 2016, the company did not receive declaration of lower or upper threshold being crossed.

No other provision in the articles of association affects shareholders' rights which may only be modified in accordance with the law.

# Existence of an agreement the implementation of which could bring about a change of control of the company or could have the effect of delaying, deferring or preventing a change of control

The company is not aware of any agreement the implementation of which could lead at a later date to a change of control.

There currently does not exist any provision in any instrument of incorporation, in the articles of association or in a charter or regulation which could have the effect of delaying, deferring or preventing a change of control.

#### Measures taken by the company to ensure that control is not exercised in an abusive manner

The measures taken by the company to ensure that control is not exercised in an abusive manner are described in the Registration Document on the following pages:

- Section 5 of the Registration Document: report from the chairman of the board relating to internal control;
- Section 5 of the Registration Document: existence of independent directors on the board and on specialist committees;
- Section 5: 'Conflicts of interest'

#### Significant contracts and transactions with related parties

See section 7.2.2.2 below for information regarding significant contracts.

With regard to related-party transactions, they are described in Note 20 to the consolidated financial statements in section 6.1 of this Registration Document.



#### Property, plant and equipment

Due to the large-scale use of subcontracting for the manufacture of its products, the Group's activities do not justify the ownership of plant or industrial equipment or facilities.

The Company leases its offices and laboratories, with a total area of 2,500 m<sup>2</sup> in the building housing its registered office in Paris, and an area of 580 m<sup>2</sup> in Copenhagen in Denmark.

In addition, in accordance with a temporary agreement to occupy public state-owned land entered into with the Châtenay-Malabry Faculty of Pharmacy and Paris XI University signed in 2006, the Company has a research and development laboratory located on the premises of the Châtenay-Malabry Faculty of Pharmacy. This laboratory, which occupies an area of approximately 60 m2, has a clean room (a vacuum chamber enabling work with genotoxics) that the Company uses to conduct certain experiments on its products.

#### Elements that could have an impact on a public offer

In accordance with Article L 225-100-3 of the French Commercial Code, the elements that could have an impact on a public tender offer are listed below:

- The capital structure of the Company has no characteristics that are likely to have an impact on a public tender offer;
- There are no restrictions imposed by the articles of incorporation on the exercise of the voting rights and the transfer of shares, and there are no clauses included in agreements brought to the Company's attention pursuant to Article L 233-11 of the Commercial Code;
- No declaration made pursuant to Articles L 233-7 and L 233-12 of the French Commercial Code mentions any direct or indirect shareholdings in the Company's capital that could have an impact on a public tender offer;
- There are no securities carrying special control rights;
- There is no employee ownership system;
- The Company is not aware of any shareholder agreements that could lead to restrictions on the transfer of shares and the exercise of voting rights;
- And under Article 14 of the articles of incorporation, the members of the Board of Directors are appointed for a term of four years by the annual shareholders' meeting. In case of vacancy by death or resignation of one or more board seats, the Board of Directors may, between annual shareholders' meetings, make appointments on an interim basis, which are subject to ratification by the next annual meeting. The Company's articles of incorporation may be amended only by an extraordinary shareholders' meeting;
- The Board of Directors benefits from authorizations set forth in the paragraph "Authorized, non-issued capital/debt securities" hereinafter;
- The Company has concluded certain agreements explicitly containing a clause with regard to change in control. These are in particular collaboration and licensing agreements which include a clause requiring prior approval by the contractor in the event of a change in control of Onxeo;

To date, there has been no agreement providing for indemnities for members of the Executive Committee or employees, if they resign or are dismissed without just and serious cause or if their employment ends due to a public tender offer.

# Information from third parties, expert statements and declaration of interest None.

- 7.2.2.2 Significant contracts
- 7.2.2.2.1 Partnership and licensing agreements
- 7.2.2.2.1.1 Partnership agreement with the Institut Curie, the Centre National de la Recherche Scientifique (CNRS) and the Inserm Transfert SA



On 1 January 2014, DNA Therapeutics (fused with Onxeo in March 2016) entered into a partnership agreement with the Institut Curie, the CNRS and INSERM Transfert the terms of which seek to give effect to a research and development program between the parties relating the new technology Dbait which corresponds to a family of non-coding nucleic acid molecules capable of interfering with cellular damage repair mechanisms so as to better the treatment of cancer patient who do not respond well to traditional treatments.

The agreement provides for Onxeo to financially contribute to the research program.

Each party is liable for its own costs in the relation to the realization of the research program.

The rights stemming from all results of this program will be shared equally between the parties.

The partnership agreement came into force on 1 January 2014 for a maximum period of five years. At each anniversary date, it will be tacitly renewed for successive one year periods, unless one of the parties wish to repudiate by giving at least 6 month notice prior to that renewal.

The agreement can be terminated by one party in case of breach of contract by another party or for any other reasonable cause. This termination will only become effective three months following the complaining-party having sent a letter by first class recorded delivery explaining the grounds for termination, unless the negligent-party can, within this timeframe, remedy his breach or bring proof of a force majeur cause leading to the breach.

Onxeo may also terminate the agreement, at any time, subject to having given 3 months' notice, as soon as there is reasonable cause to do so with regards to the development of Onxeo, such as a change of control in case of an acquisition by a pharmaceutical company, or an objective interest to reorganize its research programs.

