

A société anonyme (French corporation) with capital of €13,704,097 Registered Office: 49, boulevard du Général Martial Valin – 75015 Paris 410 910 095 Trade & Companies Register of Paris

# 2018 REGISTRATION DOCUMENT

# INCLUDING THE ANNUAL FINANCIAL REPORT AND THE MANAGEMENT REPORT



This document was submitted to the *Autorité des marchés financiers* (AMF) on April 5, 2019 in accordance with Article 212-13 of its General Regulation. 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 from Onxeo's registered office located at 49, boulevard du général Martial Valin – 75015 Paris, and from the Onxeo website: <a href="www.onxeo.com">www.onxeo.com</a> and from 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 2018", dated 5 April, 2019.

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#### Note

In this registration document and unless indicated otherwise:

- The term "Reference document" means this registration document;
  - The terms "Company" or "Onxeo" mean Onxeo whose registered office is 49, boulevard du Général Martial Valin, 75015 Paris, France, listed on the Paris Trade & Companies Register under number 410 910 095;
  - The term "Group" means the group of companies comprised of the Company and its subsidiaries.

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

#### Disclaimer

#### <u>Information on the market and competition</u>

The Registration Document contains, particularly in Chapter 2 "Activities of the Company in 2018", information on the Group's markets and its competitor situation. Such information is taken in particular from studies carried out by external sources. Publicly available information, which the Company considers reliable, has not been checked by an independent expert and the Company cannot guarantee that a third party using different methods to compile, analyze or calculate data on the markets would obtain the same results.

#### Forward-looking statements

The Reference document contains forward-looking statements concerning the outlook and development strategy of the Group. Such forward-looking statements are identified by the use of the future or conditional tenses or by forward-looking terminology, such as "consider", "envisage", "think", "have the objective of", "in expectation of", "understand", "should", "aim", "estimate", "believe", "hope", "may", "promising", "encouraging", "interesting" or the negative form of these terms, or any other variations or similar terminology. Such information is not historical data and should not be interpreted as a guarantee that the facts or data will occur. Such information is based on data, assumptions and estimates considered reasonable by the Company. It is liable to change or to be altered due to uncertainties surrounding the economic, financial, competitive and regulatory environment. Such information is mentioned in various sections of this Registration Document and contains data relating to the Group's intentions, estimates and objectives, particularly those concerning the market in which it operates and its strategy, growth, results, financial position, cash flow and forecasts. The forward-looking statements contained in the Registration Document are current as of the date of the Registration Document. The Group operates in an environment that is competitive and constantly changing. The Group therefore cannot anticipate all risks, uncertainties or other factors that may affect its activity, their potential impact on its activity, or even the extent to which the appearance of a risk or combination of risks may lead to results significantly different from those mentioned in the forward-looking statements, bearing in mind that no forward-looking statement constitutes a guarantee of actual performance.

# Risk factors

Investors are invited to pay special attention to the risk factors described in Section 5.7.1.4 "Risk factors" of this Registration Document before making any investment decision. Should any or all of these risks materialize, they may have a negative impact on the Group's activity, financial position, profits or outlook. In addition, other risks that are neither identified nor considered material by the Company on the date of the Registration Document could also have a significant adverse impact.



# KEY INFORMATION ON THE GROUP

# 1.1 PROFILE AND STRATEGY

Onxeo is a French clinical trial biotechnology company that develops new drugs aimed at fighting cancer by targeting the functions of tumor DNA using the only mechanisms of their kind in the heavily researched field of DNA Damage Response (DDR).

The Company focuses on developing innovative or disruptive compounds from the preclinical research (called translational) up to clinical concept tests in humans, which represents its know-how and its area of expertise.

It thus conducts its programs up to the most value-creating and attractive inflection points for potential partners.

Onxeo is listed on both the Euronext Paris and Nasdaq Copenhagen exchanges.

The Company's portfolio includes:

- AsiDNA™, a first-in-class inhibitor of the repair of breaks in tumor DNA, which is based on a unique agonist decoy mechanism. AsiDNA™ was already successfully evaluated in a phase 1 trial in metastatic melanoma by local administration and is currently undergoing clinical development for treating other solid tumors by systemic administration (IV).
- platON™, the Onxeo decoy oligonucleotides platform. The purpose of PlatON™ is to extend the Company's pipeline by generating new compounds based on this same unique decoy action mechanism and by taking advantage of the expertise which the Company has developed on oligonucleotides.
- Belinostat, a HDAC (epigenetic) inhibitor that already has conditional approval by the FDA for the 2<sup>nd</sup> line treatment of patients suffering from peripheral T-cell lymphoma and is sold in the United States in this indication under the name of Beleodag®.

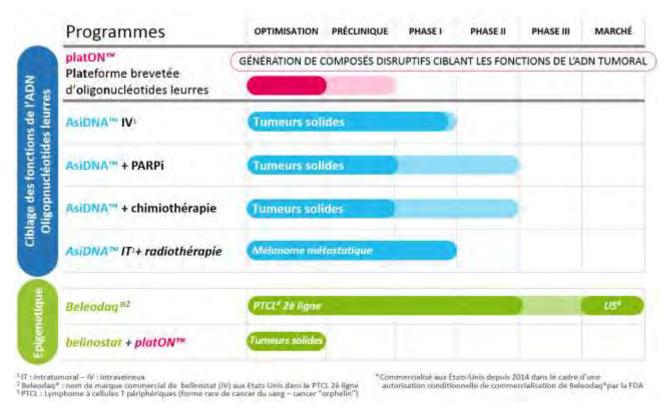
This portfolio, through innovative, high scientific value treatment approaches, makes Onxeo a key player in one of the most important fields in oncology.

To implement its growth strategy, the Group has strong assets and distinctive expertise that form the foundation for its future growth:

- A unique biotechnology company profile with a portfolio composed of products developed from particularly promising technologies. Used alone or combined with other anti-cancer treatments, these programs offer development outlooks on different indications which offer great market potential in oncology.
- A highly skilled team of scientists and doctors, which has repeatedly been able to lead programs in Europe and the United States through to the approval stage; This team is headed up by a management team and a board of directors with a high profile and international experience.
- Cutting-edge translational know-how and experience in clinical trials conducted in Europe and the United States, collaborations with international level academic and scientific opinion leaders and international business partners.

The pipeline is detailed in the graph below:





Detailed information on each product can be found in paragraph 4.2.1 of this Registration Document.

# 1.2 MANAGEMENT AND SUPERVISORY BODIES

# 1.2.1 BOARD OF DIRECTORS

Chairman of the Board of Directors and independent director: Joseph Zakrzewski

Chief Executive Officer:
Judith Greciet

Independent directors:
Danièle Guyot-Caparros
Thomas Hofstaetter
Jean-Pierre Kinet
Jean-Pierre Bizzari
Christine Garnier
Elvira Sanz Urgoiti

Director representing the shareholders: Financière de la Montagne SARL, represented by Nicolas Trebouta



#### 1.2.2 MANAGEMENT COMMITTEES

#### **Executive Committee**

Chaired by Ms. Judith Greciet, Chief Executive Officer, the Executive Committee determines the Company's strategy, the direction and the growth scenarios in collaboration with the Board of Directors. It defines the allocations of resources and means which are able to implement those decisions. In this context it systematically reviews the development plans of the R&D programs as well as their progress and implements any necessary trade-offs based on the recommendations on the operational committee (see below). Finally, it 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.

#### **Operational Committee**

Composed of the operational R&D departments and the project coordinators, in addition to *ad hoc* project teams, it sets the operating strategy, systematically reviews and validates progress of projects, and coordinates the teams. It validates any operational decisions having an impact on the projects and shares its recommendations with the Executive Committee on strategic decisions. Special attention is paid to achieving objectives, quality and development timetables. The Operational Committee meets once a week.

# **Risk 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 sur Seine

Represented by Mr. Samuel Clochard, member of the Versailles Institute of Statutory Auditors.

#### **Ernst & Young Audit**

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

Represented by Mr. Frank Sebag, member of the Versailles Institute of Statutory Auditors.



# 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 December 31, 2017 and December 31, 2018.

The key figures presented below are commented on in Chapter 3 and should be read in conjunction with Chapter 6 of the Registration Document.

Consolidated financial statements (IFRS standards) In € thousands	12/31/2018	12/31/2017
Revenue, of which	6,127	9,505
Recurring revenue	2,310	3,042
Non-recurring revenue	3,817	6,463
Operating expenses, of which	(9,654)	(28,694)
Research and development costs	(7,585)	(18,857)
Research tax credit	2,454	3,699
Other operating expenses	(4,523)	(13,536)
Operating profit (loss) before non-recurring items	(3,527)	(19,189)
Non-recurring operating profit (loss), of which	(12,117)	(47,188)
Impairment of R&D assets relating to Beleodaq®	(8,550)	(38,111)
Financial profit (loss)	(691)	(491)
Tax expenses	1,760	7,797
Net profit (loss)	(9,399)	(59,071)
Free Cash Flow	11,253	14,277



# COMPANY ACTIVITY IN 2018

# 2.1 2018 HIGHLIGHTS

# 2.1.1 GROUP COMPANIES

On 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
- Topotarget UK
- BioAlliance Pharma Switzerland
- Topotarget Switzerland
- SpeBio B.V. (subsidiary 50%-owned with SpePharm)





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

During the financial year, the Company actively continued the development of its key assets, in particular AsiDNA™, its first-in-class tumor DNA damage response inhibitor, which has enabled a phase 1 study to be carried out on AsiDNA™ in different doses in France and Belgium as a systemic single therapy. Initial conclusive activity and tolerance results were obtained in November 2018, allowing the Company to start on the clinical development, particularly in association with other anti-cancerous agents.

In parallel, the works to optimize new compounds from platON™, the Company's proprietary decoy oligonucleotides' platform, have allowed it to identify several candidates, the first of which will start the regulatory preclinical phase in the first half of 2019.

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

# 2.1.2.1 *R&D Programs*

# 2.1.2.1.1 AsiDNA™

AsiDNA™ is a *first-in class* product which interferes with the repair of tumor DNA through an agonist decoy mechanism. It is composed of 64 nucleotides (fragment of DNA) constituted of two strands of 32 nucleotides, of complementary and specific sequence.

AsiDNA™ is protected internationally by several patent families covering the chemical composition of the product, its method of use or of administration as well as some associations with other anti-cancer products. The patents protect all the analogue compounds of between 40 and 400 nucleotides, irrespective of their sequence, in addition to the associated pharmaceutical compositions and the related methods for treating cancer. They give Onxeo a very wide field of protection in this class of compounds.

The main patent will expire mid-2031 and may be extended until 2036 via the different supplemental protection systems prevailing in the United States and in Europe. The latest patents on methods of use or associations will be valid until 2036, before an extension period.

In 2018, the Group actively pursued the preclinical and clinical development of this candidate as a systemic single therapy and in combination with other treatments in various types of solid tumors, achieving several key milestones:

#### **Intellectual Property**

In January 2018, Onxeo received a notification from the European Patent Office (EPO) informing the Company of its intent to grant a new patent covering AsiDNA™ in all member states of the European Union (EU), considerably strengthening the Company's intellectual property portfolio around the AsiDNA™ program. It protects the various compounds and pharmaceutical formulations as well as their therapeutic uses, particularly in the treatment of cancers, both alone and in combination with other agents that target tumor DNA (e.g. radiotherapy, chemotherapy or other agents that damage tumor DNA).

In December 2018, Onxeo received a notification indicating the EPO's intent to grant a new patent protecting the combination of AsiDNA™ with any PARP inhibitor. This combination patent will protect AsiDNA™ in Europe until 2036, before potential extension periods.

# At the preclinical level

- In April 2018, the Company presented at the AACR (American Association for Cancer Research) meeting two preclinical studies that show the unique approach AsiDNA™ has in inhibiting the repair of tumor DNA by activating the enzymes involved in DNA damage signaling and distracting them from their target.

The results of a study into repeated, long-term administration of AsiDNA™ showed an increase in tumor cells' sensitivity to the treatment. The lines of tumor cells tested became more sensitive to AsiDNA™, with no resistance appearing following repeated treatments. The repeated treatments likewise had no impact on healthy cells. This self-sensitization during treatment represents a never-before-observed phenomenon in anti-cancer treatments (which eventually all lead to resistance). Thanks to this unique property, AsiDNA™



could be used in maintenance therapy to prevent the development of acquired resistance during treatment. Onxeo has filed a patent request claiming priority for the use of  $AsiDNA^{TM}$  as a maintenance treatment on the basis of this recently identified property.

In July 2018, Onxeo announced new preclinical results for AsiDNA™ that showed a strong synergy when
administered in combination with PARP inhibitors and a reversion of tumor resistance associated with the
use of PARP inhibitors.

The data shows that, in *in vitro* triple negative breast cancer (TNBC) and small cell lung cancer (SCLC) models, AsiDNA™ maintains the expression of PARP1, the repair enzyme inhibited by PARP inhibitors, and prevents resistance to PARP inhibitors from emerging. When in the presence of a PARP inhibitor, the cell adapts and reduces expression of the PARP enzyme, this constituting one of the resistance mechanisms to PARP inhibitors. Insofar as AsiDNA™ hyperactivates repair enzymes, it creates a positive regulation of the expression of PARP. When combined with a PARP inhibitor, AsiDNA™ could therefore maintain sensitivity to treatment by counteracting the natural resistance mechanism. In vivo, this synergy was found between olaparib and AsiDNA™, with a complete response rate more than doubled compared with the rate observed with olaparib alone in a triple negative breast cancer model known as HR+, which is naturally resistant to PARP inhibitors. Strong inhibition of tumor growth was also found in a mouse xenograft model of olaparibresistant human ovarian cancer tumor cells. Patient-derived xenograft (PDX) models are considered to be strong predictors of clinical behavior.

The trial on the combination of AsiDNA™ with PARP inhibitors is particularly relevant for the Company as their action mechanisms are highly complementary and they target indications where unmet medical needs are still important. Other combinations are also being studied, particularly with chemotherapy which, when used in combination with AsiDNA™, is showing highly conclusive results. All this data is key to preparing for future clinical protocols once the active doses and the tolerance profile of AsiDNA™ are validated in the clinics.



#### At the clinical level

- In April 2018, the Company announced the launch of DRIIV (DNA Repair Inhibitor administered IntraVenously), a phase 1 clinical trial of AsiDNA™ in advanced solid tumors and first-patient treatment. The purpose of this trial is to assess AsiDNA™ tolerance and the optimum dose, as well as to determine its active dose at the level of the tumor in patients with advanced solid cancer and where AsiDNA™ is administered intravenously. The DRIIV trial is being carried out at three of the most prestigious centers in France and Belgium with the initial interim results expected in the second half of 2018.
- In November 2018, the Company, on schedule, announced the positive interim results of the first three doses out of six tested in this study. These positive results show that, from the second dose, AsiDNA™ results in sustained engagement of its biological targets in patients' tumor cells, confirming the activity of AsiDNA™ when administered intravenously. In addition, the quantification of the Ki67 biomarker, which reflects tumor proliferation, shows a net reduction in the rate of tumor proliferation in three patients and stabilization in one patient. Finally, a favorable safety profile was observed, with no serious adverse drug-related events nor any dose-limiting toxicity at these first three doses. Based on this data, and in particular the determination of active doses, the Company intends to extend the AsiDNA™ clinical program in association with the targeted indications from the first half of 2019.

Whether as a monotherapy or in combination, AsiDNA™ shows highly significant potential, with a particularly broad range of indications. The Group wishes to add value to AsiDNA™ through partnerships in order to generate numerous growth and value catalysts for the Company and its shareholders.

#### 2.1.2.1.2 platON™

AsiDNA™ is the first compound sourced from platON™, Onxeo's patented platform of oligonucleotides.

PlatON™ is a chemistry platform that allows new molecules to be constructed by modifying three compounds: the oligonucleotide (a double-strand fragment of DNA), a link between the two strands to ensure the fragment's stability and a vector, the purpose of which is to encourage cellular penetration (a cholesterol molecule in the case of AsiDNA™).

With platON™, Onxeo has the means by which to enrich its portfolio with highly innovative drug candidates while at the same time harvesting the expertise and knowledge it has gained over several years in the field of oligonucleotides and DNA repair mechanisms.

The Group is convinced of the major therapeutic potential of its decoy oligonucleotide technology, particularly by interfering with the tumor DNA repair signals, and of the disruptive innovation it represents, which could open up the way to a new cancer treatment paradigm.

Throughout 2018, the Company has continued to select and optimize several highly innovative compounds and is aiming to enter the preclinical phase with the most promising compound in the first half of 2019.

# 2.1.2.1.3 Beleodag® (intravenously administered Belinostat)

Belinostat is a histone deacetylase inhibitor (HDACi). Belinostat, in its injectable form, has been marketed in the US since 2014 under the name Beleodaq® as part of a conditional approval by the FDA for use in the 2<sup>nd</sup>-line treatment of patients with peripheral T cell lymphoma.

In April 2018, a preclinical study was presented to the annual meeting of the AACR (American Association for Cancer Research), which brought to light an anti-tumor activity synergy brought about by the combination of AsiDNA™ with belinostat in several tumor models. In the course of exploring the best possible combinations with AsiDNA™, it appears that the combination of Beleodaq® with other platON™-derived compounds would likely be the most relevant from a clinical perspective.



# 2.1.2.2 Other products dedicated to partnerships

Continuing with its strategic repositioning on the development of highly differentiated products in oncology, in 2017, the Company sold the products Sitavig® and Loramyc® to Vectans Pharma and granted a global license for Validive® to Monopar Therapeutics Inc.

The agreement to sell Sitavig® and Loramyc® to Vectans Pharma, entered into in July 2017, provided for an initial payment of €4 million in addition to a profit-sharing clause concerning future sales, based on the cumulated commercial performance of the two products worldwide. Furthermore, in 2018 Onxeo collected and will continue to collect over the next two years, from its existing partners at the time of the sale, certain payments relating to pre-defined or regulatory milestones or else to sales performances.

In the context of the global Validive® license granted to Monopar Therapeutics Inc. in September 2017, Onxeo received immediate payment of a licensing right of \$1.0M. It is also due to receive subsequent milestone payments which could reach \$108M subject to achieving the agreed milestones, particularly payments relating to regulatory milestones, from phase III to registration, for \$15.5M. The agreement also provides for the payment of increasing royalties on sales, which could experience double-digit percentage growth.