# 7.2.2.2.1.2 Partnership agreement with licensing option with the Royal College of Surgeons in Ireland (RCSI) and Dublin City University (DCU)

On 14 June 2016, Onxeo entered into a partnership with the RCSI and DCU, with an option to license.

The partnership generates cross-licensing right which are exclusive, non-transferable, non-sub-licensable, and free between the RCIS, DCU and ONXEO in order to evaluate the Cu(Phen)(Belisnotat) chemotypes technology.

The agreement also contains an option for ONXEO to demand that RCSI and DCU grant an exclusive license over their intellectual property rights existing prior to the partnership agreement and those created during this agreement so that ONXEO may manufacture, develop, use and sale the products resulting from its development activities in the alternative uses of Belinostat and of the HDAC inhibitors.

The partnership agreement was entered into for a period lasting the duration of the development project, which is a maximum of eighteen months starting from 14 June 2016, subject to the early termination by early accomplishment of the project, or prolongation by agreement of both parties. The agreement allows for each party to terminate the agreement if: (i) there is a breach of contract by another party which is not remedied within 30 calendar days and (ii) in case of insolvency for any one of the parties. The parties have the right to terminate the agreement early and unilaterally by giving 2 month of notice.

This agreement may not be assigned, in whole or in part, to third parties or successors in title by a party without the prior consent of the other party.

#### 7.2.2.2.1.3 License Agreement with PINT

On 27 July 2016, Onxeo entered into a commercial license agreement with PINT. This agreement grants PINT the exclusive license, with royalties, allowing it to sub-license, in order to use, sale, offer to sale, having sold or imported (excluding the right to manufacture or export) the products, for the treatment of refractory or relapsed PTCL in humans via a molecule conceived for injection in the following territories: Argentina, Brazil, Chile, Colombia, Venezuela, Equator, and Peru.

This agreement will last until PINT has satisfied the entirety of its payment obligations under the terms of the agreement to ONXEO, country by country, subject to an early realization of its contractual commitment.

The agreement further provides for the possibility for Onxeo to terminate the agreement if: (i) there is a default of payment, (ii) PINT fails to achieve its objectives in terms of regulatory compliance or cannot generate enough

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income from the sale of the product in a humanitarian-program, (iii) for failing to reach the minimum threshold for royalties, (iv) if PINT changes control, (v) and if PINT contest Onxeo's patents.

The agreement further provides a right of early termination for each party in case of insolvency proceedings and in case of breach of a contractual term not remedied within 60 days (or 10 days in case of default of payments).

Finally, the agreement provides for a right of assignment to third parties. However, if PINT assigns the agreement to one of its subsidiaries or affiliates, PINT will remain entirely liable for compliance with the terms of the agreement as originally contracted between PINT and Onxeo on behalf on the assignees.

#### 7.2.2.2.2 Main subcontracting agreements

#### Framework Service Agreement (manufacturing) with Avecia

On 7 October 2016, DNA Therapeutics (fused with Onxeo in March 2016) entered into a master service agreement with Avecia relating the manufacturing of its product AsiDNA.

Under the terms of this framework agreement, Avecia is responsible for the manufacturing of the active substance of AsiDNA including the development and optimization of the processes, analytical methods and manufacturing of technical and clinical tools.

The intellectual property generated, developed, discovered or invented as a result of the performance of obligations under this agreement belongs to Onxeo.

This agreement came into force on 7 October 2016 for a maximum period of 3 years. At each anniversary date, it will be tacitly renewed for successive one year periods.

Each party may terminate the agreement in case of a force majeure.

The parties can also terminate the agreement by mutual consent. They can also terminate unilaterally subject to a written notice of 90 days for Onxeo and 12 days for Avecia.

The agreement also provides that each party may terminate the agreement in case of a breach of contract by the other party which has not been remedied within 30 days from the date of a letter give notice of the breach.

#### 7.2.2.3 Supplementary Information on the share capital

At 31 December 2015, the company's share capital amounted to 11,760,851.00 Euros divided into 47,043,404 shares each of a nominal value of 0.25 Euros, all of the same class and fully paid up. They represent 47,043,404 voting rights, after treasury shares. There are no shares not evidencing the capital of the company.

At the date of the Registration Document, the company's share capital amounted to 11,760,851.00 Euros divided into 47,043,404 shares each of a nominal value of 0.25 Euros, all of the same class and fully paid up

#### 7.2.2.3.1 Cross-shareholdings and treasury shares held

The Company did not carry out any transactions covered by Articles L 233-29 and L 233-30 of the Commercial Code.

#### 7.2.2.3.2 Acquisition by the Company of its own shares

#### 7.2.2.3.2.1 Share buyback program

#### Objectives of the share buyback program and use made of the shares bought back

In accordance with the provisions of Articles L. 225-209 et seq. of the French Commercial Code, the Company was authorized by its shareholders to trade in its own shares, up to a maximum of 10% of the share capital. This authorization was granted to it for a period of eighteen months, by the Company's ordinary and extraordinary shareholders' meeting of 20 May 2015 under the terms of its sixth resolution and then renewed for a period of eighteen months by the Company's ordinary and extraordinary shareholders' meeting of April 6, 2016 under the terms of its thirteenth resolution.



During the financial year ending December 31, 2016, the Board of Directors successively implemented the program authorized by the General Meeting of 20 May 2015 and, as of 7 April 2016, the program authorized by the General Meeting of 6 April 2016.

The objectives pursued by this buyback program, in decreasing order of priority, concern the following situations:

- The liquidity of the company's shares with an investment service provider acting independently within the scope of a liquidity contract in accordance with the ethics charter of the French Association of Financial Markets (AMAFI), recognized by the AMF;
- To implement any company share purchase option plan within the scope of the provisions of articles L 225-177 et seq. of the Commercial Code;
- To award free shares to employees and corporate officers;
- To grant shares to employees and, where applicable, corporate officers under profit-sharing agreements and to implement any employee savings plan, under the conditions provided for by law, in particular within the scope of articles L 3332-18 of the French Labor Code;
- To purchase shares to retain them and tender them subsequently in exchange or as payment within the scope of external growth transactions within the limit of 5% of the share capital;
- To provide shares upon the exercise of rights attached to securities granting immediate or future rights to capital;
- To cancel the shares thus bought back within the limits set by law and subject to the condition precedent of the adoption of resolution 11 of this meeting.

The details of this share buyback program are available at the Company's registered office or on its website.

#### Implementation of the share buyback program – Liquidity agreement

In accordance with the provisions of Article L 225-211 of the Commercial Code, the methods of the share buyback program carried out during the past financial year are presented hereafter.

During the 2015 financial year, this share buyback program was exclusively used within the scope of a liquidity contract aimed at entering into a share management process with regard to, or preserving the liquidity of, the company's shares with an investment services provider. Under the regulations in force, and in particular the provisions of European Regulation No. 2273/2003 of 22 December 2003, on 2 January 2007 the company concluded a liquidity contract with CM-CIC Securities that complied with the ethics charter of the French Association of Financial Markets (Association Française des Marchés Financiers, AMAFI), recognized by the Autorité des Marchés Financiers. This contract is still in force as of the date of this Registration Document. €400,000 was allocated to the liquidity account and trading expenses amounted to €27,000 for the year.

Under the share buyback program, the company made the following purchases and sales of its own shares, between the beginning and end dates of the last financial year:

	Number of shares purchased	Number of shares sold	Average price on purchase	Average sale price	Number of shares registered in the Company's name	Proportion of capital
Pure buyback program	0	0	0	0	0	0
Liquidity contract						
January 2016	89 626	106 847	3,17	3,03	14 645	0,04%
February 2016	91 980	92 423	2,91	2,90	14 202	0,04%
March 2016	64 931	49 020	3,26	3,31	30 113	0,07%
April 2016	47 062	61 852	3,33	3,39	15 323	0,04%
May 2016	42 141	14 827	3,20	3,26	42 637	0,10%
June 2016	72 231	81 961	2,67	2,69	32 907	0,08%
July 2016	112 797	125 683	3,26	3,21	20 021	0,05%

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August 2016	50 651	38 943	3,13	3,14	31 729	0,08%
September 2016	62 206	40 977	3,02	3,24	52 958	0,13%
October 2016	50 457	69 253	2,51	2,52	34 162	0,07%
November 2016	172 824	165 468	2,44	2,46	41 518	0,09%
December 2016	33 434	51 152	2,44	2,43	23 800	0,05%
Total 2016	890 340	898 406	2.91 <sup>(1)</sup>	2.89 <sup>(1)</sup>	354 015	

<sup>(1)</sup> Weighted average calculated over the year

The Company held 23,800 treasury shares on 31 December 2016, with a total nominal value of €5,950 and a total book value of €57,891 valued at their purchase price.

#### 7.2.2.3.2.2 Shares held by the company (excluding liquidity contract)

At 31 December 2016, the company held 4,908 of its own shares, with a total nominal value of €1.227 and a total book value of €37,559.89

All purchases and sales made by the company with respect to its shares since they were admitted for trading on the Paris Euronext regulated market have been made within the scope of the liquidity contract in order to stabilize the share price.

#### 7.2.2.3.3 Authorized share capital/debt securities, not yet issued

The Company has authorized the capital increases, not effected at the date of filing of this registration document, which could result from the warrants, stock options and free shares described in Chapter 5 of this Registration Document.

#### **General Meeting of 6 April 2016**

Resolution	Object of the resolution	Maximum nominal amount in euros	Terms for determining the issue price	Authorization duration and expiry
15th resolution	•	e capital increase v €5,069,010 <sup>(1)</sup> s Nominal amount		6 June 2018 (26 months)
16th resolution	Delegation to the Board of Directors with a view to increasing the amount of any issue with or without preferential subscription rights decided under the 15th resolution	e of the initial issue (1)		
17th resolution	Delegation of authority to the board of directors with a view to issuing shares or any securities giving access to the capital with removal or shareholders' preferential subscription rights for the benefit or a category of a specific category or investors	g capital increas g €3,041,406 f Nominal amount I bonds and ot f debt securities giv	of At least equal to the ses: average of the prices weighted be of the volumes of the last 3 trading daying preceding the setting of the issurance less, where applicable, the maximum discounce of 25%	e (18 months) y e e s e e e