#### 2.1.3 FINANCING

In June 2018, the Company announced two financing operations:

- Firstly, Onxeo signed a royalty agreement with SWK Holdings Corporation, a US company specialized in financing in the life sciences sector. According to the terms of the agreement, Onxeo issued bonds in an amount of \$7.5 million, fully subscribed by SWK Holdings Corporation. The terms for repaying the bonds will allow the latter to directly receive the royalties and milestone payments on the sales stemming from the marketing of Beleodaq® (belinostat) by Spectrum Pharmaceuticals, Inc. for an amount of \$13.5 million. The remaining details of the transaction have not been disclosed.
- On the other hand, on June 15, 2018, the Company set up an equity line of credit, including an incentive plan, by issuing new shares over a period of 10 months, for a maximum amount of €5.4 million together with the company Nice & Green. In accordance with the terms of the agreement, Nice & Green, in its capacity as a specialized investor, this investment not intended to be a permanent stake in the Company's capital, has undertaken, for a 10-month period, to subscribe for and exercise each month, on Onxeo's initiative, share warrants corresponding to minimum monthly financing of €500,000 up to a limit of 4,700,000 shares over the term of the contract. The shares will be issued on the basis of the average share price weighted by volumes over the first three trading days prior to each issue, less a maximum discount of 5.0%. In the event that this line of credit is used up in full¹, any shareholder that held 1.00% of Onxeo's capital before it was set up would see its holding drop to 0.92% of the capital². Onxeo retains the option of suspending drawdowns or of terminating this agreement at any time.

Nice & Green and Onxeo have also agreed on an incentive plan that consists of the allocation in cash, to the Company, of a share of any added value realized by Nice & Green through the sale of shares resulting from the exercise of the warrants.

# 2.1.4 GOVERNANCE

On May 16, 2018, the Ordinary General Shareholders' Meeting renewed Mr. Thomas Hofstaetter's term of office as a director for 3 years. Mr. Hofstaetter is also Chairman of Onxeo's Remunerations Committee and Scientific and Business Development Committee.

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<sup>&</sup>lt;sup>1</sup> In this case, 4,700,000 new shares would be issued.

<sup>&</sup>lt;sup>2</sup> On the basis of the 50,695,653 shares comprised in Onxeo's capital at December 31, 2017.



#### 2.1.5 DISPUTE

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®.

In a partial arbitral award 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. Onxeo then had summons served on SpeBio for contractual liability before the Commercial Court. Onxeo then lodged a forcible joinder with the Commercial Court to add SpePharm as a co-defendant on criminal grounds, and, by a ruling dated May 3, 2016, the Paris Commercial Court granted Onxeo's forcible joinder adding SpePharm as a co-defendant and consolidating the Onxeo v. SpeBio and Onxeo v. SpePharm proceedings. In a counterclaim, SpeBio and SpePharm filed claims for damages.

On October 17, 2017, the Paris Commercial Court handed down a judgment ordering Onxeo to pay to SpeBio the sum of €8.6 million for costs sustained prior to the termination with interest at the statutory rate from June 30, 2014 with compound interest (in addition to €250,000 on the basis of Article 700 of the French Code of Civil Procedure) and to SpePharm the sum of €50,000 in damages (in addition to €15,000 on the basis of Article 700 of the French Code of Civil Procedure). This judgment was handed down along with provisional enforcement and, as a result, a total amount of €9.2 million was paid by Onxeo at the start of 2018. It should be noted that SpeBio is 50% owned by Onxeo and SpePharm jointly.

On October 20, 2017, Onxeo lodged an appeal against this ruling and lodged its submissions with the Court of Appeal of Paris on January 9, 2018, in order to ensure that the appeal proceedings are dealt with promptly in the interest of its shareholders. In December 2018, the Court of Appeal handed down a decision ordering Onxeo to pay SpeBio the additional sum of around €2.8 million as compensation for the damage suffered in terms of expenses incurred and loss of opportunity. The Court did, however, overturn the order that required Onxeo to pay €50,000 to SpePharm BV in damages. The Company paid the amount of €2.8 million at the start of 2019.

It should be recalled that the initial proceedings before the Court of Arbitration of the International Chamber of Commerce (ICC) have been suspended whilst awaiting the decision of the Commercial Court and the French Court of Appeal. These proceedings will therefore resume and Onxeo will do its utmost to obtain damages from SpePharm.



# 2.1.6 TIMELINE SUMMARY OF SIGNIFICANT EVENTS IN FISCAL 2018

Summarized below are the events which were reported in a press release on the Company's initiative during fiscal 2018:

January 23	Onxeo provides update on litigation with SpeBio/SpePharm
January 25	Onxeo receives EPO Intent-to-Grant Notice for key AsiDNA™ patent
March 14	Onxeo provides financial update
March 15	Onxeo to present results of two studies highlighting potential of AsiDNA™ as anti-cancer treatment at 2018 AACR Annual Meeting
March 29	Onxeo reports Full-Year 2017 financial results and provides business update
April 9	Onxeo to present corporate overview at the H.C. Wainwright Annual Global Life Sciences Conference.
April 24	Onxeo announces initiation of DRIIV Phase 1 Clinical Trial of AsiDNA™ for treatment of advanced solid tumors
May 16	Ordinary General Meeting of May 16, 2018 and deferment of the Extraordinary General Meeting on Second Notice to June 19, 2018.
May 16	Onxeo provides business update and reports First Quarter 2018 Financial Information
May 23	Onxeo to present at BIO International Convention in Boston
June 7	Onxeo secures \$7.5 Million of non-dilutive capital from SWK Holdings Corporation through sale of rights related to future Beleodaq® royalties
June 15	Onxeo implements an equity line of credit including an incentive plan with Nice & Green
July 12	New preclinical results on Onxeo's AsiDNA™, first-in-class DNA repair inhibitor, point to strong synergy and reversion of tumor resistance when combined to PARP inhibitors
July 27	Onxeo reports Half-Year 2018 financial results and provides business outlook
October 3	Onxeo to present at the 11th Edition of the "Rencontres de la Cancérologie Française" Oncology Conference
October 18	Onxeo to present overview of AsiDNA™ for treatment of solid tumors at DNA Damage Response Therapeutics Summit 2019
November 5	Onxeo announces positive interim results from Phase 1 Study of AsiDNA™, a first-Inclass DNA Damage Response Inhibitor
December 13	Onxeo reports decision from the Paris Court of Appeal in the lawsuit against SpeBio/SpePharm
December 20	Onxeo receives EPO Intent-to-Grant Notice for new patent protecting AsiDNA™ in combination with any PARP inhibitor

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



# 2.2 SIGNIFICANT POST-BALANCE SHEET EVENTS SINCE END OF 2018

On January 3, 2019, the Company announced the identification of predictive biomarkers for AsiDNA™, its first-in-class DNA damage response (DDR) inhibitor, enabling the Company to consider customized medicine approaches in both single therapy and in combination. A signature for AsiDNA™ sensitivity was established with the aid of bioinformatic analyses stemming from transcriptomic experiments. This signature was then validated *in vitro* on several cellular lines. Finally, genes that showed an expression profile correlating strongly with sensitivity to AsiDNA™ were analyzed. These studies showed that sensitivity to AsiDNA™ correlates to the level of expression of the DNA repair genes in the tumor, also identifying several genes in which the expression level correlated most strongly to AsiDNA™. As a result, the analysis of these genes may be used to select those patients with the greatest sensitivity to treatment and, therefore, the greatest probability of responding in the forthcoming clinical trials.

On February 13, 2019, the Company announced the presentation of the results of five preclinical studies showing the differentiated profile of AsiDNA™, the first-in-class DNA damage response inhibitor, strengthening its clinical potential and demonstrating its unique action mechanism, during the next AACR (American Association for Cancer Research) Annual Meeting, which will be held from March 29 to April 3, 2019 in Atlanta (Georgia), United States.

On March 1, 2019, Spectrum Pharmaceuticals (SPPI) announced the completion of the sale of its seven hematology/oncology products approved by the FDA, including Beleodaq®, to Acrotech Biopharma LLC. Based on the information provided to date by Spectrum, the Company does not foresee any significant impact of this transaction on the activities and results of Beleodaq® for Onxeo.

# 2.3 FORESEEABLE DEVELOPMENTS AND FUTURE PROSPECTS

The Company will continue its value creation strategy based on developing innovative therapeutics for severe or rare cancers, and is planning on the following major catalysts for growth in 2019:

- AsiDNA™: finalization of the DRIIV-1 study and publications during international scientific congresses; initiation of a new AsiDNA™ phase 1b/2 clinical study of AsiDNA™ in combination with chemotherapy and/or PARP inhibitors in order to demonstrate the synergy and efficacy of the combination in humans, with preliminary results expected before the end of 2019; based on resources and the progress of the programs, the Company could also begin a clinical study in combination with a PARP inhibitor, the second particularly promising combination for AsiDNA™. The Company also intends to begin academic collaborations in order to accelerate the development of the vast potential of AsiDNA™, both on its own and in combination. In particular, it potentially intends to file a clinical trial authorization request in the United States (IND) in the second half of the year in order to begin development on the American continent.
- platON™: selection and start of preclinical phase of a new, highly innovative molecule in the first half of 2019; proof of preclinical concept expected as of 2019.

Onxeo considers that, in light of its current activities, it has no specific comments to make on trends that might affect its revenue and its general operating conditions from the date of the last financial year ending December 31, 2018, up to the publication date of this Registration Document.

The Company's main investments will focus on research and development. The cash flow amounts to €11,253K at December 31, 2018.

To guarantee sufficient financial resources to support the Company's activities after the critical stages expected in the next 12 months and to obtain financial visibility up to the 2nd quarter of 2020, the Company has decided to negotiate an extension of the equity line of credit in place with Nice & Green. Details of this financing will be reported when the transaction is launched.

The Company is also looking into the opportunity of consolidating its financial resources through new, non-dilutive financing or fundraising, together with the continued search for new licensing agreements.



# RESULTS AND FINANCING

# Financial background

Information describing the change in the financial situation and the result of transactions made during the financial years corresponding to historical financial data is included by reference in this Registration Document:

- Chapter 3, 'Results and financing', on pages 32 to 39 of the 2017 Registration Document filed with the AMF on April 25, 2018 under number D.18-0389.
- Chapter 3, 'Results and financing', on pages 30 to 35 of the 2016 Registration Document filed with the AMF on April 24, 2017 under number D.17-0423.

This chapter has been extracted from the Management Report approved by the Board of Directors on March 12, 2019. The data it contains should be read in conjunction with the information presented in Chapter 6 of the Registration Document.

# 3.1 RESULTS

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

The Company's annual financial statements have been prepared in accordance with the presentation rules and evaluation methods provided by the regulations in force.

# 3.1.1.1 Review of the financial statements and results

For the financial year ended December 31, 2018, the Company made revenue of €549K compared to €895K for the financial year ended December 31, 2017. This revenue corresponds mainly to sales of products as part of a managed access program – also known as the named patient program – for Beleodaq®.

Other income totaled €5,186K, compared with the €8,393K recorded for 2017. This decrease is mainly due to the recording, in 2017, of the partial sale of goodwill to Vectans Pharma for an amount of €4 million, this corresponding to two of the Company's historical products. Other income includes the royalties calculated on sales made by licensing partners for €1,508K, the proportionate share of payments received on the signing of partnership agreements spread over time in the amount of €616K and other contractual payments within the framework of the licensing agreements in place for an amount of €2,720K.

Operating costs of the financial year amount to €16,463K, compared with €31,918K for the financial year 2017. This significant fall is mainly due to the reduction in R&D expenditure, which fell from €19,677K in 2017 to €7,539K in 2018 as a result of the conclusion of the phase III ReLive study in September 2017 and the workforce reduction plan implemented at the end of 2017. The level of R&D expenditure in 2018 once again demonstrates Onxeo's new profile, as the company is now committed to development at earlier stages of the AsiDNA™ and platON™ programs. Other operating expenses amounted to €8,924K, down from €12,241K in 2017, this change reflecting a continuous cost-controlling policy.

Operating income showed a loss of €(7,800)K, compared with a loss of €(21,611)K for the financial year 2017.

Financial income recorded a loss of €(395)K, compared with a loss of €(638)K in the financial year 2017. This loss mainly comes from the interest charge of €588K linked to the debenture loan put in place in June 2018 with SWK Holdings.

There is a pre-tax loss of €(8,195)K, compared with a loss of €(22,249)K in the financial year 2017.

Net extraordinary items showed a loss of €(7,197K), mainly comprising the impairment of R&D assets related to Beleodaq® in the amount of €7,783K, and in the amount of the order issued in the appeal in the context of the dispute with the companies SpeBio and SpePharm amounting to €2,868K, which was partly offset by the recognition in operating profit of the advance paid by Bpifrance for the Livatag® program as part of the NICE consortium for an amount of €4,037Kfollowing acknowledgement of said program's commercial failure.

The Company recognized a €2,436K research tax credit in the financial year 2018.



As a result of these various revenue and expense items, the net P&L for the period showed a loss of €12,955K against a loss of €66,425K in 2017.

# 3.1.1.2 Allocation of results

We propose that the General Meeting of April 26, 2019 allocate the loss for the year 2018 amounting to €12,955,413 to the 'losses carried forward' account, which will thus increase from €0 to €12,955,413.

In accordance with the provisions of Article 243 *bis* of the French General Tax Code, we remind you that no dividend was distributed in the last three financial years.

# 3.1.1.3 Non-deductible expenses

In accordance with the provisions of Article 223 *quater* 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 223 *quinquies* of the French General Tax Code which are not listed in the special statement have been noted.

# 3.1.1.4 Financial Summary

A table showing the Company's results for the last five financial years is presented in section 6.3 of the Registration Document, in accordance with Article R. 225-102 (2) of the French Commercial Code.

# 3.1.1.5 Equity investments and controlling interests at year-end

In accordance with the provisions of Article L. 233-6 of the French Commercial Code, we inform you that in the financial year 2018, 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 terms for the Company's suppliers for the financial year ended December 31, 2018.



# Invoices issued and received by the closing date of the fiscal year for which the payment deadline has passed

	Article D.4		es received by	_		al year for	Article D.441 I-2°: Invoices issued by the closing date of the fiscal year for which the payment deadline has passed					
	0 days	1 to 30 days	31 to 60 days	61 to 90 days	91 days and over	Total (1 day and over)	0 days	1 to 30 days	31 to 60 days	61 to 90 days	91 days and over	Total (1 day and over)
(A) Late payment tr	anches	<u> </u>	,	<u>,                                     </u>		,		'	,	,	1	,
Number of invoices concerned	1,432					1,351	8					19
Total amount of the invoices concerned, excl. tax	7,226,147	5,825,391	1,195,645	51,066	200,242	7,272,344	713,247	472,325	114,930	54,600	9,108	650,963
Percentage of the total amount of purchases for the year, excl. tax	49.8%	40.2%	8.2%	0.4%	1.4%	50.2%						
Percentage of the year's revenue, excl. tax							52.3%	34.6%	8.4%	4.0%	0.7%	47.7%
Number of excluded invoices									7	4		
Total amount of excluded invoices									352,9	69.58		
(C) Reference paym	ent deadline us	ed (contractu	al or legal dea	dline—Article	L. 441-6 or A	rticle L. 443-1 c	f the French Co	mmercial Cod	le)			
Payment terms used to calculate late payments	Contractual deadline. This						Contractual deadlines: Each invoice issued is followed with its own contractual deadline. This deadline is 30 days end of month for sales of goods and 45 to 60 days for other services depending on the contract.					



# Invoices received and issued having late payments during the fiscal year

	Artic	e D.441 I-1: inv	oices <u>received</u>	d but paid late	e in the financ	ial year	Article D.441 I-2: invoices issued but paid late in the financial year					
	0 days	1 to 30 days	31 to 60	61 to 90	91 days	Total (1 day	0 days	1 to 30	31 to 60	61 to 90	91 days	Total (1 day
			days	days	and over	and over)		days	days	days	and over	and over)
(A) Late payment tra	anches											
Number of												
invoices	1,432			<		1,351	8					19
concerned												
Total amount of												
the invoices	7,226,147	5,825,391	1,195,645	51,066	200,242	7,272,344	713,247	472,325	114,930	54,600	9,108	650,963
concerned, excl.	, -,	-,,	,,-	,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	,	, ,-	-,	,	,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	, , , ,	,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,
tax												
Percentage of the												
total amount of	49.8%	40.2%	8.2%	0.4%	1.40/	50.2%						
invoices received	49.8%	40.2%	8.2%	0.4%	1.4%	50.2%						
in the year, excl. tax												
Percentage of the								I			T	
total amount of												
invoices issued in							52.3%	34.6%	8.4%	4.0%	0.7%	47.7%
the year, excl. tax												
, ,									1	1		
Number of												
excluded invoices												
Total amount of												
excluded invoices												
(C) Reference paym	ent deadline ι	used (contractu	al or legal dea	dline—Articl	e L. 441-6 or A	rticle L. 443-1 o	f the French Co	mmercial Cod	le)			
Payment terms												
used to calculate	■ Contractu	al deadlines: Ea	ich invoice is f	ollowed with	its own contr	actual	Contractual deadlines: Each invoice issued is followed with its own contractual					
late payments		is deadline usu					deadline. This deadline is 30 days end of month for sales of goods and 45 to 60 days for other services depending on the contract.					nd 45 to 60



# 3.1.1.7 Amount of loans with term of less than two years granted by the Company

Art. L. 511-6, 3 *bis* para. 2 and R. 511-2-1-1 and R. 511-2-1-2 of the French Monetary and Financial Code None.

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

The Onxeo Group's consolidated financial statements, which we submit for your approval, have been prepared in accordance with the International Financial Reporting Standards (IFRS).

The consolidated financial statements posted revenue of €6,127K, compared with €9,505K in 2017. This change comes mainly from the impact of the sale of the historical products, Loramyc® and Sitavig® to Vectans Pharma for €4 million, which was recorded as non-recurring revenue in 2017. Recurring revenue amounts to €2,310K and represents revenue from sales by the partner Spectrum Pharmaceuticals in the US, as well as sales in the context of the managed access program implemented in Europe. The decrease in recurring revenue compared to the €3,041K recorded in 2017 is a direct result of the sale of the aforementioned historical products. Operational charges amounted to €9,654K, compared with €28,694K in 2017, as a result of decreased R&D expenses following the conclusion of the phase 3 ReLive study in September 2017, the workforce reduction plan implemented at the end of 2017 and, more generally speaking, strict control of all expenses. Other non-current operating income and expense amounted to €12,117K, essentially consisting of the impairment of R&D assets related to Beleodag® in the amount of €8,550K and for the amount of the order issued by the Paris Court of Appeal in the appeal in the context of the dispute with the companies SpeBio and SpePharm, this amounting to €2,868K. Net financial income showed a loss of €691K. As a result of the impairment of the Beleodag®-related R & D assets, subject to Danish tax, the Group reduced the amount of its deferred tax liability, leading to the recording of tax income of €1,764K. After taking into account these various income and expense items, net result was a loss of €9,399K, compared with a loss of €59,071K recorded for the previous financial year.