Resolution	Object of the resolution	Maximum nominal amount in euros	Terms for determining the issue price	Authorization duration and expiry
19th resolution	Delegation of authority to the board of directors with a view to increasing the share capital within limit of 10% of the capital in remuneration of contributions in kind of any equity securities of securities giving access to the capital of third-party companies not within the context of a public exchange offer	o of the company a capital <sup>(1)</sup> In Nominal amount on bonds and other debt securities giving all access to the capital $n \in 12.000.000 \in (1)$	of er og	6 June 2018 (26 months)
22 <sup>nd</sup> resolution	Authorization of the board of directors to grant share subscription or purchase options	, , ,	(3)	6 June 2019 (38 months)
23 <sup>rd</sup> resolution	Authorization of the board of directors to allocate free shares whether existing or to be issued	, , ,	to N/A	6 June 2019 (38 months)
24 <sup>th</sup> resolution	Delegation to the board of director to issue and allocate share warrant to the benefit of the following category of persons: (i) member and observers of the company' board of directors in office as of the warrant allocation date who are neither employees nor executives of the company or of any of it subsidiaries, (ii) consultants and service providers to the Company	s 405,520 shares) g s s e e e of s	to <sup>(4)</sup>	6 October 2017 (18 months)

- (1) These amounts are not cumulative, the maximum total amount of capital increases permitted to be implemented under the delegations made under the terms of the 15th, 16th, 17th and 19th resolutions is set at 5,069,010 euros. The maximum nominal amount of debt securities permitted to be issued under the aforementioned delegations is set at 60,000,000 euros.
- (2) These amounts are not cumulative, the maximum total amount of capital increases permitted to be implemented under the delegations made under the terms of the 22nd et 23rd resolutions is set at 152,070 euros.
- (3) The purchase or subscription price per share shall be set by the board on the day when the option is granted and may not be less than (i) for new share subscription warrants at the average of the prices quoted on the 20 trading days preceding the day when the option is granted, and (ii) for options on existing shares, at the average of the quoted prices on the 20 trading days preceding the day when the option is granted or less than the average purchase price of shares held by the company on the day when the option is granted in accordance with Articles L. 225-208 and L.225-209 of the Commercial Code.
- (4) The subscription price of an ordinary share in the company on exercise of a warrant, which shall be set by the board of directors at the time of warrant allocation, must be at least equal to the average of the quoted prices on the 20 trading days preceding the day of warrant allocation by the board of directors.

The complete text of the resolutions of the company's general meetings is available on the website of Bulletin d'Annonces Légales Obligatoires: http://www.journal-officiel.gouv.fr/balo.

#### 7.2.2.4 Supplementary information about the auditing of the accounts

#### 7.2.2.4.1 Audit of the accounts

The statutory auditors of **Onxeo** carry out certification of the company's accounts in accordance with legislation on commercial companies. The statutory auditors are appointed by shareholders' general meeting.



#### **Statutory Auditors**

#### **Grant Thornton**

French member of Grant Thornton International 29, rue du Pont 92200 Neuilly sur Seine

Represented by Mr. Samuel Clochard, member of the regional association of statutory auditors of Versailles.

The mandate of Grant Thornton was renewed by the shareholders' meeting of 6 April 2016 meeting to approve the financial statements for the year ending 31 December 2015. Its mandate will expire at at the close of the 2022 shareholders' meeting approving the financial statements for the year ending 31 December 2021.

#### **Ernst & Young Audit**

Tour Ernst & Young, Faubourg de l'Arche, Tour First, 1/2 place des Saisons 92400 Courbevoie, Paris-La Défense 1.

Represented by Mr. Frank Sebag, member of the *member of the regional association of statutory auditors of Versailles*.

Ernst & Young's mandate was renewed by the General Meeting on 29 June 2011 for a period of 6 financial years. This mandate will expire after the General Meeting approving the accounts for FY 2016.

#### **Alternate Auditors**

IGEC, Institut de gestion et d'expertise comptable 3, rue Léon Jost 75017 Paris

The mandate of IGEC was renewed by the shareholders' meeting of 6 April 2016. It will expire at the close of the shareholders' meeting to approve the financial statements for the year ending 31 December 2021.

Société Auditex SA Tour First, 1 /2 place des Saisons 92400 Courbevoie, Paris-La Défense 1

The mandate of Auditex SA was renewed at general meeting held on 29 June 2011 for a period of six financial years. This appointment expires at the close of the shareholders' meeting to approve the financial statements for the year ending 31 December 2016.

The appointing of an alternate auditors is not required when the statutory auditor is neither a physical nor a unipersonal moral person. The renewal of Auditex is therefore not necessary.

Statutory auditors have not resigned and their appointments have not terminated during the period covered by the referenced historical information.

#### 7.2.2.4.2 Fees paid to auditors and members of their networks

The table of fees paid to the statutory auditors and members of their networks as recognized in expenses by the company between 1 January and 31 December 2015 is provided in Note 22 to the consolidated financial statements, included in section 6.1 of this Registration Document.

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# 8. PERSONS RESPONSIBLE

#### 8.1 PERSON RESPONSIBLE FOR THE REGISTRATION DOCUMENT

Mrs. Judith Greciet, Chief Executive Officer

#### 8.2 DECLARATION BY THE PERSON RESPONSIBLE

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

I certify that, to my knowledge, the financial statements are prepared in accordance with applicable accounting standards (IFRS as adopted by the EU for the consolidated financial statements and French GAAP for the annual financial statements) and give a true and fair picture of the assets and liabilities, the financial position and the results of the Company and the undertakings included in consolidation, and that the management report presents a true picture of the changes in the business, the results and the financial position of the Company and the undertakings included in the consolidation, along with a description of the principal risks and uncertainties they face.