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

- Onxeo is the main contributor, with revenue of €5,734K. The Company covered all research and development expenditures as well as overhead costs, generating a consolidated loss of €14,338K.
- The contribution of the subsidiary Topotarget UK, which, as the holder of certain patents, receives a
  proportionate share of Beleodaq® income, recorded a loss of €715K, mainly related to the impact of the
  impairment of Beleodaq®-related R & D assets.
- The contribution of the Swiss subsidiary Topotarget Switzerland, which holds certain licensed assets, is a profit of €945K, taking into account the income recorded on these assets over the course of the financial year 2018.
- SpeBio's positive contribution of €5,176K due to penalties paid by Onxeo as part of the dispute with this subsidiary.
- The Group's other subsidiaries had limited activity and their contribution to consolidated income was a loss of €433K, essentially representing the operating costs of the US subsidiary Onxeo US.

The impact of restating the Group's financial under IFRS was a loss of €25K, which mainly breaks down as follows:

- Income of €1,764K relating to the decrease in deferred tax liabilities resulting from the impairment of Beleodag®-related R & D assets;
- A €927K charge corresponding to the warrants and stock options as well as the bonus shares awarded during the year;
- An expense of €119K relating to the revaluation of interest on bond debt;
- An expense of €491K relating to the reclassification to reserves of deferred license income in accordance with the IFRS 15 standard.
- An expense of €315K corresponding to the valuation of the share subscription warrants as part of the ownequity line of credit with Nice & Green.



# 3.2 CASH FLOW AND FINANCING

This section should be read in conjunction with the figures set out in Chapter 6 of the Registration Document, and in particular the Consolidated Cash Flow Statement and the Consolidated Statement of Shareholders' Equity.

#### 3.2.1 THE GROUP'S FINANCIAL PROFILE

As a biotechnologies company focused on the development of innovative drugs, the Group has to finance sometimes long and expensive trials, which induces a specific financial profile with cash flow generated by the activity generally negative for several years. The innovative oncology products developed by the Group should nevertheless generate strong growth in the medium/long term and high profitability, through partnership covering the advanced stages of clinical development and the marketing phases. These partnerships with larger pharmaceutical groups could thus contribute to Onxeo payments at key stages of the development and marketing of the products.

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

The Group has cash flow amounting to €11,253K at the balance sheet date and benefits from an equity line of credit (partially used as at December 31, 2018) that will allow it to receive supplementary cash contributions in 2019. In early 2019, the Group paid the penalty of €2.8 million handed down by the Court of Appeal of Paris as part of the dispute against SpeBio and SpePharm after offsetting against the inter-companies loan of €1.5 million due by SpeBio. Since Onxeo owns 50% of SpeBio, it is entitled to receive half the distributable cash of this subsidiary, valued at approximately €5 million. Since the date of this payment is uncertain, the Group was able to secure additional financing (extension of the current own equity line of credit) allowing it to finance its activities up to Q2 2020 based on its financing plan.

The Group took on bond debt through bonds issued to the company SWK Holdings in June 2018 for an initial amount of \$7.5 million (€6.2 million, the balance of which at the end of 2018 was €5.9 million). This debt will be repaid through royalties on sales of Beleodaq® paid by the American partner Spectrum Pharmaceuticals for a total amount of \$13.5 million, including a repayment bonus of \$6 million. Onxeo also has public aid for an amount of €485K relating to the AsiDNA™ project, which will be repaid in full by 2021.

#### 3.2.3 RESEARCH AND DEVELOPMENT COSTS

Changes in spending on research and development over the last five years are presented in the table below:

R&D costs	In € thousands
2014	14,834
2015	16,350
2016	18,075
2017	18,857
2018	7,539

The level of R&D expenditure in 2018 once again demonstrates Onxeo's new profile, as the company is now committed to development at earlier stages of the AsiDNA™ and platON™ programs.

The main research and development costs related to clinical trials and industrial-scale development of medicines.

The cost of a clinical trial varies but generally remains proportional to the number of subjects involved in the trial. When the development strategy for a new product is defined, trials are initially carried out on a small number of patients before being extended to a wider patient population if there are no contra-indications.

The development of the Group's products requires ever broader trials, which therefore become ever more costly as they progress. Consequently, a product progressing through the various stages of clinical development will require an increasing amount of resources as it nears marketing. The clinical trials conducted to date, in



Europe and the United States in particular, were conducted using internal resources, through partnerships with public research institutes and also, to a great extent, through subcontracting.

The industrial development phase enables production processes developed during preclinical and clinical trials to be reproduced on a large scale, in readiness for product marketing. This phase is generally initiated only when the products have proved their efficacy. The Group relies on qualified subcontractors to make these changes of scale and, depending on agreements with such subcontractors, is likely to support specific investments.

#### 3.2.4 WORKING CAPITAL

The Group's working capital requirement is positive at December 31, 2018, in the amount of €0.3 million, compared to €7.0 million in the previous year. This change is mainly related to the surrender of a refundable advance by BPIfrance, recognized as revenue in the amount of €4 million, due to the commercial failure of the program financed (Livatag®) with no impact on cash flow, as well as a fall in trade payables in the amount of €1.8 million due to the reduction in operating costs. Changes in other debt and receivable items are offset in full.

Changes in R&D expenses and the new licensing agreements which the Group will have to sign on its products are some of the main factors which will influence the change in WCR in the coming years.

### 3.2.5 INVESTMENTS

The Group's historical main investment relates to the acquisition by merger in 2014 of Topotarget, for a total amount of €88 million (IFRS standards). This external growth policy was continued in 2016 with the finalization in the month of March of the acquisition of DNA Therapeutics, for an amount of €1.7 million. The two transactions were financed in full by the issue of new shares.

Apart from these extraordinary transactions and the R&D costs incurred by the Company, commented on above and recognized as a cost until the Group has obtained the MA, the investments are limited and will remain limited in coming years. The Group has made the strategic choice of working with external partners for all its basic research activities, for some of its development activities (clinical trials) and also for the production, storage and distribution of its products. Accordingly, the Group's activity is not highly capital-intensive, the only fixed assets being various fixtures and fittings, as well as office and laboratory equipment, IT equipment and office furniture. At December 31, 2018, total fixed assets represented a net value of €0.3 million.

In order to prevent its financial resources being too heavily tied up, 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.

Further, no investment was the object of a firm commitment from the Group.

#### 3.2.6 FINANCING

# 3.2.6.1 Funds raised - Equity contributions

Up until now, 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 €208.6M as of the end of December 2018. 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 2017, the Company successfully raised secondary funds on several occasions (capital increase with maintenance or removal of the preferential subscription right) for an additional amount of over €145 million. In June 2018, the Company put an own equity line of credit in place which generated an additional amount of €2.7 million at December 31, 2018. The capital increases from this, benefitting the Company through the conversion of the warrants/options issued, are added to this amount alongside certain partnership contracts.

# 3.2.6.2 Research tax credit



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

In the last five years, the amount declared for CIR in France and for the similar mechanism in force in Denmark changed as follows:

In € thousands	2014	2015	2016	2017	2018
CIR France	2.083	3.508	3.769	3.620	2.412
CIR Denmark		306	186	79	42
Total	2.083	3.814	3.955	3.699	2.454

In accordance with legal provisions in France and Denmark, the Company expects to receive the 2018 research tax credit reimbursement before the end of 2019.

#### 3.2.7 GRANTS AND REFUNDABLE ADVANCES

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 refundable advances mostly granted by Bpifrance. In general, the grants obtained by the Company are paid based on the state of progress of the research and development projects, on the basis of expenditure actually incurred. In this respect, the Company regularly submits to the organizations concerned financial assessments on the basis of which the various tranches of funding are paid. In the case of refundable advances, a reimbursement timetable is drawn up based on achievement of the milestones defined in the research and development programs being financed. In the event of a total or partial failure, the sums do not usually have to be reimbursed by the Company.

The amount of refundable public aid recognized at December 31, 2018 is €485 million and corresponds to advances from BPIfrance for the development of AsiDNA™. The advances are in the process of being repaid.

#### 3.2.8 DESCRIPTION OF CASH FLOWS

In the financial year 2018, the cash flow generated by the activity amounted to -€11.3 million, compared to -€28.3 million in the previous year. This situation is directly linked to the development of the activity and particularly the sharp fall in R&D costs, to the extraordinary impairment of R&D assets related to Beleodaq® in the 2017 financial statements and to the change in working capital requirement explained above.

Cash flow related to investment transactions is almost non-existent.

Cash flow related to financing transactions amounts to €8.3 million over the period, due to the putting in place of a debenture loan and an own equity line of credit in June 2018 for a total net amount of €8.6 million.

# 3.2.9 INTRA-GROUP FLOWS

Information on loans and advances granted by the Company to its subsidiaries is presented in note 7 to the Company's annual financial statements provided in section 6.3 of the Registration Document.



# 4. FROM RESEARCH TO DEVELOPMENT

# 4.1 RESEARCH & DEVELOPMENT

#### 4.1.1 PRINCIPLES AND ORGANIZATION

The Group currently has approximately thirty salaried staff with a high level of expertise, almost two-thirds of whom are in R&D and who carry out and coordinate the various activities associated with research, development, quality assurance, registration and industrial protection, in addition to various strategic marketing activities, market surveys, corporate development and support services (finance, human resources and communication).

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

The Group has a research laboratory on its Parisian site where the teams carry out different optimization activities and preclinical trials.

The regulatory framework summarized below (paragraph 4.1.2) is the general framework which covers the entire development process of a drug up to its registration and its reimbursement. It should be noted that the Group's strategy is focused on developing innovative or disruptive compounds from the preclinical research (called translational) up to clinical concept tests in humans (phases Ib or II), which represents its know-how and its area of expertise. Within the framework of this strategy corresponding to the model to increase the value of a biotechnology company, the subsequent development stages (phases III, registration, reimbursement, etc.) are carried out in collaboration with or delegated to partners under licensing agreements.

#### 4.1.2 REGULATORY FRAMEWORK

Regulatory provisions 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, 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 Group operates is based on the procedures defined by the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH).

Health products cannot be marketed in a jurisdiction without having obtained technical and administrative authorization from the authorities of the country in question, and without having at least obtained a prior MA. In order to obtain an MA for a product, the Group must provide proof regarding its efficacy and safety, including detailed information about its composition and manufacturing process. This forms the framework for conducting 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). Similarly, they may also demand supplementary tolerance or efficacy tests after obtaining the MA, involving particular populations or impose conditions able to restrict 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



Clinical trials on humans are normally conducted in three phases known as phase 1, phase 2 and phase 3, which are generally sequential but may also overlap.

**Phase I:** phase 1 consists of administering the product, most often in oncology to subjects with cancer, in order to identify its initial utilization safety profile, to validate the maximum or optimum doses and its distribution and metabolism.

**Phase II:** in phase 2, the drug is studied within a restricted population of patients suffering from a targeted disease in order to establish its preliminary efficacy, its optimum dosage and to fine tune its tolerance profile.

**Phase III:** the phase 3 trial is carried out in a large number of patients suffering from a targeted disease to compare the treatment in the trial to the reference treatment in order to produce enough data to be able to establish the benefit-risk ratio of the product.

Clinical trials can sometimes be required after the products have been marketed 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 Phase IV post MA trials.

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

The carrying out of a phase 1, phase 2 or phase 3 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 European Directive 536/2014. When companies requesting permission to test products submit clinical trial protocols, the regulatory authorities may either accept or refuse such trials, or demand that major changes be made to the protocol. Additionally, every 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 noncompliance with any regulatory provisions.

# 4.1.2.2 Marketing Authorization

In order to be marketed, every drug must be covered by a Marketing Authorization issued by the competent national or supranational health authority (ANSM in France, EMA in Europe, FDA in the US, etc.) which assesses the product according to scientific criteria of quality, safety and efficacy.

The application for an MA is comprised of detailed and accurate information on the product, particularly its composition, its action mechanism, the manufacturing process, the associated quality elements, its toxicity, its efficacy and its safety. ...The quality of this information is assured by carefully supervised preclinical and clinical studies. The extent and nature of these trials vary in line with a number of factors such as the nature of the product evaluated, the treatment developed, the sought-after indications and the healthcare standards.

The preparation of these applications and their evaluation by the competent authorities are an expensive process that may 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 under the mutual recognition procedure or be decentralized within other Member States or, for certain products, directly with EMA within the context of so-called centralized procedure. The centralized procedure involves an application, a review 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 that grants marketing authorization following a New Drug Application (NDA) or a Biological Licence Application (BLA).

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World Medical Association (WMA) Declaration of Helsinki, "Recommendations Guiding Physicians in Biomedical Research Involving Human Subjects."



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 possible in Europe under a similar law for drugs intended to treat a disease that affects 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, drugs pricing is controlled by the State which sets the absolute level or prevents local authorities making reimbursement over a given amount. Medical-economic data are requested increasingly often by the healthcare authorities in order to determine the cost-effectiveness ratio of a new product in relation to existing alternatives. International benchmarks on the prices practiced are also frequently used to control price increases.

# 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 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 RESEARCH & DEVELOPMENT PROJECTS

The Group develops products in oncology, and more specifically targets types of tumor for which there is a high medical need. This involves innovative products for the treatment of rare or resistant cancers, severe diseases for which new therapeutic approaches are in demand and which constitute markets of high potential. As of the date of this registration document, this portfolio consists of the following main products:

### 4.1.3.1 Clinical phase products

- AsiDNA™: first-in-class product from the platON™ platform, DAN repair inhibitor in tumor cells. An intravenous single-therapy AsiDNA™ (DRIIV-1) phase 1 trial is under way, in patients whose treatment for advanced / metastatic forms of solid tumors has failed. The first positive activity reports of the first three doses were published in November 2018 allowing for determining the active doses. In parallel, preclinical trials demonstrating the synergy of AsiDNA™ in association with other anti-cancerous agents, particularly carboplatin and PARP inhibitors have been carried out. A phase 1b trial in association with carboplatin (chemotherapy) associated or not with paclitaxel is being prepared and should start in the coming weeks..
- Beleodaq® (belinostat) for treating peripheral T-cell lymphoma (PTCL). After a positive phase II trial which led to a conditional FDA approval (see below), the partner Spectrum is in charge of continuing the clinical development.
- Validive® for treating severe mucositis in patients treated for a head and neck cancer; after a positive phase 2 trial, the Company signed a global licensing agreement with the laboratory Monopar Therapeutics which is now in charge of continuing its further development.

# 4.1.3.2 Registered products

- Beleodaq® (belinostat) for treating relapsed or refractory peripheral T-cell lymphoma (PTCL) has been registered and is marketed in the US (conditional MA).
  - Beleodaq® has, since 2017, been part of an NPP program (Named Patient Program) in Europe, which allows it to be prescribed in certain countries.

On March 1, 2019, Spectrum Pharmaceuticals (SPPI), the Company's partner in the United States, announced the completion of the sale of its seven hematology/oncology products approved by the FDA, including Beleodaq®, to Acrotech Biopharma LLC. Based on the information provided to date by Spectrum, the Company does not foresee any significant impact of this transaction on the activities and results of Beleodaq® for Onxeo.



These products are presented in detail in section 4.2 of the Registration Document.

Furthermore, two products, Loramyc®/Oravig® (miconazole Lauriad®), for treating esophageal candidiasis, and Sitavig®/Labiriad® (acyclovir Lauriad®) for treating recurring labial herpes, were sold in 2017 to the laboratory Vectans and are therefore no longer part of the Company's drug portfolio. The sale agreement did, however, provide for the collection by the Company of certain milestone payments: they are therefore mentioned only in reference to these future payments.



### 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 research and development projects. As at December 31, 2018, the Group's license portfolio is composed of 16 patent families that are already published or being reviewed by the international patent organizations, concerning innovative products or technologies and protecting the Group's assets abroad in the long term.

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 out licensing rights on its products Beleodaq® and Validive® (respectively described in sections 4.2.2 and 4.2.3 of this document).

Specifically, the Company filed in 2018 two new patent applications (patent families vii and viii in the table below), one relating to biomarkers predictive of treatment with a Dbait molecule - with an expiration date estimated at 2038 -, the other on a combination of a DBait molecule with an HDAC inhibitor - extending the patent protection of AsiDNA  $^{\text{TM}}$  in these fields of application until 2038.

#### Patents portfolio for products that are marketed or undergoing clinical development

Products	Main therapeutic areas	Protections	Expiry date	Status						
	Histone deacetylase inhibitor (HDACi) technology									
	Peripheral T-cell lymphoma (PTCL)	lymphoma substance		Issued (EP, US, JP, etc.)						
Beleodaq®				Issued (EP, US, JP, etc.)						
		iii) Production of the active substance	Q2 2030 US, Q3 2028 elsewhere	Issued (EP, US)						



Products	Main therapeutic areas	Protections	Expiry date	Status
	Dbait Tech	nology: "DNA strand break bait" (	(Dbait) molecu	ıles
		i) Treatment of cancer by the administration of Dbait molecules in combination (radio/chemotherapy)	Q3 2024	Issued (EP, US, JP, CN, etc.)
		ii) Specific Dbait molecules	Q3 2027	Issued (EP, US, JP, CN, etc.)
		iii) Treatment of cancer by single administration of Dbait molecules	Q1 2028	Issued (EP, US, JP, CN, etc.)
AsiDNA™	Treatment of cancer	iv) Dbait molecules optimized for better <i>in vivo</i> administration (AsiDNA™ and other Dbait molecules combined)	Q2 2031	Issued (US, EP, CN, etc.) Filed (EP, US, etc.)
	cancer	(v) Dbait molecules in combination with PARP inhibitors	Q3 2036	Issued (agreement for issue EP, JP) Filed (US, CN, etc.)
		(vi) Systemic administration of Dbait molecules	Q1 2037	Filed (EP, US, JP, CN, etc.)
		(vii) Predictive biomarker	Q1 2038	Filed
		(viii) Dbait molecules in combination with HDAC inhibitors	Q4 2038	Filed
		(ix) Prevention and reversal of acquired resistances	Q1 2039	Filed

# 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's trademarks are the names of its products that are marketed or under clinical development as well as, in particular, the names of its plat $ON^{\text{TM}}$  oligonucleotides platform, 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.



## Trademarks portfolio for products that are marketed or under clinical development

Trademarks	Products	Main countries in which the trademark is registered or pending registration
Beleodaq®*	belinostat	USA, Europe, Japan, China, Australia, Russian Federation, Mexico, Norway, Oman, Serbia, Singapore, Switzerland, Turkey, Vietnam, Israel, India, Canada, South America (Argentina, Brazil, Chile, Columbia, Ecuador, Venezuela)
AsiDNA™	etidaligide	France, European Union, Japan, United States
platON™	New product generation platform	Europe, United States

<sup>\*</sup> the Beleodaq® trademark is in the process of being transferred to Acrotech Pharma LLC, exclusive licensee of the Group for selling belinostat in the United States, Canada, Mexico, and India, due to the sale under way between Spectrum and Acrotech.