We have received a letter from the statutory auditors prepared at the conclusion of their work, in which they state that they have audited the information about the financial position and financial statements provided in this Registration Document, and have read the entire Registration Document.

Financial information on the consolidated and annual accounts presented in this Document is the subject of reports from the statutory auditors:

- The statutory auditor's report on the consolidated financial statements at 31 December 2016 emphasize note 3.1 and note 5.1 "liquidity risk" of the annexes related to terms with the principle of ongoing business was established.
- The statutory auditor's report on the consolidated financial statements at 31 December 2014, containing observations which describe the merger transaction that took place during the period and the accounting impact on the financial statements for the year ended 31 December 2014, and the incidence of the impact of the "Change of method" applied during the period regarding the first application of the IFRS 11 standard.

Done on 24 April 2017

Judith Greciet, Chief Executive Officer

#### 8.3 PERSON RESPONSIBLE FOR THE FINANCIAL INFORMATION

Mr. Nicolas Fellmann - Chief Financial Officer Address: 49 boulevard Valin – 75015 Paris – France

Telephone: +33 (0)1 45 58 76 00 - Fax: +33 (0)1 45 58 08 81 - Email: contact@onxeo.com

#### 8.4 HISTORICAL FINANCIAL INFORMATION INCORPORATED BY REFERENCE

In accordance with Article 28 of Commission Regulation (EC) No 809/2004, the following information are incorporated by reference in the Registration Document:

- The consolidated financial statements and the relevant statutory auditors' report thereon at pages 118 to 153 of the 2015 Registration Document filed with the AMF on 29 April 2014 under number D.16-0452.
- The consolidated financial statements and the relevant statutory auditors' report thereon at pages 110 to 160 of the 2014 Registration Document filed with the AMF on 14 April 2015 under number D.15-0036.



# 9. CROSS-REFERENCING TABLE WITH INFORMATION REQUIRED IN THE ANNUAL FINANCIAL STATEMENTS

In order to enhance the readability of this Registration Document, the cross-referencing table below enables information in this Registration Document to be identified which its homologues in the annual financial report that listed companies are required to publish in accordance with Article L. 451-1-2 of the Monetary and Financial Code and Article 22-3 of the General Regulations of the AMF.

ANNUAL FINANCIAL STATEMENTS	SECTIONS (PAGES)
1. Persons responsible	8.2 (p. 183)
2. Annual Financial Statements (French GAAP Standard)	6.3 (p. 131)
3. Consolidated Financial Statements (IFRS Standard)	6.1 (p. 95)
4. Annual Management Report	See sub-section below
5. Chairman's report on corporate governance and internal control	5.1, 5.2 et 7.2.2. (p. 58, 71 et 172)
6. Fees paid to auditors and members of their networks	7.2.2.4 (p. 181)
7. Statutory auditors' report on the consolidated financial statements	6.2 (p. 128) 6.4 (p. 159)
8. Statutory auditors' report on the chairman's report	5.6 (p. 93)
ANNUAL MANAGEMENT REPORT	SECTIONS (PAGES)
Company activity during the financial year	2 (p. 11)
2. Analysis of the results and financial position – Appropriations –	3.1.1 (p.30)
Dividends – Non-tax deductible expenses	
3. Information related to payment delays for contractors	3.1.1.6 (p. 31)
4. Key risks and uncertainties for the Company / Utilization of the Company's financial instruments	5.5.1.4 (p. 80)
5. R&D activity	4.1 (p. 36)
6. Future development and strategy	2.3 (p. 16)
7. Significant events since the end of the financial year	2.2 (p. 15)
8. Employee holdings of share capital	2.4.1 (p. 17)
9. Company's executive committee	5.2 (p. 71)
10. Information relating to corporate officers	5.1.2.1 (p. 64)
11. Significant share purchase of French-based companies, or take-overs of such companies; sale of such assets	2.1.1 (p. 11)
12. Subsidiaries' activities	2.1.1 (p. 11)
13. Information related to the share capital distribution and self-control – Share buyOback program	7.1.2 et 7.2.2.3 (p. 168 and 178)
14. Changes in the share capital	7.1.2 et 7.2.2.3 (p. 168 and 178)



15. Summary of the corporate officers' transactions and those persons concerned under Article L. 621-18-2 of the French Monetary and Financial Code on the Company's securities during the financial year	5.4 (p. 78)
16. Relevant information in case of a public offer	7.2.2.1 (p. 172)
17. Information on agreement between a corporate officer and a significant shareholder or a Group subsidiary	7.2.2.1 (p. 172)
18. Social and environmental information	2.4 (p. 16)
19. Table of results for the last five financial years	6.3 (p. 131)
20. Delegation of powers to increase share capital	7.2.2.3 (p. 178)



# 10. CROSS-REFERENCING TABLE FOR THE REGISTRATION DOCUMENT

This cross-reference table shows, as regards each of the headings provided by Annex I of European Commission Regulation (EC) No 809/2004 of 29 April 2004, the numbers of the paragraphs(s) of this registration document in which is mentioned information related to each of the regulation's headings.