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

Onxeo is a biotechnology company that develops innovative oncology drugs, based on tumor DNA-targeting, an area in which its scientific teams have cutting-edge expertise. This model is intended to transform scientific innovations into breakthrough clinical treatments thanks to tried-and-tested translational expertise, by developing its products up to an attractive stage that is highly valued by pharmaceutical partners. This means developing the preclinical stage products (1 to 2 years before the clinical stage starts) to optimum inflection points in terms of value (generally phase Ib or II proof of clinical concept). Once proof of concept is established in humans, Onxeo seeks to monetize its products through partnerships.

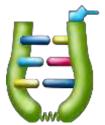
#### 4.2.1 ASIDNA™ AND THE DNA REPAIR INHIBITORS' MARKET

# 4.2.1.1 A first-in-class product from the acquisition of DNA Therapeutics

AsiDNA™ is the first product of a new class of drugs (first in class) from the signal interfering DNA repair technology (siDNA). The inhibition of DNA repair mechanisms in tumor cells is today recognized as one of the most promising steps in cancer treatment.

The cancerous cells do in fact have biological defense mechanisms allowing them to respond to DNA alterations caused spontaneously in the case of certain genetically unstable tumors, or resulting from treatment using genotoxic substances (chemotherapy or radiotherapy for example).

These repair processes contribute to the aggressiveness of cancers and to resistance to treatments.

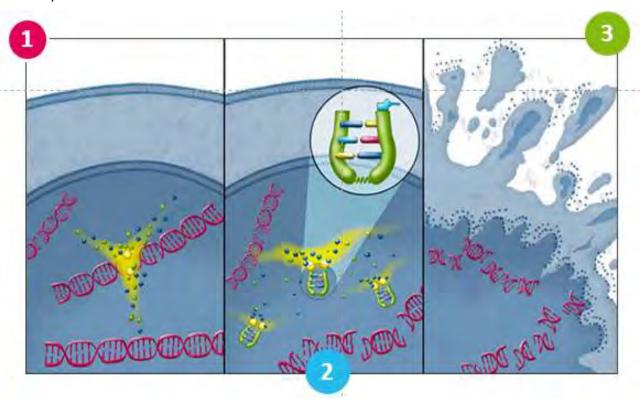


AsiDNA™ is a fragment of DNA (double-strand) which acts like a decoy to counteract the DNA repair cycle in tumor cells: it sends a false lesion signal which mobilizes the detection, signaling and repair enzymes (proteins) of DNA breaks and thus prevents the repair of real DNA lesions, whether they are endogenous or induced by genotoxic anticancer treatments. Since cancerous cells have lost the capacity to interrupt the cellular division, they therefore continue to split up with a damaged DNA, which in the end leads to cell death. Healthy cells, on the other hand, have retained the capacity to

suspend their splitting whilst waiting for the disappearance of the product of the cell, and may then resume their splitting cycle.



This single action mechanism, also known as "Dbait", was developed by Marie Dutreix, Director of Research at CNRS, and Jian-Sheng Sun, Professor at the National Natural History Museum of Paris, and mostly conducted in the laboratories of Professor Dutreix at the Institut Curie. It is illustrated below.



- Several DNA repair pathways are activated in the cancerous cells via the recruitment of enzymes allowing them to effectively repair their damaged DNA and avoid cell death;
- AsiDNA™ imitates a DNA break in the cancer cells and activates the DNA damage signaling enzymes, thus triggering a false "damage" signal which prevents the repair enzymes from being recruited on the site where they should act to repair the damage on the chromosomes of the tumor cell;
- The cancerous cells are no longer able to split up with a damaged DNA, which leads to cell death through mitotic catastrophe.

# 4.2.1.2 The therapeutic approach targeting DNA Damage Response (DDR) in oncology

DNA damage response Inhibition is a relatively new field in oncology. The cancerous cells build up over time and, due to their high proliferation, a certain amount of DNA damage related to replication errors. Their survival is therefore highly dependent on repair mechanisms so much so that by inhibiting these mechanisms, the cancerous cell is deprived of any ability to repair its DNA which inevitably leads to its death by mitotic catastrophe.

As can be seen in the table<sup>4</sup> below, DNA breaks may manifest themselves either on a single strand, or simultaneously on the two strands, and each type of damage calls for a very specific repair mechanism. To correctly repair, the cell has to be capable of correctly detecting and identifying the type of breach, in order to activate the correct signaling and repair agents (i.e. proteins).

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<sup>&</sup>lt;sup>4</sup> Targeting DNA Repair in Cancer: Beyond PARP Inhibitors – Jessica S. Brown, Brent O'Carrigan, Stephen P. Jackson, and Timothy A. Yap – Cancer Discovery January 2017



		Cassures	double b	rin		Cassures simple brin					
Voie de réparation	NHEJ	HR	alt-NHEJ MMEJ	SSA	ICL repair	SSB repair	BER	TLS	NER	MMR	
Proteines capteurs de dommage	Ku70/Ku80	MRN	PARP	MRN	FA core complex (FANCA, B, C, E, F, G, L and M)	PARP	DNA Glycolases, APE1	PCNA	XPC DDB2 CSA	MSH2, MSH3 MSH6, MLH1 PMS2	
Protéines de signalisation	DNAPK	ATM, ATR, MK2, CtIP, BRCA1/BARD1, BRCA2, PALB2, RPA		CtIP	FANCD1 [BRCA2] D2,I J [BRIP1] N [PALB2] O [RAD51C] P [SLX4]			RAD6 RAD18	XPA, XPF, RPA		
Protéines effectrices	XRCC4 XLF LIG4 APLF Artemis PAXX WRN	RAD51 MUS81/EME1 SLX1/SLX4 RTEL1 BLM TOPOIII POLQ PARI RECQL5 FANCJ, BLM	XRCC1 LIG3, LIG1 CtIP POLQ	RAD52, others ?	Shared with HR, TLS, and NER	XRCC1 PNKP POL FEN1, TDP1 Aprataxin LIG1, LIG3A	As for SSB repair	REV1, POLH, POLI, POLK	XPG ERCC1 POLE POLD1 LIG1, LIG3	EXO1 POLD LIG1	

NHEJ: non-homologous end-joining; HR: homologous recombination; alt-NHEJ: alternative non-homologous end-joining; MMEJ: microhomology-mediated end-joining; SSA: single-strand annealing; ICL: interstrand cross-link; SSB: single-strand break; BER: base excision repair; TLS: translesion synthesis; NER: nucleotide excision repair; MMR: mismatch repair.

Only simultaneous damage to the two chains of the DNA molecule (we then talk of a double-strand break) generates genomic instability, which itself leads to cell death. Thus, the strategy to develop drugs inhibiting DNA double-strand break pathways seems the most interesting.

DNA damage response is a complex cascade of events which, in a simplified manner, is organized in three stages:

- 1/ detection and identification of the damage with "sensor" proteins;
- 2/ signaling with enzymatic proteins whose role is essential in coordinating the most appropriate response (this response may be the repair of the DNA break, but it may also be the activation of apoptosis when the damage is too great);
- 3/ repair with effector proteins which will suitably repair the DNA molecule (resection, replication, insertion).

Currently, the drugs or candidate-drugs which are developed in this DDR inhibition approach target specific proteins intervening in a repair pathway by an inhibitor mechanism: these are "targeted" therapies, which inhibit a specific protein, such as the PARP inhibitors.

On the other hand, AsiDNA™ inhibits all the repair pathways by sequestering and bypassing all of the proteins necessary for the initiation of the response cascade. After sequestering these proteins, it overactivates them (agonist), thus decoying the cell which will not be able to make a difference between a real damage signal / repair signal, and the false signal induced by AsiDNA™.

Thus, through this dual mechanism of decoy and agonist of the entire natural biological response process to damage to its DNA, the tumor cell cannot develop resistance by using alternative repair pathways, as is the case with all targeted therapies. Indeed, if we target and inhibit a protein X, the tumor cell will progressively cease to produce it and use protein Y instead to resist the inhibition of X; the treatment targeting X then becomes ineffective. This is called acquired resistance.

The capacity of AsiDNA™ to block upstream all the repair pathways, without giving the cell the possibility to repair its DNA, and its very specific property of not inducing resistance, are major points of differentiation in respect of the competition.



# 4.2.1.3 Market and competition in DDR (DNA Damage Response)

AsiDNA™ is currently the only compound under development which does not target a specific protein of the DNA damage response cascade.

The previous table named all the proteins which can be activated at the time of the DNA damage response, and which are therefore potential targets for drugs. To this list we need to add the candidate-drugs which target some cell cycle regulatory proteins (particularly CHK1 and CHK2) which are themselves activated by the DDR signaling pathways. The main development targets are shown in red in the table.

# PARP (poly(ADP-ribose) polymerase) inhibitors

The DNA repair inhibitors' market was initially invested by PARP inhibitors on which several products on the market and under development are based.

Company	Molecule	Trading name	Status	Indications (approved and undergoing clinical trials)
				Ovarian Cancer Breast Cancer
AstraZeneca	olaparib	Lynparza®	Marketed	Prostate cancer (phase III)
				Pancreatic cancer (phase III)
Clovis Oncology	rucaparib	Rubraca®	Marketed	Ovarian Cancer
Tesaro	niraparib	Zejula®	Marketed	Ovarian Cancer
		,		Breast Cancer
Pfizer	talazoparib	Talzenna®	Marketed	Prostate cancer (phases II and III)
				Lung cancer (phase I)
				Breast Cancer
	veliparib		Phase III	Lung Cancer
Abbvie				Ovarian Cancer
	ABT-767		Phase I	Solid tumors
				Ovarian cancer (phase III)
BeiGene	pamiparib		Phase III	Gastric cancer (phase III)
				Solid tumors (phase II)
lianani HanaDui	fluncacarile		Phase II	Ovarian cancer (phase II)
Jiangsu HengRui	fluzoparib		Phase II	Gastric cancer (phase I)
Oncology Venture	2X-121		Phase II	Breast Cancer
Checkpoint Tx	CEP-9722		Phase I	Solid tumors
Humanwell Healthcare	HWH-340		Phase I	Solid tumors
Humanweii Healthcare	WB1-340		Phase I	Cancer
Impact Tx	IMP-4297		Phase I	Solid tumors
Jeil Pharmaceutical	JPI-547		Phase I	Solid tumors
Ildong	IDX-1197		Phase I	Solid tumors
Shanghai De Novo Pharmatech	DN-1 (SC- 10914)		Phase I	Solid tumors
Allist Pharmaceuticals	AST-6828		Preclinical	-
Nerviano Medical Sciences	NMS-P293		Preclinical	-
NewGen Tx	NT-125		Preclinical	-
Ribon Tx	PARP inhib		Preclinical	F

Source: Pharmaprojects

The inhibition of the PARP enzyme prevents the recruitment of the damaged DNA site of the BER (base excision repair) pathway; this leads to an accumulation of single-strand breaks which are not lethal for the cell. This accumulation, in turn, will lead to the formation of double-strand breaks and therefore to the activation of the most efficacious repair pathway for this type of damage, the HR (homologous recombination) pathway. When this HR pathway is functional, the damage caused by the PARP inhibitors ends up being repaired and the cancerous cell does not die. To be fully efficacious, the PARP inhibitors

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need the HR pathway to be inactivated or deficient, which is the case when the patient carries certain mutations, particularly those of the BRCA 1 and 2 genes.

We talk about synthetic lethality to describe this dual therapeutic approach (inhibition of the PARP enzyme by the drug and inactivation of the HR repair pathway by mutation).

Unlike PARP inhibitors, AsiDNA<sup>™</sup> does not need for such or such repair pathway to be inactivated or deficient in order to function. Its action mechanism is not dependent on the mutational status of the tumors; it is not therefore limited in its use to prior knowledge of the genetic profile of patients.

In the first 9 months of 2018, the three PARP inhibitors on the market (Lynparza®, Rubraca® and Zejula®) totaled turnover of \$670M.

# DNA-PK (DNA-dependent serine/threonine protein kinase) inhibitors

Company	Molecule	Trading name	Status	Indications (approved and undergoing clinical trials)
Merck KGaA	nedisertib		Phase II	Small cell lung cancer
Celgene	CC-115		Phase I	Cancer
Vertex Pharmaceuticals	VX-984		Phase I	Cancer
Boryung	BR-101801		Preclinical	DNA-PK and PI3K delta double inhibitor

# ATR (ATM- and Rad3-related kinase) inhibitors

Company	Molecule	Trading name	Status	Indications (approved and undergoing clinical trials)
AstraZeneca	AZD-6738		Phase II	Different cancers
AA I/C-A	VX-970		Phase II	Different cancers
Merck KGaA	VX-803		Phase I	Solid tumors
Bayer	BAY-1895344		Phase I	Solid tumors

# ATM (ataxia telangiectasia mutated kinase) inhibitors

Company	Molecule	Trading name	Status	Indications (approved and undergoing clinical trials)
	AZD-0156		Phase I	Solid tumors
AstraZeneca	AZD-1390		Phase I	Glioblastoma, brain metastases
	AZ-31		Preclinical	-
Merck KGaA	M-3541		Phase I	Solid tumors

# CHK1 and/or CHK2 (Checkpoint Kinase 1 or 2) inhibitors

Company	Molecule	Trading name	Status	Indications (approved and undergoing clinical trials)
Eli Lilly	prexasertib		Phase II	Lung cancer and other locations
Esperas Pharma	ESP-01		Phase II	Solid tumors
Sierra Oncology	PNT-737		Phase II	Different locations
Cancer Research Technology	CCT-241533		Preclinical	-
Vernalis	VER-250840		Preclinical	-



## Wee1 protein kinase inhibitors

Company	Molecule	Trading name	Status	Indications (approved and undergoing clinical trials)
AstraZeneca	adavosertib		Phase II	Different locations
Debiopharm	Debio-0123		Preclinical	-

# DNA polymerase theta (POL $\theta$ or POLQ) inhibitors

Company	Molecule	Trading name	Status	Indications (approved and undergoing clinical trials)
Artios			Preclinical	-
Repare Tx			Preclinical	-

Source: Pharmaprojects

AstraZeneca and Merk KGaA are highly committed to DDR, with respectively 6 and 4 products in their portfolio targeting this field.

The field of DDR is of interest to many players and is part of a big partnership and licensing activity, due to the potential combinations it offers with other types of therapies.

#### Since 2018:

- licensing agreement between Repare Therapeutics and Ono Pharmaceuticals for a POLQ inhibitor
- clinical collaboration agreement between CStone Pharmaceutical and Impact Therapeutix on the PARP inhibitor IMP-4297;
- acquisition of Tesaro (niraparib) by GSK;
- clinical collaboration agreement between Roche/Genentech and Tesaro to test the PARP inhibitor niraparib in combination with atezolizumab;
- clinical collaboration agreement between Immunomedics and Clovis Oncology to test the PARP inhibitor rucaparib in combination.

# Before 2018;

- strategic partnership between AstraZenica and Merck & Co of July 2017 which, inter alia, aims to explore the combinations between PARP and MEK inhibitors with anti-PD-1 / PD-L1 antibodies;
- licensing agreement between Tesaro and Takeda for the exploitation of niraparib in Japan (July 2017);
- licensing agreement between Tesaro and Janssen Pharmaceuticals for the development of niraparib in prostate cancer (April 2016);
- clinical collaboration agreement between Clovis Oncology and BMS to evaluate the combination between rucaparib and nivolumab (July 2017).

This collaboration and partnership phase was preceded by much more significant operations such as mergers and acquisitions, with a certain number of medium-sized and large-sized pharmaceutical groups betting on this promising new approach in oncology:

- Acquisition of KuDos Pharmaceuticals (inventor of olaparib) by AstraZeneca in 2005;
- Acquisition of Biomarin Pharmaceuticals (inventor of talazoparib) by Medivation in 2015, then acquisition of Medivation by Pfizer in 2017;
- Acquisition of 3 Vertex DDR programs by Merck KGaA (2017).

Onxeo, in its acquisition of DNA Therapeutics in 2016, therefore clearly positioned itself on a therapeutic area under massive development and generating a strong partnership activity in the widest meaning of the term.

# 4.2.1.4 Development of the project to date and next steps

## 4.2.1.4.1 Preclinical program

In 2017, the Company conducted numerous in vitro and in vivo studies of AsiDNA™, in monotherapy and in association with other molecules showing its in vivo activity after systemic injection. Activity biomarkers were validated and their quantification in tumors showed proportionality with the circulating doses of the



molecule. In a complementary manner, the synergy of AsiDNA™ anti-tumor activity with carboplatin, with the PARP inhibitors (PARPi) and with the HDAC inhibitors (HDACi) has been demonstrated in vitro or in vivo

In 2018, the Company initially set about confirming the synergy with the PARPi in vitro and was able to show a very significant increase in the efficacy of the association of AsiDNA™ with olaparib (a PARPi), in a triple negative breast tumor implanted in mice, in relation to the efficacy of each compound administrated alone.

Interestingly, Onxeo also confirmed that AsiDNA™, unlike PARPis, did not induce acquired resistance but, on the contrary, that repeated treatments with AsiDNA™, both in vitro and in vivo, led to an increased sensitivity of tumor cells and tumors. This result points to a potential use of AsiDNA™ in maintenance therapies.

The Company also proved that repeated treatments with AsiDNA™ in association with a PARP inhibitor or carboplatin inhibit the appearance of acquired resistances for these two types of molecules, suggesting that AsiDNA™ could therefore prolong the efficacy of these therapies.

In 2018, Onxeo also conducted a study aimed at searching for predictive biomarkers of the anti-tumor response to AsiDNA™. To do this, transcriptomic studies were conducted on tumor cells treated or not with AsiDNA™. A transcriptomic signature of AsiDNA™ was thus determined. In using this signature in bio-IT studies supported by public databases, it was determined that the negative regulation of 6 genes, all coding for proteins involved in DNA repair, was correlated to the response of tumors to AsiDNA™. In vitro experiments were able to confirm this correlation.