	Annex I of EC Regulation no. 809/2004	Registration Document
		Chapter(s)/ Section(s)
I.	Persons responsible	8 (p. 183)
II.	Statutory Auditors	1.2.3 (p. 9) 7.2.2.4 (p. 181)
III.	Selected financial data	
1.	Selected historical financial data	1.3 (p. 10)
2.	Selected financial data for interim periods and comparative data covering the same periods of the preceding financial year	N/A
IV.	Risk factors	<b>5.5.1.4</b> (p. 80)
V.	Details of issuer	
1.	Corporate history and development	7.2.1 (p. 171)
	1.1. Registered name and trade name	7.2.2.1 (p. 172)
	1.2. Location and company registration number of the issuer	7.2.2.1 (p. 172)
	1.3. Date of incorporation and term of the issuer	7.2.2.1 (p. 172)
	1.4. Registered office and legal form of the issuer, legislation governing its activities, country of origin, address and telephone number	7.2.2.1 (p. 172)
	1.5. Significant events in the development of the issuer's activity	2.1 (p. 11) 7.2.1 (p. 171)
2.	Investments	2.3 (p. 16) 3.2 (p. 32)
VI.	Business overview	
1.	Main activities	1.1 (p. 7)
	1.1. Type of operations carried out by the issuer and its main activities	1.1 (p. 7)
	1.2. Important new product or service launched on the market	4.2 (p. 42)
2.	Main markets	4.2 (p. 42)
3.	Events that have influenced the information supplied in accordance with points VI and VI.2	N/A
4.	Issuer's degree of independence as regards patents or licenses, industrial, commercial or financial contracts or new manufacturing processes	4.1.4 (p. 39)
5.	Basis of any declaration by the issuer concerning its competitive position	4.2 (p. 42)
VII.	Organization chart	2.1.1 (p. 11)
VIII.	Property, plant and equipment	7.2.2.1 (p. 172)
	Environmental impact	2.4.2 (p. 26)
IX.	Examination of the financial situation and operating income	3 (p. 30)



Х.	Cash and capital	3.2 (p. 32)
XI.	Research and development, patents and licenses	4 (p. 36)
VII		4.1.4 (p. 39)
XII.	Information on trends Profit forecasts or estimate	2.3 (p. 16)
XIII.	Administrative, management and supervisory bodies and general	N/A
AIV.	management	
1.	Information on activities, absence of any conviction and terms of	5.1.2 (p. 64)
	office	5.1.2.1 (p. 64)
2.	Information on conflicts of interest, agreements concluded with	5.1.2.2 (p. 70)
	third parties and restriction on the sale of shares	5.1.2.5 (p. 71)
		5.1.2.6 (p. 71)
XV.	Remuneration and benefits of the persons referred to in point	5.1.2.4 (p. 70)
	XIV.1	5.2.2 (p. 72)
XVI.	Functioning of the administrative and management bodies	
1.	Expiry date of the current term of office of members of the	5.1.2.1 (p. 64)
<u> </u>	administrative, management and supervisory bodies	E 1 2 7 /n 71)
2.	Information on service contracts involving members of the administrative, management and supervisory bodies of the issuer or	5.1.2.7 (p. 71)
	of any of its subsidiaries	
3.	Information on the issuer's audit committee and remuneration	5.1.1.3 (p. 60)
3.	committee	3.1.1.3 (p. 00)
4.	Compliance with the corporate governance regime in force	5 (p. 58)
		7.2.2.1 (p. 172)
XVII.	Employees	,
1.	Number of employees at the end of the period covered by the	2.4.1 (p. 17)
	historical financial data or average number during each financial	
	year of this period and distribution of employees	
2.	Holdings and stock options: for each of the persons referred to in	2.4.1.1.4 (p. 20)
	point XIV.1, information on the participations that he or she holds in	5.2.2 (p. 72)
•	the issuer's share capital and any option existing over its shares	7.0.0.0 ( .170)
3.	Agreement providing for employee participation in the issuer's capital	7.2.2.3 (p. 178)
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	Shares with double voting rights, shareholder pacts or agreements,	7.2.2.1 (p. 172)
	crossings of statutory thresholds, Existence of an agreement the	7.2.2.1 (p. 172)
	implementation of which could bring about a change of control of	7.2.2.1 (p. 172)
	the company	
XIX	Transactions with related companies	7.2.2.1 (p. 172)
XX.	Financial data on the issuer's assets and liabilities, financial	6.1 (p. 95)
λλ.	situation and operating income	
1.	Historical financial information	6 (p. 95)
2.	Pro forma financial data and description of the effect of the	N/A
۷.	restructuring	IN/A
3.	Annual financial statements (individual company and consolidated	6.1 (p. 95)
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4.	Verification of historical financial data	- (I I
	4.1 Declaration certifying that the historical financial data has been	6.2 (p. 128)
	verified	6.4 (p. 159)
	4.2 Other information contained in the registration document and	6.5 (p. 162)
	verified by the statutory auditors	6.6 (p. 163)
	4.3 When financial data appearing in the registration document is	N/A
	not derived from financial statements verified by the issuer, state its	
г	source and stipulate that it is not verified	C F / 453\
5.	Date of latest financial data verified	6.5 (p. 162)