The Company presented the results of five of these preclinical studies showing the differentiated profile of AsiDNA™, strengthening its clinical potential and demonstrating its unique action mechanism, during the AACR (<u>American Association for Cancer Research</u>) Annual Meeting, held from 29 March to 3 April 2019 in Atlanta (Georgia), United States. The presentations in poster-form were entitled:

- AsiDNA™, a targeted treatment without acquired resistance
- AsiDNA™ overrides acquired resistance to PARP inhibitors
- Molecular analysis of the AsiDNA™ action mechanism provides new indications on the regulation of DNA damage response
- Development of a patient selection strategy based on biomarkers for treatment by AsiDNA™ (in collaboration with the Institut Curie)
- AsiDNA™, a new DNA repair inhibitor to sensitize aggressive sub-types of medulloblastoma (*Institut Curie*)

AsiDNA™ is the first-in-class molecule from a patented chemical "decoy" oligonucleotides platform which the company named platON™ and presented in October 2017. The components of this platform are built on the basis of a double strand oligonucleotides sequence, a binding molecule and a molecule encouraging intra-cell penetration. Each of these three components can be modified to generate various compounds expressing different properties and/or activities, with the common feature of targeting tumor DNA functions through a decoy mechanism.

In 2018, the Company in particular identified a new compound from this platform with pharmacological properties different from AsiDNA™ and belonging to a new chemical family for which an invention patent application has been filed. This new compound is being optimized in order to enter into preclinical in vitro studies as of the 1st quarter 2019.



# 4.2.1.4.2 Clinical program

An initial phase 1/2a (DRIM⁵) clinical trial of AsiDNA™, in association with radiotherapy in patients suffering from metastatic melanoma has already demonstrated good tolerance and safety by intra-tumor and sub-cutaneous administration, in addition to initial indications of efficacy.

The clinical demonstration of this same activity after systemic administration would give the product a very wide scope of application in terms of target tumors, without limitation to those only accessible by local administration. An authorization application for a new intravenous AsiDNA™ phase 1 study was thus filed in December 2017 with the Belgian and French health authorities and with the ethics committees of the clinical centers concerned.

In April 2018, Onxeo announced that it had recruited and treated the first patient of the phase 1 DRIIV (DNA Repair Inhibitor administered IntraVenously) clinical trial of AsiDNA™.

This trial, carried out in some of the most prestigious centers in France and Belgium, is intended to evaluate the tolerance of AsiDNA™ and the optimum clinical dose and to determine its active dose at tumor level, in patients whose treatment for advanced / metastatic forms of solid tumors has been unsuccessful.

In November 2018 and as planned, Onxeo announced the positive interim results of the first three-dose levels already tested on the six ones planned for AsiDNA™ in the DRIIV study.

A total of 10 patients with advanced solid tumors received 112 infusions of AsiDNA™, ranging from 200mg (dose 1) to 600mg (dose 3).

The Cmax data (maximum concentration) and AUC data (area under curve) show a proportional effect to the dose from dose 1 to dose 3, with a systemic exposure increasing in proportion to the dose.

In accordance with the study protocol, biopsies were taken during cycle 2 of treatment with AsiDNA™ and analyzed in comparison with reference biopsies (pre-treatment). The activation of the targets by AsiDNA™ was measured by quantifying by immunohistochemistry two recognized biological markers of the DNA-PK activation, one of the main targets of AsiDNA™, gH2AX and pHSP90.

The biopsies pre- and post-treatment of four patients were able to be analyzed (two from the second dose level group and two from the third dose level group). In these patients, the biopsies revealed a significant activation of the target DNA-PK, as evidenced by the significant increase in the quantification of the two activity biomarkers in the tumor tissue of the patients after administration of AsiDNA™. These data confirmed a strong activation of the targets and strong activity in the tumors, with these two doses of AsiDNA™. In addition, the quantification of an established biomarker of the tumor proliferation, the Ki67 marker, showed a net reduction in the rate of tumor proliferation in three patients and stabilization in one patient.

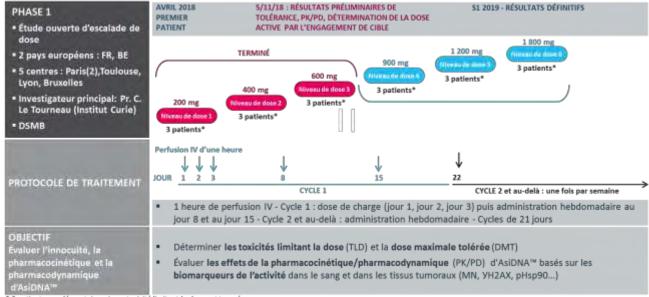
Finally, the intravenous administration of AsiDNA™ was generally well tolerated in the first three doses, without a serious side effect linked to the drug and without toxicity limiting the dose.

The table below summarizes the conception of the DRIIV-1 trial:

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<sup>&</sup>lt;sup>5</sup> Le Tourneau et al. Br J Cancer. May 24, 2016;114(11):1199-205





\* 3 patients supplémentaires si une toxicité limitant la dose est trouvée

All of the data from the DRIIV-1 trial is expected in the first half of 2019. Nevertheless, these initial tolerance and proof of mechanism data confirm the activity and the good tolerance profile of AsiDNA™ by systemic administration and validate moving on to the next stage of the clinical development i.e. the initiation of phase Ib/II trials on the efficacy of AsiDNA™ in association with other treatments, particularly with DNA-damaging substances such as platins and taxans. An initial phase 1B trial is expected to start in the first half of 2019.

# 4.2.2 BELINOSTAT AND BELEODAQ® (INTRAVENOUSLY ADMINISTERED BELINOSTAT)

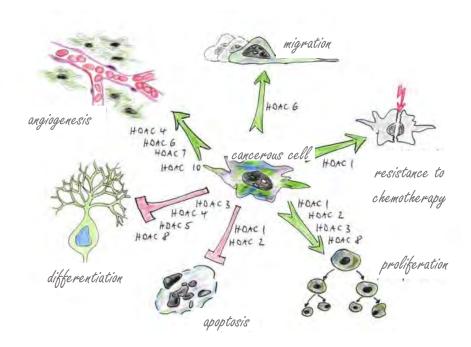
# 4.2.2.1 Belinostat, a HDAC inhibitor with great potential

Belinostat is a histone deacetylase inhibitor (HDACi) which, via an enzymatic process, typically normalizes genetic disfunctions which are characteristic of cancer cells. It acts by inhibiting these enzymes (HDAC) particularly involved in cell proliferation.

Belinostat acts on several types of HDAC (HDAC 1, 2, 3, 6) thus giving it an activity potential on different processes of the development of a tumor, as illustrated<sup>6</sup> below.

<sup>&</sup>lt;sup>6</sup> adapted from Olaff, Witt et al., Cancer Letters 277 (2009) 8-21





Thanks to their pleiotropic action, HDAC inhibitors can simultaneously target several crucial channels for the survival of the cancer cells. In preclinical studies, the HDACi 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<sup>7 8</sup>.

Relying on a strong and well-documented mechanistic rationale in favor of a combination between the epigenetic approach and the DNA repair inhibition approach, the Company tested, in a preclinical stage, on in vitro models, the association of belinostat (and other HDAC inhibitors) and AsiDNA™. The promising results of these experiments were presented to the AACR Meeting in Chicago in April 2018. They show a significant level of synergy between these two types of molecule. Other experiments are planned with new compounds from the platON™ platform.

# 4.2.2.2 Relapsed or refractory T-cell lymphoma (Beleodag®: IV form of belinostat)

## 4.2.2.2.1 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 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, Hydroxyadriamycin, 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.

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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



# 4.2.2.2.2 Epidemiology

Non-Hodgkins lymphomas, quite rare worldwide (incidence of 5 / 100,000, 386,000 cases in 2012), are however quite frequent in countries marked by an ageing population. The incidence is thus 20.1 / 100,000 in North America (70,000 cases) and 15.6 / 100,000 in the European Union (79,000 cases). PTCL cases account for between 10 and 15% of NHL cases, namely between 38,000 and 58,000 new cases globally. In Western countries, this proportion is lower - 5 to 10% of NHL cases - than in Asian countries (15 to 20%).

In the main pharmaceuticals markets (US, Europe, Japan and China) there are therefore between 17,000 and 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, amounting to an estimate of between 22,000 and 36,000 cases by 2030<sup>11</sup>

The indication approved in the USA concerns refractory patients or those in relapse following first-line treatment (CHOP), and second-line candidates, namely around 60% of patients diagnosed with a PTCL. For the US, this market is estimated at approximately 187 million dollars in 2015 (according to a market study commissioned by the Company in 2016<sup>12</sup>).

# 4.2.2.2.3 Competition

In the USA, three products have been approved by the Food and Drug Administration for 2nd-line treatment of PTCL: Beleodaq®, Istodax® (romidepsin, Celgene) and Folotyn® (pralatrexate, Spectrum Pharmaceuticals). In Europe, no drug to date has obtained MA on the market for this indication. It should be noted that two authorized generics of Istodax® were launched in the US in 2018, one by Pfizer and the other by Teva.

In addition to the 3 products approved for PTCL in the USA, we should mention Adcetris® (brentuximab vedotin, Seattle Genetics) which is approved (in the US and in Europe) for a sub-type of PTCL, systemic anaplasic large-cell lymphoma where relapsed or refractory in adults. On the Asian market, two products have MA for refractory or relapsed PTCL: Epidaza® (chidamide), approved in China; and Poteligeo® (mogamulizumab), approved in Japan.

The products at advanced clinical development stage (phase II / III), which are currently being tested (active status or being recruited), in the 2nd-line treatment indication of PTCL are:

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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)

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>&</sup>lt;sup>11</sup> Ihid

<sup>12</sup> Navigant Consulting Inc



Reference clinical trials.gov	Molecule	Company (Sponsor)	Title or subject of the trial	Phases
NCT02464228	tipifarnib	Kura Oncology	Study of Tipifarnib in Subjects with Relapsed or Refractory PTCL	Phase II
NCT02264613	ALRN-6924	Aileron Tx	A Phase 1/2a Open-Label Study to Determine the Safety and Tolerability of ALRN-6924 in Patients With Advanced Solid Tumors or Lymphomas Expressing Wild-Type p53 Protein	Phase I/II
NCT03590574	AUTO4	Autolus	A Single Arm, Open Label, Multi-centre, Phase I/II Study Evaluating the Safety and Clinical Activity of AUTO4, a CAR T-cell Treatment Targeting TRBC1, in Patients With Relapsed or Refractory TRBC1 Positive Selected T Cell Non-Hodgkin Lymphoma	Phase I/II
NCT02953652	chidamide	Huya Bioscience	Efficacy and safety of oral HBI-8000 in Pts with R/R PTCL	Phase II
NCT 03372057	duvelisib	Verastem	A study of duvelisib in Pts with R/R PTCL	Phase II
NCT02676778	Deleukin diftitox	Eisai	Study of E7777 in Pts with R/R PTCL and CTCL	Phase II
NCT03502629	genolimzumab	Genor Biopharma	Phase II clinical study to evaluate the efficacy and safety of GB226 for the treatment of relapsed and refractory peripheral T cell lymphoma (PTCL), and to evaluate the immunogenicity of GB226.	Phase II
NCT03776279	mitoxantrone	CSPC Pharmaceutical	Single-arm, Open and Multi-center Phase II Study of Liposome-entrapped Mitoxantrone Hydrochloride Injection in Relapsed/Refractory Peripheral T-cell Lymphoma and NK/T-cell Lymphoma	Phase II
NCT03770000	tenalisib	Rhizen Pharmaceuticals SA	An Open Label, Phase I/II Study to Evaluate the Safety and Efficacy of Tenalisib (RP6530), a Novel PI3K $\delta/\gamma$ Dual Inhibitor Given in Combination With a Histone Deacetylase (HDAC) Inhibitor, Romidepsin in Adult Patients With Relapsed/Refractory T-cell Lymphoma	Phase I/II
NCT03075553	nivolumab	NCI	Nivolumab in treating pts with R/R PTCL	Phase II
NCTO20460E2	avol: mah	Dfiana	Avalumah in B/B DTCI	Dhasa !!
NCT03046953 NCT03493451	avelumab tislelizumab	Pfizer  Beigene / Celgene	Avelumab in R/R PTCL  A Phase 2, Open-Label Study of BGB-A317 in Patients With Relapsed or Refractory Mature T- and NK- Neoplasms	Phase II Phase II
NCT02925000	TLC-178	Taiwan Liposome Company	A Phase I/IIa, Open Label, Dose-escalation Study Investigating the Safety, Tolerability, and Pharmacokinetics of Intravenous Liposomal Vinorelbine Tartrate Injection in Patients With Advanced Malignancy	Phase I/II

Non-exhaustive list (search on the website Clinical Trials.gov of current clinical trials using the key words PTCL, Peripheral T-Cell Lymphoma, and looking at the Pharmaprojects database.



# 4.2.2.2.4 Partnerships

#### **Spectrum Pharmaceuticals.**

As part of a collaboration and licensing agreement entered into in 2010, Spectrum Pharmaceuticals is co-developing Beleodaq® in partnership with the Group and is in charge of its promotion to oncology and hematology experts in the USA.

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

In February 2014, the FDA granted the admissibility of the US registration application for Beleodaq® coupled with a priority review program to allow conditional approval for a drug that treats a life-threatening disease, based 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 the MA from the FDA for the treatment of peripheral T-cell lymphoma. This registration is based on the results of the phase 2 BELIEF clinical trial which included 129 patients with refractory peripheral T-cell lymphoma or in relapse after at least an initial systematic administered treatment. Since August 2014, Spectrum Pharmaceutical teams have started marketing Beleodaq® to hematologists, generating the first sales figures in the second half of 2014, thereby initiating the Group's royalty flow. A second \$25-million milestone payment was paid to the Group in November 2014 following registration of the product by the FDA.

To respond to FDA requirements within the framework of the conditional MA obtained in 2014, Spectrum Pharmaceuticals is preparing a phase 3 clinical trial which would allow for extending the indication of belinostat to first-line treatment of PTCL. Spectrum Pharmaceuticals, as holder of the marketing authorization in the US, will be the sponsor of this study.

First of all, a study evaluating the tolerance of the association Beleodaq® + CHOP was carried out (phase 1) (belinostat plus cyclophosphamide, hydroxydaunorubicine, oncovin, and prednisone) by Spectrum and the results published in December 2015 during the 57th Annual Meeting of the ASH.

Other than the fact that the tolerated maximum dose was found (1000mg/m², i.e. the same dose as the one authorized in single therapy), the Group announced positive results in terms of response with 85% overall response and 67% full response.

The start of this phase 3 clinical trial is still conditional on the carrying out of the same dose and tolerance research study of the association Folotyn + CHOP, with Folotyn being the other Spectrum product in PTCL for which the FDA has also given a conditional MA and which should therefore be included in the same confirming phase 3 as Beleodaq<sup>®</sup>.

On January 17, 2019, Spectrum Pharmaceuticals signed an agreement with the Aurobindo Group and its subsidiary in the US, Acrotech, providing for the sale to Acrotech of several of its hematology / oncology products including Beleodaq®. On March 1, 2019, Spectrum Pharmaceuticals (SPPI) announced the completion of the sale of its seven hematology/oncology products approved by the FDA, including Beleodaq®, to Acrotech Biopharma LLC. The transfer terms of the obligations relating to the Beleodaq® activities between Spectrum Pharmaceuticals and Acrotech are still being finalized. On the date of publication of this document and based on the information provided to date by Spectrum, the Company does not foresee any significant impact of this transaction on the activities and results of Beleodaq® for Onxeo.

# **Pint Pharma**

In 2016, the Company signed a licensing agreement with Pint Pharma for the registration and marketing of Beleodag® in PTCL in Latin America (Argentina, Brazil, Chile, Colombia, Ecuador, Peru, and Venezuela).

This agreement gave rise to an initial payment on signature and provides for payments based on regulatory and revenue milestones, as well as royalties on net sales of Beleodaq®, for a total value greater than \$20 million.

# **Clinigen Group**



In April 2017, Onxeo and Clinigen Group - through its IDIS Managed Access division - joined forces to launch, in Europe, an early access program to a Named Patient Program-type product. This program allows for the use of Beleodaq® on the request of doctors and only for certain named patients, even though the product does not have a marketing authorization. This derogation from the general regime is obviously strictly regulated and only patients who have no other therapeutic option can benefit from this program if their doctor so requests.

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

Partner	Territory	Phase	Amounts already generated by the Group	Total to be generated from the agreement
Spectrum Pharmaceuticals. Licensing and collaboration agreement in 2010*	United States, Canada, Mexico, and India	Marketed in the USA as a 2nd-line treatment for PTCL Undergoing development in other indications	65 million dollars + 1 million Spectrum shares + royalties on sales	320 million dollars + royalties on sales
Pint Pharma Licensing agreement	LATAM (Argentina, Brazil, Chile, Colombia, Ecuador, Peru, and Venezuela	Pre-registration	Initial payment of 3 million dollars generated in 2016	20 million dollars + royalties on sales

<sup>\*</sup> Sale to Acrotech completed March 1, 2019 Please refer to the previous page, para. Spectrum Pharmaceuticals

# 4.2.3 OTHER PRODUCTS

#### 4.2.3.1 *Validive*®

The Group developed Validive® for the treatment of oral mucositis induced by radiotherapy or chemotherapy in patients suffering from a head and neck cancer. This is a new muco-adhesive therapeutic application of clonidine, patented by the Group. Apart from being an agonist of alpha2-adrenergic receptors traditionally used as an anti-hypertensive, clonidine also acts as an agonist of alpha2-adrenergic receptors with an anti-inflammatory effect which was sought-after here.

The Group carried out a randomized clinical Phase II trial, double blind against placebo, comparing the efficacy and tolerance of the mucoadhesive tablet Validive® in doses of  $50\mu g$  and  $100\mu g$ , administered once a day, with that of a placebo in the prevention of severe oral mucositis induced by radiotherapy and/or chemotherapy in 183 patients suffering from a head and neck cancer in post-chemotherapy and post-radiotherapy mucositis. The trial was carried out in Europe and the US and the recruitment of patients was finalized in May 2014.

In terms of efficacy, the phase 2a trial showed a fall in the incidence of severe oral mucositis (grades 3 and 4) in the group of patients treated with Validive® compared to the control group, a delay in terms of the appearance of severe oral mucositis in the patients treated with Validive and no significant difference in terms of efficacy between the Validive® 50µg and Validive® 100µg 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.

The continued development, and particularly the carrying out of a pivotal phase 2 allowing for registration, was entrusted to an American partner to which a global license was granted. It is therefore Monopar Therapeutics (Chicago, Illinois) which will be in charge of the clinical and regulatory activities to complete the development of the product, and of the marketing activities in case of success. The characteristics of the agreement signed between Onxeo and Monopar Therapeutics are summarized in the table below.



Partner	Territory	Phase	Amounts already generated by the Group	Total to be generated from the agreement
Monopar Therapeutics Licensing agreement in 2017	World	Under development	Initial payment of 1 million dollars generated in 2017	108 million dollars + royalties on sales

# 4.2.3.2 Loramyc® / Oravig® et Sitavig®

In July 2017, the Company announced the sale of two historic products, Sitavig® and Loramyc®, to the private laboratory Vectans Pharma which develops and markets innovative therapies for buccal diseases. As part of this transaction, Onxeo sold to Vectans Pharma all the assets associated with the two drugs in question, particularly the patents, regulatory authorizations and pending contracts.

This transaction is part of the company's strategy to refocus on the development of innovative anti-cancer drugs with a high potential for creating value, such as  $AsiDNA^{TM}$ , and allows for the redeployment of financial and human resources in line with this new strategy.



# CORPORATE GOVERNANCE

Some sections of chapters 5 and 7 of the Registration Document constitute the Corporate Governance Report prepared for the financial year 2018 (please refer to the corresponding cross-reference table in Chapter 10). This report was approved by the Board of Directors on March 12, 2019; it was forwarded to the AMF alongside the registration document and is available from the Onxeo website: <a href="https://www.onxeo.com">www.onxeo.com</a>.

This report also covers the composition, conditions for preparing and organizing the work of the Board of Directors during the financial year 2018.

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 factors likely to have an influence in the event of a public offering.

This report was prepared and written in accordance with French law no. 2008-649 of July 3, 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="www.middlenext.com">www.middlenext.com</a>. The Board declares that it has fully taken into account all of the elements of this code in the section "Points de vigilance" (areas of vigilance).

# 5.1 THE BOARD OF DIRECTORS

## 5.1.1 COMPOSITION AND ACTIVITIES 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.

The General Shareholders' Meeting of May 16, 2018 renewed the term of office of Mr. Thomas Hofstaetter.

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.

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

Joseph Zakrzewski Independent Director, Chairperson Judith Greciet Director, Chief Executive Officer

Danièle Guyot-Caparros Independent Director
Thomas Hofstaetter Independent Director
Jean-Pierre Kinet Independent Director
Mr. Jean-Pierre Bizarri Independent Director
Christine Garnier Independent Director
Elvira Sanz Independent Director

Financière de la Montagne SARL Director and shareholder, whose permanent

representative is Mr. Nicolas Trebouta.

The Board of Directors also appointed among its members a senior independent Director, Ms. Danielle Guyot-Caparros. This Director shall ensure that the Company complies at all times with the applicable practices of good governance, 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 French law of January 27, 2011 referring to proportionate gender balance on corporate boards, stipulating that the percentage of members of either sex may not be less than 40% as of January 1, 2017, the Board of Directors has among its members today four women who make up 44% of its members. 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 biotechnology 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 Chapter 5.1.2.1 of this document.

# 5.1.1.2 Missions 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 www.onxeo.com, determine the mission of the Board, its committees and organizes their work.

These rules specify the Board's operating methods and the procedures for implementing 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 fully fulfill its duties:

- (i) The Chief Executive Officer and the Chairman of the Board, as well as the Chairman of each committee, shall be responsible for conveying useful information to other members of the Board;
- (ii) Board and Committee meetings shall be 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 the Directors' decision-making, and in accordance with the law, the Board's rules of procedure authorize the use of video conferencing and teleconferencing systems.

# 5.1.1.3 Organization and report on the Board's activities in 2018

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

- the Audit Committee,
- the Remuneration Committee,
- the Appointments and Governance Committee, and



- the Scientific and Business Development Committee.

# 5.1.1.3.1 The Board's activity report

Five board meetings were held in 2018. The participation rate was 100%.

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 2018:

The Board meeting of March 29, 2018, in particular, approved the separate and consolidated financial statements for 2017, together with the terms of the associated press release. It approved the annual report, the report of the Chairman on corporate governance, internal control and risk management, as well as special reports on the award of stock options or purchase of shares and the bonus shares. The Board examined statutory agreements. It approved the draft resolutions and convened the Annual General Meeting. The minutes of the various committees were presented to the Board. The Board also adopted the Employee option plan 2017-2 and the AGA Plan 2017-2, as well as awarding share and bonus share option plans. It also provided an update on its activity.

The Board meeting of May 16, 2018, in particular, approved the sales figures for Q1 2018, together with the terms of the associated press release and acted on the Company's professional equality and equal pay policy. The minutes of the various committees were presented to the Board. It also provided an update on its activity.

**The Board meeting of July 27, 2018**, in particular, approved the half-yearly financial statements at June 30, 2018 and approved the interim financial report, together with the terms of the associated press release.

## The Board also:

- conducted the semi-annual review of the objectives of the senior management,
- reviewed the achievement of the performance conditions of subscription plans and of the bonus share award plan of July 28, 2017,
- decided on the plans awarding bonus shares and share options to employees of the Onxeo Group and the Chief Executive Officer;
- decided on the issuance of share subscription warrants for non-salaried non-executive Board members;
- recorded the cancellation of securities giving access to capital that took place over the first half of 2018:
- recorded the capital increase resulting from the final acquisition of the bonus shares awarded on June 15 and July 28, 2017, consequently amending the Company's Articles of Association.

The works of the different committees were presented to the Board.

**The Board meeting of October 25, 2018** approved the revenue for Q3 2018, together with the terms of the associated press release.

#### The Board also:

- provided an update on the Company's activities and its financing;
- decided on the issuance of share subscription warrants for non-salaried non-executive Board members;
- recorded the capital increase resulting from the exercise of share options, consequently amending the Company's Articles of Association;
- recorded the cancellation of securities giving access to capital that took place over Q3 2018.

The work of the Appointment and Governance Committee were presented.

## The Board meeting of December 19, 2018:

- approved the 2019 budget,
- recorded the cancellation of securities giving access to capital that took place over Q4 2018,



- determined (i) the variable remuneration of the Chief Executive Officer for 2018 and (ii) the objectives of the Chief Executive Officer and her remuneration for 2019.

The works of the different committees were presented to the Board.

#### 5.1.1.3.2 The 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, one at least of whom must have specific financial or accounting skills and be independent.

The Audit Committee is presently composed of three members: Danielle Guyot-Caparros, who chairs the committee, Joseph Zakrzewski and Nicolas Trebouta, permanent representative of Société Financière de la Montagne. Ms. Judith Greciet, Managing Director, 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

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 July 22, 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 annual and interim financial statements. In 2018, 3 sessions were held with an 89% attendance rate.

The Committee met on **March 21, 2018**, at which time the 2017 consolidated financial statements and the audit of the 2017 accounts were presented and thoroughly reviewed. It also reviewed the new statutory auditor's report, which was prepared in the context of the European audit reform.

During its meeting of **July 24, 2018**, the Committee reviewed all documents related to the half-year results.

During its meeting of **December 14, 2018**, the Committee reviewed the draft budget for 2019 and the Company's short-term financing plan.



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 Remuneration Committee

# Composition

The members of the Remuneration Committee are selected from among Onxeo's directors or outside 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 Remuneration Committee is composed of three members:

Thomas Hofstaetter, who chairs the committee, Elvira Sanz and Nicolas Trebouta, permanent representative of Société Financière de la Montagne. There are thus two independent directors including the chairman. Ms. Judith Greciet, Managing Director, attends the meetings as an invitee of the Audit Committee.

#### Mission

The Remuneration 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 award plans of stock options, share purchase warrants and bonus shares.

## Organization of work

The Remuneration Committee meets at least once a year. In 2018, 3 sessions were held with a 100% attendance rate.

At its meeting of **March 28, 2018**, the Committee reviewed the policy for awarding share options, bonus shares and share subscription warrants, with a view to fostering the teams' loyalty in the face of the significant challenges faced by the Company over the period 2018-2019.

At its meeting on **July 25, 2018**, the Committee reviewed the attainment of the performance conditions of the 2018 share option and bonus share award plans for employees and the Chief Executive Officer.

It examined the conditions for awarding new share options and bonus shares to executives and employees of the Group. The Committee also reviewed the conditions of the warrant plan for non-salaried non-executive Board members of the Company.

At its meeting on **December 18, 2018**, the committee examined the variable remuneration of the Chief Executive Officer for 2018 and her objectives for 2019. It also discussed the Chief Executive Officer's remuneration for FY 2019. Finally, it reviewed the principles of distributing directors' fees for the financial year 2019.

# 5.1.1.3.4 Appointments and Governance Committee

# Composition

The members of the Appointments and Governance Committee are selected from among Onxeo's Directors or outside 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 Appointments and Governance Committee is composed of four members: Danièle Guyot-Caparros, who chairs the committee, Christine Garnier, Jean-Pierre Bizzari and Jean-Pierre Kinet. It is made up of four independent Directors, including its Chairman. An additional member may be appointed on a temporary basis to the Appointments and Governance Committee if his/her profile is



suited to the subject at hand. Ms. Judith Greciet, Managing Director, attends the meetings as an invitee of the Audit Committee.

#### Mission

The Appointments and Governance Committee's mission 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 shall be 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';
- Examining potential conflicts of interest;
- 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, with Management, the profiles of candidates for a position on the Executive Committee and participating, if necessary, in the interview process.

# Organization of work

The Appointments and Governance Committee meet in an ad hoc manner, but at least once a year. In 2018, it held 1 session with a 100% attendance rate.

# 5.1.1.3.5 The Scientific Business Development Committee

# Composition

The Scientific and 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 is composed of Thomas Hofstaetter who chairs the committee, Elvira Sanz, Christine Garnier, Jean-Pierre Bizzari and Jean-Pierre Kinet. There are thus five independent directors, including the Chairman. Ms. Judith Greciet, Managing Director, attends the meetings as an invitee of the Audit Committee.

# Mission

The Scientific and Business Development Committee supports and assists the executive management on acquisition projects and strengthening the product pipeline, sale or licensing agreements, as well as the Company's strategic direction.

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, assess and evaluate the strategic plan proposed by the Chief Executive Officer to the Board of
  Directors including the research program issues and the associated strategic choices with regard to
  the external and internal business context,
- investigate, 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 on investments belonging to the Company.

## Organization of work

The Scientific and Business Development Committee meets at least once a year. In 2018, it held two sessions with an 80% participation rate.

# 5.1.1.4 Assessment of the Board of Directors



In accordance with recommendation No 11 of the Middlenext corporate governance code to which the Company adheres, once a year, the Chairman of the Board requests that each member expresses their opinions on the Board's functioning and the preparation of its work.

Further to the entry of two new members, the evaluation made in 2018 allowed the Board to review and change the organization of the specialized committees, particularly with the creation of a scientific and business development committee. The Board also recognized the general satisfaction with the level of preparation for meetings, the quality of discussions in it and the effectiveness of the decision-making processes.

## 5.1.2 INFORMATION ON DIRECTORS

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

Excluding Ms. Judith Greciet, also CEO of the Company, no board member exercises any executive or salaried function for Onxeo or for any company directly or indirectly controlled by Onxeo.

No family relationship exists between any Board members. No Director has been sentenced for fraud, none has been involved in a management 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 offices and/or functions of the directors indicated below are on the basis of the declarations of the interested parties. The Company specifies that it may not be held liable for the information provided by the directors or corporate officers.

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# 5.1.2.1 Corporate offices

At the time of the Registration Document, the Board of Directors is composed of the following members: The terms of office are indicated to the Company's best knowledge.

Director	Terms of Office and Functions
Joseph Zakrzewski	Within the Company
Joseph Zakrzewski serves as Chairman of Onxeo since January 22, 2016. His term of office will expire at the 2019 General	
Shareholders' Meeting.	<ul> <li>Outside the Company</li> <li>Director of Acceleron Pharmaceuticals Inc. (USA)</li> </ul>
Born December 30, 1962, Mr. Zakrzewski has over 25 years of experience in the biotechnology and the pharmaceutical industries. He is a member of the Board of	<ul> <li>Director of Amarin Pharmaceuticals Inc. (USA)</li> <li>Director of Sangamo Therapeutics (USA)</li> </ul>
Directors of several listed and unlisted companies. He advises many entities, and also	
engages in various philanthropic activities.  Mr. Zakrzewski was a Venture Partner in 2010 and 2011 at OrbiMed, the largest fund dedicated to health in the world. From 1988 to 2004, Mr. Zakrzewski held various positions at Eli Lilly & Company, especially in R&D, production, finance, and business development for the biotechnology and protein divisions.	<ul> <li>5 years and no longer performed</li> <li>Director of Liposcience Inc. (USA)</li> <li>Director of I Corporation (USA)</li> <li>Director of Insulet Corporation (USA)</li> </ul>
Business address 715 Street Road, New Hope, PA 18938 United States	



Director	Terms of Office and Functions
Judith Greciet  Judith Greciet joined Onxeo on March 1, 2011, as Chief Operating Officer in charge of R&D and Operations. She has been Managing Director and a Director of the company since June 29, 2011. Her term of office will expire at the 2020 General Shareholders' Meeting.  Born on 10/27/1968, Judith Greciet's career has been spent in various laboratories (including Eisai, Zeneca, and Wyeth), occupying important managerial and strategic international positions in the growing field of oncology and immunology, and working on innovative products. She has a doctorate in Pharmacy and is a graduate in business administration and pharmaceutical marketing.  Business address Onxeo 49, Boulevard du Général Martial Valin 75015 Paris	<ul> <li>President of Onxeo Inc. (United States)</li> <li>Other directorships and positions held over the past previous</li> <li>5 years and no longer performed</li> <li>Director of Theravectys SA, France</li> <li>Chairperson of Laboratoires BioAlliance Pharma SA</li> </ul>



Director	Terms of Office and Functions
Danièle Guyot-Caparros	Within the Company
Danielle Guyot-Caparros has been a Director of Onxeo since June 26, 2013. Her term of office will expire at the 2019 General Shareholders' Meeting.	<ul> <li>Director of Onxeo SA</li> <li><u>Outside the Company</u></li> <li>Director of Supersonic Imagine SA (France)</li> </ul>
Danielle Guyot-Caparros was born October 16, 1958. After working for 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.	Other directorships and positions held over the past previous  5 years and no longer performed  • Member of the Supervisory Board of Diaxonhit SA (France)
Chief Life Sciences Adviser for Deloitte since 2008, she has a Masters in Financing / Accountancy and a DECF (diplôme d'expertise comptable—degree in accountancy).	
Business address 4, rue d'Eblé 75007 Paris France	



#### **Christine Garnier**

Christine Garnier has been a Director of Onxeo since April 26, 2017. Her term of office will expire at the 2020 General Shareholders' Meeting.

Born February 28, 1961, Christine Garnier is co-founder of the firm AEC Partners and has been Managing Partner since 1998. A graduate of ESCP Europe, her consultant activity is specialized in corporate, international and operational strategies, evolutions in business models organizations, and the optimization of performance across the life science industry. During the last twenty years, Christine Garnier has managed more than 200 assignments on primary and specialty care products, vaccine products, as well as medical devices and OTC. She assists executive committees and operational and functional management in the development of vision, their strategies and changes to their organizations. The scope of her activity is centered on Europe and fast developing countries (South East Asia, Latin America, etc.) as well as international and corporate headquarters. She provides her clients with expertise in strong strategy organization, coupled with her skill to identify and initiate necessary transformations. Before joining Partners, Christine Garnier previously worked for 12 years in the pharmaceutical industry holding marketing positions in Wyeth and international marketing and strategic planning at Rhône Poulenc Rorer.

# **Business address**

AEC Partners 27 avenue Pierre 1er de Serbie 75116 Paris France

# **Terms of Office and Functions**

# Within the Company

• Director of Onxeo SA

## Outside the Company

- Managing director of AEC General Partners
- Managing director of AEC Limited
- Director of AEC Asia

Other directorships and positions held over the past previous

# 5 years and no longer performed

None

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# **Elvira Sanz Urgoiti**

Elvira Sanz has been a Director of Onxeo since April 26, 2017. Her term of office will expire at the 2020 General Shareholders' Meeting.

Born on April 10, 1959, Elvira Sanz is a Doctor in Pharmacy who graduated from the Complutense University of Madrid, with Extraordinary Prize of End of Career and graduated with an International MBA from the Business School ESDEN, first in her class. She has undertaken postgraduate courses at prestigious universities and international business schools, such as the Harvard Business School and Wharton University.

She has extensive experience in the pharmaceutical industry which she has accumulated over 25 years, starting as a Research Scientist and occupying positions of growing responsibility across different business areas for MSD, Roche and Cyanamid. In 1994, she joined Wyeth Farma as Director of Registrations and New Products. In 1996, she was appointed as Marketing Director and subsequently, in 1998, Deputy Director General until 2000, when she was appointed as Director General for Spain. In 2005, she joined Wyeth's US headquarters to develop a global project, reporting to the CEO of the company, for the restructuring of Wyeth's affiliates at global level. In 2007, she returned to Spain as General Director for Spain and Portugal. Following the acquisition of Wyeth by Pfizer in October 2009, she was named President and Director General, a position she held until 2015.

Business address Bolonia 1 28028 Madrid Spain

# **Terms of Office and Functions**

#### Within the Company

• Director of Onxeo SA

# Outside the Company

- Administration Board member "Universidad Europea de Madrid"
- Board member "Save the Children"

# Other directorships and positions held over the past previous 5 years and no longer performed

- President Pfizer SL
- President Pfizer GEP SL
- President Laboratorios Parke Davis SL
- President Wyeth Farma SA
- President Vinci Farma SA
- President Hospira Invicta SA
- President Pharmacia Nostrum SA
- President Binesa 2002 SL
- Board member Zoetis Spain SL



Director	Terms of Office and Functions
Thomas Hofstaetter  Thomas Hofstaetter has been a director of Onxeo since May 31, 2012. His term of office will expire at the 2021 General Shareholders' Meeting.	<ul> <li>Within the Company</li> <li>■ Director of Onxeo SA</li> <li>Outside the Company</li> <li>■ None</li> </ul>
Born on June 4, 1948, Thomas Hofstaetter holds a doctorate in molecular biology from the University of Tubingen, Germany. He has over thirty years' experience in corporate development and mergers and acquisitions of pharmaceutical and biotechnology companies, particularly with Wyeth, Inc., Aventis, VaxInnate Corporation and Geron Corporation.	<ul> <li><u>5 years and no longer performed</u></li> <li>Director of Bionor Pharma ASA, Norway</li> </ul>
Business address: Thomas Hofstaetter Lindenstr. 37 60325 Frankfurt, Germany	

# Financière de la Montagne, represented by Nicolas Trebouta

Financière de la Montagne has been a director since June 29, 2011. Its term of office will expire at the 2020 General Shareholders' Meeting.

Born on May 29, 1963, Nicolas Trebouta, has managed investments since 2004 directly through his company, Financière de la Montagne, or through biotech funds. Cofounder of Chevrillon and Associates in 2000, he participated via this organization in several LBO operations including Picard Surgelés, the printer CPI, and Albingia Insurance. He is a medical doctor and has been a shareholder of Onxeo since 2008.