7.	Interim and other financial data  Dividend distribution policy	6.5 (p. 162) 6.5 (p. 162)
8.	Legal and arbitration proceedings	6.1 (p. 95) 6.3 (p. 131)
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XXI.	Supplementary information	
1.	Share capital	7.1.2 (p. 168) 7.2.2.3 (p. 178)
	1.1. Amount of capital subscribed, number of shares issued, nominal value per share and reconciliation of the number of shares outstanding at the beginning and end of the financial year	
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	1.3. Number, book value and nominal value of shares held by the issuer or its subsidiaries	7.2.2.3 (p. 178)
	1.4. Securities that are convertible or exchangeable or come with subscription warrants	7.2.2.3 (p. 178)
	1.5. Information on the conditions governing any right of acquisition and obligation attached to capital subscribed but not paid up, or on any undertaking aimed at increasing capital	7.2.2.1 (p. 172)
	1.6. Information on the capital of any member of the Group that is the subject of an option or agreement providing for it to be placed under option	7.2.2.3 (p. 178)
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XXII.	Sizeable contracts	7.2.2.2 (p. 176)
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# 11. CROSS-REFERENCING TABLE WITH "ESG" DECREE

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		Section(s)
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	Employment	2.4.1.1 (p. 17)
	Employee breakdown by gender, age and geographical area	2.4.1.1.2 (p. 17)
	Recruitments	2.4.1.1.3 (p. 19)
	Redundancies	2.4.1.1.3 (p. 19)
	Remuneration trends	2.4.1.1.4 (p. 20)
	Organization of work	2.4.1.2 (p. 21)
	Organization of working time	2.4.1.2.1 (p. 21)
	Absenteeism	2.4.1.2.2 (p. 21)
	Labor relations	2.4.1.3 (p. 21)
	Organization of employee dialogue (rules and procedures for employee notification, consultation and negotiation)	2.4.1.3 (p. 21)
	Summary of collective bargaining agreements	2.4.1.3.1 (p. 21)
	Health & Safety	2.4.1.4 (p. 22)
	Conditions of health and safety at work	2.4.1.4.1 (p. 22)
	Summary of agreements signed with unions and personnel representatives in the area of health and safety at work	2.4.1.4.5 (p. 24)
	Rate of frequency and seriousness of working accidents and occupational diseases	2.4.1.4.6 (p. 24)
	Training	2.4.1.5 (p. 25)
	Training policies implemented	2.4.1.5 (p. 25)
	Total number of training hours	2.4.1.5 (p. 25)
	Equal treatment	2.4.1.6 (p. 25)
	Measures taken in the area of gender equality	2.4.1.6 (p. 25)
	Measures taken in the area of inclusion of the disabled in the workplace	2.4.1.6.1 (p. 26)
	Policy in the fight against discrimination	2.4.1.6.2 (p. 26)
2	Environmental information	
2		<b>2.4.2</b> (p. 26)
	General environmental policy	2.4.2.1 (p. 26)
	Organization of the company and assessment or certification initiatives	2.4.2.1 (p. 26)
	Employee training and awareness in the area of environmental protection	2.4.2.1.1 (p. 27)
	Resources devoted to the prevention of environmental risks and pollution	2.4.2.1.2(p. 27)
	Amount of provisions and guarantees for environmental risks	2.4.2.1.3 (p. 27)
	Pollution and waste management	2.4.2.2 (p. 27)
	Prevention, reduction or remediation of emissions into the air, water or soil with a serious environmental impact	2.4.2.2.1 (p. 27)
	Prevention of the production, recycling and disposal of waste	2.4.2.2.2 (p. 27)
	Recognition of noise pollution	N/A
	Recognition of any other form of pollution related to an activity	N/A
	Durable utilization of resources	



	Water consumption and supply in accordance with local constraints	N/A
	Consumption of raw materials and measures taken to enhance their efficient utilization	N/A
	Consumption of energy, measures taken to improve energy efficiency and utilization of renewable energy	N/A
	Soil utilization	N/A
	Climate change	N/A
	Greenhouse gas emissions	N/A
	Adaptation to the consequences of climate change	N/A
	Protection of biodiversity	N/A
	Measures taken to limit damage to biological balances, natural environments and protected animal and plant species	N/A
3	Societal information	<b>2.4.3</b> (p. 28)
	Local, economic and social impact of the activity	N/A
	Impact of activities on local employment and development	N/A
	Impact of the activity on neighboring or local populations	N/A
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	Conditions of dialogue with stakeholders	2.4.3.1 (p. 28)
	Partnership and sponsorship activities	2.4.3.1.2 (p. 28)
	Outsourcing and suppliers	2.4.3.2 (p. 28)
	Incorporation within the purchasing policy of social and environmental issues	2.4.3.3 (p. 29)
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	Action taken to prevent all forms of corruption	2.4.3.3.1 (p. 29)
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	Protection of human rights	2.4.3.3.4 (p. 30)