# **Business address**

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

#### **Terms of Office and Functions**

# Within the Company

• Director of Onxeo SA

## Outside the Company

- Manager of Financière de la Montagne SARL
- Manager of the SCI Fleurus Immobilier
- Manager of the SCI 5 rue de la Liberté
- Chairman of the SAS Dragon 8
- Managing partner of the SC Financière des Associés
- Director of the GIE IO
- Chairman of the Supervisory Board of the SCA Chevrillon & Associés
- Manager of the EARL Ferme de Bissy
- Managing Partner of the SC Valois
- Manager of the SCI du Trillon
- Representative of FDM, director of Onxeo (formerly Bioalliance)
- Manager of the SC Aster
- Manager of the SCI du Chardonnet

# Other directorships and positions held over the past previous 5 years and no longer performed

 Chairman & CEO of the SICAV Mercure Epargne Longue (dissolved in May 2014)



# Jean-Pierre Bizzari

Jean-Pierre Bizzari has been a Director since April 6, 2016. His term of office will expire at the 2019 General Shareholders' Meeting.

Born October 29, 1954, Doctor Jean-Pierre Bizzari was Executive Vice President and Director of clinical development in Oncology for the United States, Europe, Asia and Japan for Celgene from 2008 to 2015. He participated in the clinical development of several anti-cancer agents such Taxotere®, Eloxatin® and Abraxane®, and Irinotecan® (CPT-11). A world-renowned Oncology expert, he is a member of the Scientific Advisory Council of the National Institute of Cancer (INCa), of the European Organization for Research and Treatment of Cancer (EORTC), and President of the New Drug Advisory Committee. Dr. Bizzari is also an active member of the Board of Directors of several biotechnology companies in France and the United States. He has published over 70 articles in reputable scientific journals and presented more than 160 "abstracts" at scientific congresses.

Business address 100 St Georges Road Unit 4A Ardmore. 19003. PA. USA

# **Terms of Office and Functions**

## Within the Company

· Director of Onxeo SA

#### Outside the Company

- Director of Transgene SA (France)
- Director of Halozyme Therapeutics, Inc. (USA)
- Director of Pieris Pharmaceuticals, Inc. (USA)
- Director of Nordic Nanovector ASA (Public, Norway)
- Director of Oxford BioTherapeutics Ltd (UK)
- Director of European Organisation for Research and Treatment of Cancer (EORTC)

# Other directorships and positions held over the past previous 5 years and no longer performed

- Director of Celator Pharmaceuticals (USA)
- Director of iTeos Therapeutics (Private, Belgium)



#### Jean-Pierre Kinet

Jean-Pierre Kinet has been a Director since April 6, 2016. His term of office will expire at the 2019 General Shareholders' Meeting.

Born October 23, 1953, Professor and Doctor Jean-Pierre Kinet is one of the world's most prominent experts in Immunology, mostly known for having discovered several genes and proteins constituting immunoglobulin E-receptors. His scientific discoveries have helped introduce therapies and new diagnostic tools for the treatment of diseases related to the deregulation of the immune system. He is also co-founder and founder of two biotechnology companies and member of the Board of Directors of several other European biotechnology companies. Dr. Kinet is Professor of Pathology at Harvard Medical School in Boston, USA. Jean-Pierre Kinet is also a Scientific member of the Advisorv Committee of UCB Pharma and Managing Partner at iX Life Capital.

# Business address 1950 chemin des Lauves 13100 Aix en Provence France

## **Terms of Office and Functions**

#### Within the Company

• Director of Onxeo SA

# Outside the Company

- Director of AB Science SA (France)
- Director of Pharmaleads SA (France)
- Chairman of Board of directors of Vaxon SA (France)
- Chairman of Ixlife Capital SAS (France)
- Member of the Board of the Harvard Institute of RNA Medicine (HIRM)
- Member of the Board of the Harvard-associated BIDMC Cancer Center

# <u>Other directorships and positions held over the past previous 5 years and no longer performed</u>

- Chairman of board of directors of Theravectys SA (France)
- Director of UCB Pharma SA (Belgium)

# 5.1.2.2 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 term of office, 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.

As far as the Company is aware, on the date of the Registration Document, there is no conflict of interest between the duties, with regard to the Group, of the members of the Board of Directors and their private interests and/or other duties.

# 5.1.2.3 Independence

On the date of the Registration Document, the Company considers it has seven independent directors within the meaning of the Middlenext Code. These are Danièle Guyot-Caparros, Thomas Hofstaetter, Joseph Zakrzewski, Jean-Pierre Kinet, Christine Garnier, Elvira Sanz Urgoiti and Jean-Pierre Bizzari.

# 5.1.2.4 Directors' remuneration



The remuneration of corporate officers 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 through stock options and bonus shares awarded for loyalty purposes.

Corporate officers receive no directors' fees for their position.

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 with respect to the remuneration of executives who are corporate officers of companies whose shares are admitted for trading on a regulated market.

Furthermore, in 2018 the Board of Directors decided to award 359,500 share subscription warrants to directors who are not employees or senior managers of the Company. The characteristics of these share subscription warrants are described in table 8 of section 5.2.2 of this Registration Document.

Directors' fees and other remu	neration receive	d by non-executi	ve corporate offic	cers	
Non-executive corporate officers		or FY 2018 eetings and ee meetings	Amounts for FY 2017 10 board meetings and 11 committee meetings		
	Directors' fees in € <sup>(1)</sup>	Other remuneration	Directors' fees in €	Other remuneration	
Joseph Zakrzewski	37,000	104,500 warrants	74,000	60,000 warrants	
Danièle Guyot-Caparros	10,950	42,500 warrants	23,900	40,000 warrants	
Thomas Hofstaetter	13,950	42,500 warrants	25,900	40,000 warrants	
Financière de la Montagne, represented by N. Trebouta	N/A	85,000 warrants	N/A 40,00 warra		
Jean-Pierre Kinet	9,450		19,400	-	
Jean-Pierre Bizzari	8,200		20,900	40,000 warrants	
Christine Garnier	10,450	42,500 warrants	17,310	40,000 warrants	
Elvira Sanz	11,450	42,500 warrants	18,310	40,000 warrants	
Russell Greig <sup>(2)</sup>	N/A	N/A	5,590	-	
David Solomon <sup>(2)</sup>	N/A	N/A	4,590	-	
TOTAL	101,450	359,500 warrants	209,900	300,000 warrants	

<sup>(1)</sup> By decision of the Board of Directors, only 50% of the attendance fees owed to non-executive corporate officers were paid in 2018, with payment of the balance being deferred and dependent on whether Onxeo obtains significant financing

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

# 5.1.2.5 Agreements with the main shareholders, customers or suppliers

<sup>(2)</sup> Terms of office terminated at the Combined General Meeting of April 26, 2017



As far as the Company is aware, there is no pact or agreement entered into with the main shareholders, customers or suppliers of the Group, under which a director was selected as a member of a management body, executive board or supervisory board or as a member of the senior management.

# 5.1.2.6 Restrictions accepted by the Company's corporate officers on the sale of their equity interest

As far as the Company is aware, on the date of the Registration Document there is no restriction accepted by the Company's corporate officers concerning the sale of their equity interest in the capital of the Company.

5.1.2.7 Information on service contracts involving members of the administrative, management and supervisory bodies of the Company or of any of its subsidiaries

There is no service contract binding members of the administrative, management and supervisory bodies to the Company or to one of its subsidiaries.

# 5.2 THE EXECUTIVE BOARD

As of the date of this registration document, the general 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.

# 5.2.1 LIMITATIONS IMPOSED BY THE BOARD ON THE POWERS OF THE CEO AND DEPUTY CEOS

The Board's rules of procedure, which are available on the company's website, set out the terms of exercise of the CEO's functions.

The Managing Director and the Chief Operating Officer cannot adopt certain measures or certain acts, 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 MANAGEMENT MEMBERS

The remuneration of executive management 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 through stock options and bonus shares awarded for loyalty purposes.

Members of the Executive Management are not paid directors' fees for their duties 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 Code of Corporate Governance regarding the remuneration of executive officers of companies whose shares are admitted to trading on a regulated market.

## **Judith Greciet**

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

Judith Greciet's annual fixed gross pay was set at €310,590 for the year 2018 by the Board of Directors on December 20, 2017 on the proposal and recommendation of the Appointments and Remuneration Committee.

On December 20, 2017, the Board of Directors also decided that the variable remuneration of the Chief Executive Officer would in principle represent up to 50% of the fixed salary, and that for FY 2018 it would be subject to the achievement of objectives related to research and development activities, the structuring of the corporate strategy, finance and the quality of investor relations and the organization of the Company.

After a review of the objectives for 2018, the Board on December 19, 2018 evaluated the achievement of these objectives at 100% allowing the determination of Judith Greciet's variable compensation for 2018 at a package weighed by an internal coefficient of 25% for the Company, i.e. €39,600.23, after approval by the General Shareholders' Meeting that will be held in 2019.

In 2018, Ms. Judith Greciet received no attendance fees in accordance with the rules set out in the preceding paragraphs and did not receive any other instruments providing access to capital, except for the award of stock options.

Judith Greciet did not receive any benefits in kind in 2018 other than a company car.

Onxeo considers that it complies with the recommendations of the MiddleNext Code concerning the remuneration of directors and executive directors of companies whose shares are admitted to trading on a regulated market.

The tables relating to the recommendation of the Financial Markets Authority No 2014-14 "Guide to the preparation of registration documents adapted to average values" are presented below.

Table 1

Summary table of remuneration, options and shares awarded to each executive officer (in €)								
Judith Greciet - Chief Executive Officer	Financial Year 2018	Financial Year 2017						
Remuneration payable in respect of the financial year (broken down in Table 2)	359,379	394,533						
Value of options awarded during the year	37,854	53,200						
Value of performance shares awarded during the year	153,448	202,276						

Table 2

Summary table of remuneration of each senior executive company officer (in euros)



Judith Greciet - Chief	Amounts for fina	incial year 2018	Amounts for financial year 2017			
Executive Officer	owed	paid (1)	owed	paid (1)		
- Fixed remuneration (2)	316,801	316,801	313,738	313,738		
- Variable remuneration (3)	39,600 77,648		77,648	76,125		
- exceptional remuneration	N/A	N/A	N/A	N/A		
- Directors' fees	N/A	N/A	N/A	N/A		
Benefits in kind (4):	2,978	2,978	3,147	3,147		
TOTAL	359,379	397,427	394,533	393,010		

- (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 compensation is based on the achievement of objectives related to R&D, corporate strategy, financial management, the share price, investor relations and the organization of the company; it should be noted that the variable remunerations for 2017 and 2018 were paid partly in performance shares and/or share subscription options (see tables 4 & 6 below)
- (4) Company car

Table 3

Directors' fees and other remu	neration received	d by non-executi	ve corporate offic	ers	
Non-executive corporate officers	Amounts f 5 board me 9 committe	eetings and	Amounts for FY 2017 10 board meetings and 11 committee meetings		
	Directors' fees in € <sup>(1)</sup>	Other remuneration	Directors' fees in €	Other remuneration	
Joseph Zakrzewski	37,000	104,500 warrants	74,000	60,000 warrants	
Danièle Guyot-Caparros	10,950	42,500 warrants	23,900	40,000 warrants	
Thomas Hofstaetter	13,950	42,500 warrants	25,900	40,000 warrants	
Financière de la Montagne, represented by N. Trebouta	N/A 85,000 warrants		N/A	40,000 warrants	
Jean-Pierre Kinet	9,450		19,400	-	
Jean-Pierre Bizzari	8,200		20,900	40,000 warrants	
Christine Garnier	10,450	42,500 warrants	17,310	40,000 warrants	
Elvira Sanz	11,450	42,500 warrants	18,310	40,000 warrants	
Russell Greig <sup>(2)</sup>	N/A	N/A	5,590	-	
David Solomon <sup>(2)</sup>	N/A	N/A	4,590	-	
TOTAL	101,450	359,500 warrants	209,900	300,000 warrants	

<sup>(1)</sup> By decision of the Board of Directors, only 50% of the attendance fees owed to non-executive corporate officers were paid in 2018, with payment of the balance being deferred and dependent on whether Onxeo obtains significant financing

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<sup>(2)</sup> Terms of office terminated at the Combined General Meeting of April 26, 2017



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

During FY 2018, 84,000 share options (SO) were awarded to Judith Greciet in her capacity as Executive Corporate Officer. Half of these options shall be exercisable on June 30, 2019, the other half on June 30, 2020, subject to the fulfillment of performance conditions evaluated one year after their award that relate (i) to the progress of the Company's key programs for 40% of the options, (ii) the negotiation of a strategic agreement (financing and/or industrial) for 40% of the options, (iii) the performance of the stock market price for 10% of the options and (iv) the Company's financing and organization for 10% of the options.

In addition, 66,723 subscription options (SO) were awarded to Judith Greciet, corresponding to 66% of 75% of her variable remuneration for the financial year 2018. Exercise of these options is subject to Judith Greciet being at the Company at June 30, 2019 and to the achievement of the performance conditions evaluated one year following their award.

Stock options to purchase or subscribe for shares awarded during the financial year to each corporate officer								
Name of the corporate officer	Award date	Nature of the options	Valuation of the warrants according to the Black & Scholes method (in euros)	Number of options awarded during the year	Exercise price	Expiry date		
Judith Greciet	07/27/2018	Stock options	37,854	150,723	1.187	07/27/2028		
TOTAL				150,723				

Table 5 – Share 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 2018.

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

During FY 2018, 140,778 performance shares (AGA) were awarded to Judith Greciet in her capacity as Executive Corporate Officer, broken down into:

- 65,416 AGA corresponding to the amount of her variable remuneration for FY 2017 paid in cash, to be permanently acquired on July 27, 2019, subject to a retention period that expires on July 27, 2020;
- 33,362 AGA corresponding to 25% of the theoretical variable remuneration for the financial year 2018, which will be acquired on June 30, 2019, subject to fulfillment of the performance conditions.
- 42,000 AGA as part of the 2018 award plan, to be acquired on June 30, 2019, subject to a retention period that expires on June 30, 2020, subject to the achievement of the performance conditions. The performance conditions relate to (i) the progress of the Company's key programs for 40% of the options, (ii) the negotiation of a strategic agreement (financing and/or industrial) for 40% of the options, (iii) the performance of the stock market price for 10% of the options and (iv) the Company's financing and organization for 10% of the options



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

A total of 46,322 performance shares (AGA) were awarded to Judith Greciet in her capacity as Executive Corporate Officer and vested in the financial year 2018.

# Table 8 – History of the award of warrants and share options

As part of its policy of remunerating and motivating its executives and employees, Onxeo regularly implements plans for awarding warrants and bonus share.

Independent members of the Board also benefit from successive plans awarding share subscription warrants (BSA). As of 2014, these awards were extended to all Directors not having the status of officers or employees of the Company.

Whether for share options or warrants, the exercise price is determined as the average over the last twenty trading days preceding the award date.

The conditions for exercising the options and warrants awarded to executives and corporate officers that were outstanding at December 31, 2018 are described in Table 8 below.



History of the award of financial instruments granting rights to the share capital Information on warrants and stock options (SO) awarded to executive officers								
	SO Dir. 2011	SO Dir.2012	SO Dir.2014	SO Dir.2015	SO Dir.2016	SO Dir.2017	SO Dir.2018	
Date of GM	06/29/2011	05/31/2012	06/30/2014	05/20/2015	04/06/2016	05/24/2017	06/19/2018	
Date of Board of Directors meeting	09/21/2011	09/13/2012	09/22/2014	10/27/2015	07/28/2016	07/28/2017	07/27/2018	
Exercise terms		Award	· · · · · · · · · · · · · · · · · · ·	share to performance cond	ditions		(2)	
Shares awarded to executive corporate officers (Judith Greciet) (1)	167,453	62,537	26,027	60,000	70,000	70,000	150,723	
Start date for exercise	09/21/2015	09/13/2016	09/22/2018	10/27/2016	07/28/2017	07/28/2018	(2)	
Expiry date	09/21/2021	09/13/2022	09/22/2024	10/27/2025	07/28/2026	07/28/2027	07/28/2028	
Subscription price <sup>(1)</sup>	3.63	3.75	6.17	3.61	3.16	4.00	1.187	
Shares subscribed at 12/31/2018	0	0	0	0	0	0	0	
Cancelled or lapsed shares	0	6,030	7,156	0	14,000	7,000	0	
Options remaining at 12/31/2018 <sup>(1)</sup>	167,453	56,507	18,871	60,000	56,000	63,000	150,723	

<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 July 28, 2011, November 14, 2013 and January 22, 2015)

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<sup>(2)</sup> Of the 150,723 share options awarded in 2018: a) 66,723 were awarded under the 2018 bonus to foster loyalty. Their terms of exercise are on a one option for one share basis. The exercise of these options is subject to Judith Greciet being at the Company at June 30, 2019, subject to the achievement of performance conditions evaluated one year after their award; b) 84,000 were awarded as part of the 2018 award plan. Their terms of exercise are on the customary one option for one share basis, half on June 30, 2019 and the other half on June 30, 2020, subject to the achievement of performance conditions evaluated one year after their award and relating to (i) the progress of the Company's key programs for 40% of the options, (ii) the negotiation of a strategic agreement (financing and/or industrial) for 40% of the options, (iii) the performance of the stock market price for 10% of the options and (iv) the Company's financing and organization for 10% of the options.