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# 12. GLOSSAIRE

WORDS	DEFINITIONS
ANSM	Agence Nationale de Sécurité du Médicament (French Drug agency)
AMM	Marketing Authorization
MA	Quality assurance is a concept encompassing everything individually or collectively capable of influencing product quality. Quality assurance means all the measures taken to ensure that available products are suitable for their intended use. Good practice in the areas of sampling, transport, manufacturing and preservation form part of quality assurance.
Quality Assurance	The set of measures ensuring the quality of clinical trials.
GCP	An aspect of pharmaceutical quality assurance that ensures drugs are manufactured and
(Good Clinical Practice)	controlled in a consistent manner according to quality standards suitable for the drug's intended use and in accordance with the drug's specifications.
BSA	French share purchase warrants.
CNRS	Centre National de la Recherche Scientifique (French National Scientific Research Centre).
CRO	Contract Research Organization.
Toxic Dose Limit (TDL)	Dose of a given drug at which toxicity first appears. This dose makes it possible to define the therapeutic dose, which must necessarily be lower than the TDL.
DSMB	Data Safety and Monitoring Board. International committee of experts meeting every 6 months and/or after the recruitment of the first 25 patients for the ReLive study, in order to assess the tolerance data for patients included in the study and to recommend any protocol amendments.
EMA	European Medicines Agency.
Clinical trial	The systematic study of a drug on human subjects (either healthy or sick volunteers), in order to discover or verify drug effects, adverse reactions, and to study the absorption, distribution, metabolism, and extraction of the drug in question, for the purpose of establishing its safety and efficacy.
Pharmacokinetic study	The study of a drug's kinetic parameters in various compartments (the bloodstream, tissues).
Pharmacodynamic study	The study of a drug's effective dosage and length of therapeutic efficacy.
Randomized trial	A trial in which selected patients are randomly distributed among the various groups under study.
Pivotal trial	The clinical trial used to register a drug.
Drug Adverse Effect	Any harmful and undesirable effect experienced by a participant in a clinical trial, regardless of the effect's connection to the drug(s) under study and regardless of what caused the effect.
Serious adverse effect	An adverse effect that may contribute to death or is likely to endanger life, causes disability or incapacity, or leads to or prolongs hospitalization.
FDA	Food and Drug Administration.
НСС	Hepatocellular Carcinoma – primary liver cancer.
ICH	International Conference of Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use.
IFRS	International Financial Reporting Standards.
IND	<i>Investigational New Drug</i> – Request to start a clinical trial with the FDA for innovative new medicines.
INSERM	The National Institute of Health and Medical Research, a French institution.
Investigator(s)	Natural person(s) managing and supervising the performance of the study; responsible for protecting the health and wellbeing of study volunteers. The investigator is a doctor with appropriate experience. When a trial is entrusted to multiple investigators, a coordinator is appointed by the sponsor.
In vivo	Manipulation taking place in the body of a human or animal.

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WORDS	DEFINITIONS
ISO 9000 (9001, 9002, 9003)	Quality system: A system designed to ensure quality in design, development, production, installation, and related services.
Batch	A defined quantity (of a raw material, an item used in packaging, or a product manufactured in a process or a series of processes) that may be deemed a consistent unit.
Drug	Substance or combination of substances presented as possessing curative or preventive properties regarding human disease, and any product that can be administered to humans in order to establish a medical diagnosis or to restore, mitigate or modify their biological functions.
MDR	Multi Drug Resistance gene – encoding transmembrane proteins rejecting products or drugs outside the cells.
Compliance	The patient's adherence to treatment (good therapeutic follow-up).
PCT	Patient Cooperation Treaty – an international treaty providing for standardized filing procedures for obtaining foreign patents in the signatory countries.
Phase I	This phase corresponds to the initial clinical trials. It must evaluate drug tolerance in a small number of (usually healthy) volunteer subjects and enable initial studies on the administration of the drug in the human body.
Phase II	This phase is divided into two sub-phases. The objective of Phase II-A is to study the effects of the drug on a small number of volunteer patients (usually healthy) and to complete pharmacokinetic studies. The objective of Phase II-B is to assess the tolerance (adverse effects) and efficacy of the drug on a limited number of patients and to define the optimum dosage.
Phase III	The objective of this phase is to confirm and complete the results related to the efficacy and tolerance of the drug on a sufficient number of patients. It must also enable adverse effects to be studied and the efficacy/safety relationship to be evaluated against a reference treatment.
Phase IV	This phase incorporates tests performed after the MA. It is carried out on a very large number of patients. Its objective is to fine-tune the understanding of the drug and its adverse effects, to adapt the optimum dosage for particular cases and finally to evaluate the treatment strategy.
Sponsor	Natural person or legal entity that assumes leadership of a clinical trial and is responsible for its launch and management.
Protocol	Document describing the trial's rationale, goals, methodology and statistical methods and which specifies the terms and conditions under which the trial must be conducted and managed.
Benefit/risk ratio	The ratio between a drug's expected benefits and its possible risks.
Biomedical research	Trial or experiment conceived for and conducted on human subjects with a view to developing biological or medical knowledge.
Immune response monitoring	The set of techniques used to monitor the induction and kinetics of the immune response. In the case of immunotherapy, the monitoring of T responses (via the T lymphocytes) is especially pertinent.
SO	Stock Option – Option to subscribe to shares or option to purchase shares.
Traceability	All the information and measures taken to monitor and rapidly retrace each stage of a process.
Validation	The establishment of proof that the implementation or use of any process, procedure, equipment, raw material, activity, or system actually enables the realization of planned outcomes and set specifications.

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