# Corporate Governance



# Table 8 (continued)

	Warrants 2013	Warrants 2014-1	Warrants 2014-2	Warrants 2015-1	Warrants 2015-2	Warrants 2016-1	Warrants 2016-3	Warrants 2017	Warrants 2018-	Warrants 2018- 2
Date of GM	06/29/2013	06/30/2014	06/30/2014	05/20/2015	05/20/2015	04/06/2016	04/06/2016	05/24/2017	06/19/2018	06/19/2018
Date of Board of Directors meeting	09/19/2013	09/22/2014	03/04/2015	10/27/2015	01/22/2016	07/28/2016	12/21/2016	07/28/2017	07/27/2018	10/25/2018
Exercise terms 1 warrant/ 1 share – Award over 18 months								1 warrant/1 share	1 warrant/1 share	
Shares able to be subscribed by corporate officers (1) (2)	88,490	85,886	19,000	65,000	90,000	160,000	52,500	300,000	274,500	85,000
Of which Joseph Zakrzewski	-	-	-	-	90,000	50,000	17,500	60,000	62,000	42,500
of which Thomas Hofstaetter	15,616	13,013	0	15,000	0	20,000	0	40,000	42,500	0
of which Danielle Guyot-Caparros	15,616	13,013	0	0	0	0	0	40,000	42,500	0
Of which Jean-Pierre Bizarri	-	-	-	-	-	30,000	17,500	40,000	0	0
Of which Jean-Pierre Kinet	-	-	-	-	-	30,000	0	0	0	0
of which Financière de la Montagne	-	13,013	5,500	15,000	0	30,000	17,500	40,000	42,500	42,500
Of which Christine Garnier	-	-	-	-	-	-	-	40,000	42,500	0
Of which Elvira Sanz	-	-	-	-	-	-	-	40,000	42,500	0
of which Patrick Langlois	26,026	20,821	8,000	5,000	0	-	-	-	-	-
of which David Solomon	15,616	13,013	5,500	15,000	0	0	0	-	-	-
of which Russell Greig	15,616	13,013	0	15,000	0	0	0	-	-	-
Starting date for exercise of BSAs	03/19/2014	03/22/2015	09/04/2015	04/27/2016	01/22/2016	01/28/2017	06/21/2017	04/28/2018	06/30/2019(3)	06/30/2019(3)
Expiry date	09/19/2023	09/22/2024	03/04/2025	10/27/2025	01/22/2026	07/28/2026	12/21/2026	07/28/2027	07/27/2028	10/25/2028
Issue price	€ 0.40	€ 0.64	€ 0.63	€ 0.36	€0.33	€0.26	€0.24	€ 0.20	€ 0.12	€ 0.10
Subscription price <sup>(1)</sup>	€ 3.85	€ 6.17	€ 6.26	€ 3.61	€3.33	€3.16	€2.43	€ 4.00	€ 1.187	€1.017
Shares subscribed at 12/31/2018	0	0	0	0	0	0	0	0	0	0
Total BSAs cancelled or lapsed	0	0	0	0	0	0	0	0	0	0
Warrants outstanding at end of period (1)	88,490	85,886	19,000	65,000	90,000	160,000	52,500	300,000	274,500	85,000

<sup>(1) (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 July 28, 2011, November 14, 2013 and January 22, 2015)

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- (2) The Board Meeting of October 24/25, 2016 issued, at the price of €0.26 each, 30,000 BSA in favor of two key consultants of the Company, out of which 30,000 were actually subscribed by their holders (authorization given by the General Meeting of April 6, 2016). Each warrant gives the right to subscribe to one share at the price of €2.61 each. Please refer to paragraph 7.1 and to Appendix 2 of this report.
- (3) The warrants may be exercised from June 30, 2019, provided that the beneficiary is still exercising the functions of a member of the Company's Board of Directors at that date and has attended at least 75% of the Board's meetings as at that date.



Table 9 – Share options granted during the financial year to the top ten non-executive employees or exercised by them.

Options to subscribe for or purchase shares awarded to the top ten employees other than corporate officers receiving the largest number of options	Number of options awarded	Weighted average price	Plan
Options granted during the year to the ten employees other than corporate officers receiving the largest number of options granted (overall data)	321,142	€ 1.187	2018 SO Employee Plan
Options granted during the year to the ten employees other than corporate officers receiving the largest number of options granted (overall data)	157,142	€ 1.187	2018 SO Exceptional Bonus Plan

Table 10

Executive Officers	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								
Chief Executive Officer since 06/29/2011 In office since: 06/29/2011 End of term: General Meeting called to approve the financial statements for the year ending on 12/31/2019		x	x			x		x

During the Board meeting of May 21, 2014 and on the proposal of the Appointments and Remuneration Committee dated May 16, 2014, the Board approved the suspension of the employment contract of Judith Greciet with effect from July 1, 2014 for the duration of her term of office as Chief Executive Officer.

Commitments of all kinds corresponding to elements of remuneration, indemnities or benefits due or that could be due by the Company with regard to the assumption of duties, the termination of duties or a change in duties of the executive officers or after such event: There are no such commitments in the Group that are subject to the procedure provided for in Article L 225-42-1 of the French Commercial Code.

During the year ended December 31, 2018, the Company did not award any equity or debt securities to its managers.

In accordance with the provisions of Articles L. 225-197-1 and L. 225-185 of the French Commercial Code, the Board of Directors, on the recommendation of the Remuneration Committee, set the percentage of shares (shares awarded or shares resulting from the exercise of share options) that the executive officers of Onxeo have the obligation to hold as registered shares until the termination of their duties. This percentage was set at 10% of the capital gains net of tax and related contributions obtained by the exercise of options.

In addition, the Onxeo Group's pension liabilities for executive officers at December 31, 2018 amounted to €102,245 (IFRS consolidated financial statements).



# 5.3 APPROVAL OF THE ELEMENTS OF THE COMPENSATION PACKAGE DUE OR ALLOCATED FOR THE FINANCIAL YEAR 2018 TO THE CHAIRMAN AND TO THE CHIEF EXECUTIVE OFFICER

Pursuant to the provisions of Article L. 225-100 (II) of the French Commercial Code, the elements of the fixed, variable and extraordinary compensation allocated or still to be allocated for the financial year 2018 to the Chairman and to the Chief Executive Officer for performing their term of office, as determined by the Board of Directors pursuant to the principles and criteria approved by the General Shareholders' Meeting of the Company of May 16, 2018 under its ninth and tenth resolutions and detailed in paragraph 5.2.2 of this Registration Document, shall be submitted for the approval of the shareholders during the General Meeting called to approve the financial statements of the financial year 2018.

5.4 PRINCIPLES AND CRITERIA FOR THE DETERMINATION, ALLOCATION,
AND ASSIGNMENT OF THE FIXED, VARIABLE, AND EXCEPTIONAL
ELEMENTS THAT MAKE UP TOTAL COMPENSATION AND BENEFITS OF
ANY KIND DUE TO THE CHAIRMAN AND CHIEF EXECUTIVE OFFICER FOR
THE FINANCIAL YEAR 2018

Pursuant to Article L. 225-37-2 of the French Commercial Code, the Board of Directors submits for the General Meeting's approval the principles and criteria for the determination, allocation, and assignment of the fixed, variable, and exceptional elements that make up total compensation and benefits due to the Chairman and Chief Executive Officer for the exercise of their duties during the 2018 financial year, thus constituting their remuneration policy.

These principles and criteria determined by the Board of Directors upon the recommendation of the Remuneration Committee are presented below.

Pursuant to article L. 225-100 of the French Commercial Code, the amounts determined in accordance with the implementation of said principles will be submitted for approval to the shareholders during the General Meeting that is to vote on the accounts for financial year 2018.

#### Remuneration policy of corporate officer directors

The remuneration of corporate officer directors is composed of fixed remuneration potentially supplemented by a benefit in kind (in general a company car) and variable remuneration including an annual part, fixed in accordance with annual performance criteria and which corresponds to a percentage of the fixed remuneration and part in the form of equity interest instruments, whose distribution is also subject to performance criteria and dependent on the vote of the shareholders at the General Meeting.

The remuneration is voted on by the Board of Directors every year, based on a proposal of the Remuneration Committee, which takes into account the level and the difficulty of the responsibilities, experience, the business area and the sector-based practices, internationally, through survey or benchmark of the sector.

Further, the salary increase takes account of the expected rate of inflation, sector trends and the financial budget of the Company.

At the start of the year, the Board also determines the annual objectives of the corporate officer directors, fixed in accordance with the strategic and operational plan decided upon in the Board. More qualitative objectives may also be determined. The achievement of those objectives is discussed in the Remuneration Committee each year-end, which proposes its evaluation to the Board of Directors. This evaluation may be between 0 and 135% achievement of the objectives, which then weight the expected percentage of variable remuneration. One or more group objectives may also be determined, which weight the bonus package actually paid.

A discussion may be held in case of extraordinary events which could legitimately change the evaluation of individual and/or group objectives - a decision which the Board of Directors might make on the advice and recommendation of the Remuneration Committee.



To these elements of remuneration may be added the award of share options or bonus shares, depending on the vote of the shareholders, in view of making them loyal to the Company and paid also on performance criteria.

Corporate officers receive no directors' fees for their position.

The Company does not award severance pay for the term of office or offer a supplementary retirement scheme.

Onxeo complies with the MiddleNext corporate governance code with respect to the remuneration of executives who are corporate officers of companies whose shares are admitted for trading on a regulated market.

#### Judith Greciet - Chief Executive Officer

# Remuneration 2019 (paid for 2018 for the variable part)

The gross annual fixed remuneration of Judith Greciet for financial year 2019 was set at €323,137.84 by the meeting of the Board of Directors of December 19, 2018 based on a proposal from the Remuneration Committee. This represents an increase of 2% compared with the 2018 gross remuneration.

The variable part of the remuneration of Judith Greciet is maintained in the amount of 50% of her fixed remuneration for 100% achievement of objectives and could be increased by 50%, based on achievement of additional objectives.

The evaluation by the Board of December 19, 2018 concluded as to 100% achievement giving rise to variable remuneration paid in 2019 for the year 2018 of 50% of her fixed remuneration, which will be paid 25% in cash and 75% in bonus shares, subject to the vote of the shareholders during the General Meeting planned for April 26, 2019.

Judith Greciet did not receive any benefits in kind in 2018 other than a company car.

#### Performance criteria 2019

The performance criteria determined for 2019, which will give rise to an evaluation and will weight the variable remuneration 2020 for the year 2019 are detailed below. They reflect the strategic and operational challenges of the Company in the short and medium term.

Projects	AsiDNA™	70%
	To initiate the phase I trial and organize all the activities for the trial to be finalized Q4 2019	
	To initiate a second combination trial to extend the AsiDNA™ clinical program with appropriate financial support	
	To reinforce the visibility of AsiDNA™ during scientific congresses and conferences	
	PlatON™	
	To obtain the in vivo proof of concept for the first lead candidate from $PlatON^TM$	
Business development	To value the product portfolio through a strategic partnership agreement	30%
Financing	To reinforce the company's level financing	20%
Organization	To adjust the organization to needs and to retain talented personnel	15%
Others	To optimize the capital structure	15%

In 2019, options and/or bonus shares may be awarded subject to attendance and performance conditions, as described below, and subject to shareholder approval.



#### Joseph Zakrzewski, Chairman of the Board of Directors

As all non-executive members of the Board, Joseph Zakrzewski receives directors' fees according to the following principles:

- for his duties as Chairman of the Board of Directors: a fixed amount of €36,000 annually as well as an amount of €7,000 per meeting subject to attendance
- for his duties as member of the Audit Committee: €1,000 per meeting subject to attendance

By decision of the Board of Directors, only 50% of the attendance fees owed to non-executive corporate officers were paid in 2018, with payment of the balance being deferred due to significant financing obtained by Onxeo The same regime is renewed for directors' fees due for the financial year 2019.

For the year 2018, Joseph Zakrzewski received €37,000 in directors' fees.

He may be awarded the right to subscribe to stock warrants, provided that the Company's general meeting of the shareholders that is convened to vote on the 2018 financial statements agrees to grant the board of directors a delegation for that purpose. The subscription price of the stock warrants and the subscription price for the exercise of said stock warrants will be set by the procedures determined by the general meeting.

We propose you approve the principles and criteria presented above as well as the related resolutions, reproduced below.

Pursuant to article L. 225-100 of the French Commercial Code, the amounts determined in accordance with the implementation of said principles are submitted for approval to the shareholders during the General Meeting that is to vote on the accounts for financial year 2018.

#### **Tenth resolution:**

Approval of the principles and criteria for determining, distributing and granting the fixed, variable and extraordinary elements composing the total compensation package and the benefits of any kind which can be granted to Joseph Zakrzewski as Chairman of the Board of Directors for financial year 2019

The General Meeting, resolving under the conditions of quorum and majority required for Ordinary General Meetings, after reading the report prepared pursuant to the provisions of Article L. 225-37-2 of the French Commercial Code,

approves the principles and criteria for determining, distributing and granting the fixed, variable and extraordinary elements composing the total compensation package and the benefits of any kind which can be granted for the financial year 2019 to Joseph Zakrzewski as Chairman of the Board of Directors.

#### **Eleventh resolution**

Approval of the principles and criteria for determining, distributing and allocating the fixed, variable and extraordinary elements composing the total compensation package and the benefits of any kind which can be allocated to Judith Greciet as Chief Executive Officer for financial year 2019

The General Meeting, resolving under the conditions of quorum and majority required for Ordinary General Meetings, after reading the report prepared pursuant to the provisions of Article L. 225-37-2 of the French Commercial Code,

approves the principles and criteria for determining, distributing and allocating the fixed, variable and extraordinary elements composing the total compensation package and the benefits of any kind which can be allocated for the financial year 2019 to Judith Greciet as Chief Executive Officer.



# 5.5 INTERESTS HELD BY DIRECTORS AND OFFICERS IN THE COMPANY'S SHARE CAPITAL

Interests held by directors and officers in the Company's share capital at December 31, 2018:

Interests held by directors and officers in the Company's share capital at 12/31/2018	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	114,813	0.22%	-	572,554	140,778	1.55%
Financière de la Montagne	7,723,379	14.47%	206,013	-	-	14.86%
J. Zakrzewski	37,724	0.07%	322,000	-	-	0.67%
D. Guyot-Caparros	-	-	82,500	-	-	0.15%
T. Hofstaetter	-	-	146,129	-	-	0.27%
J.P. Bizarri	-	-	87,500	-	-	0.16%
J.P. Kinet	-	-	30,000	-	-	0.06%
C. Garnier	-	-	82,500	-	-	0.15%
E. Sanz	-	-	82,500	-	-	0.15%
Total	7,875,916	14.76%	1,039,142	572,554	140,778	18.04%

# 5.6 TRANSACTIONS BY EXECUTIVES IN THE COMPANY'S SHARES

In accordance with the provisions of Article L. 621-18-2 of the French Monetary and Financial Code, we inform you of the transactions involving the Company's shares (acquisitions, divestments, subscriptions or exchanges) undertaken, as far as the Company is aware, by officers or members of the Board of Directors or people with close personal ties during FY 2018.

Concerned persons	Transaction description	Transaction date	Number of shares	Transaction amount (€)
Financière de la Montagne SARL, Director	Acquisition of shares	Aug-10-18	300,000	360,000.00
Financière de la Montagne SARL, Director	Acquisition of shares	Aug-30-18	300,000	351,000.00
Financière de la Montagne SARL, Director	Acquisition of shares	Sept-17-18	400,000	436,000.00
Financière de la Montagne SARL, Director	Warrant subscription	Aug-29-18	42,500	5,100.00
Joseph Zakrzewski, Chairman of the Board of Directors	Acquisition of shares	Sep-26-18	15,000	16,185.00
Joseph Zakrzewski, Chairman of the Board of Directors	Acquisition of shares	Sep-16-18	13,727	14,674.16



Concerned persons	Transaction description	Transaction date	Number of shares	Transaction amount (€)
Joseph Zakrzewski, Chairman of the Board of Directors	Acquisition of shares	Sep-26-18	3,997	4,280.79
Financière de la Montagne SARL, Director	Acquisition of shares	Nov-05-18	65,972	76,739.29
Financière de la Montagne SARL, Director	Acquisition of shares	Nov-06-18	234,028	282,925.81
Financière de la Montagne SARL, Director	Warrant subscription	Nov-08-18	42,500	4,250.00

# 5.7 INTERNAL CONTROL

#### 5.7.1 COMPONENTS OF THE RISK MANAGEMENT SYSTEM

# 5.7.1.1 Definition and objectives

The risk management process put in place by Onxeo aims to identify all the risks that may affect business processes and activities, and to define the means to control the occurrence of these risks and their consequences, to contain or minimize their probability of occurrence, as well as their impact on the Company's activity. This approach is intended to encompass all types of risk and apply to all activities of the Company and the Group.

Onxeo adopts the definition of risk management proposed by the French securities regulator, the AMF<sup>13</sup>, according to which risk management is a Company management tool that contributes to:

- Creating and preserving the value, assets and reputation of the Company;
- Securing decision-making and processes to promote the attainment of Company objectives;
- Promoting consistency of actions with the values of the Company;
- Involving employees based on a shared view of the main risks of the Company.

The Company has conducted a review of its risks and sees no significant risks other than those mentioned below.

# 5.7.1.2 Organizational framework

Risk management is steered by a 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 management'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.

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.

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<sup>&</sup>lt;sup>13</sup> Guide to implementation of the reference framework on internal control adapted for small and medium capitalization companies, updated on July 22, 2010.



#### 5.7.1.3 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 analyzes 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 way consistent with this risk mapping.

# 5.7.1.4 Risk factors

#### 5.7.1.4.1 Risks related to the Group's activity

#### 5.7.1.4.1.1 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 Onxeo's growth.

Within the framework of its research and development programs, the Company must conduct preclinical trials on animals and clinical trials on humans in order to demonstrate the product's safety and efficacy.

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 considered initially 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.

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

Clinical trials are generally carried out 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 enrollment, the availability of sufficient quantities of products, assistance from third parties and compliance with regulatory standards.

If, for reasons associated with one or more of the aforementioned factors, a significant delay were to occur in a trial and development times were to significantly deviate from estimates, this could have an adverse effect on the Company's ability to generate future revenue, financial position, and development.

Onxeo plans to initiate new clinical trials in 2019 with AsiDNA™: these will be small-sized phase 1 to 2 trials.

#### 5.7.1.4.1.2 Risks related to outsourcing the Company's R&D and production capabilities

The Company relies on providers involved in preclinical and clinical trials it initiates. It may use different service providers, both in France and abroad. The quality of test results depends mainly on the quality of carrying out the desired services and their compliance with the original specifications and applicable standards. The collapse of a subcontractor involved in a preclinical or clinical trial, loss of data, delays or errors in data processing could have an adverse effect on the validity of tests and compilation of regulatory filings for products being developed by the Company.



Moreover, the Company finds itself in a situation of dependency with regard to third parties for the manufacture of its products being developed. The collapse or lack of availability of these third parties to successfully complete a project could have an adverse effect on the development of products, their release times or compliance, thus affecting the trials or procedures concerning them and therefore the Company's ability to generate future revenue, financial position and development.

To address these risks, Onxeo audits its subcontractors and rigorously monitors all product development stages.

#### 5.7.1.4.1.3 Risks related to drug pricing and reimbursement policies

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

Decided by public commissions and agencies, the price of drugs is largely beyond the control of the Company and is set in relation to a flat rate deemed acceptable to the Community. 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.

Products developed by Onxeo should be sold by partners under licensing agreements. The ability of these partners and Onxeo to generate sufficient profits on the sale of 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 Company be unable to obtain an appropriate level of reimbursement, its profitability would be diminished.

#### 5.7.1.4.1.4 Risks related to commercial partnership agreements

The Company has entered into licensing agreements for the marketing of its product Beleodaq<sup>®</sup>. This product is currently sold in the United States and is being registered in various Latin American countries by the partner Pint Pharma.

Inadequate sales performance by a commercial partner may limit revenue from the company's products and impact its growth, even if the impact is not considered significant in the short term.

In general terms and to prevent risks associated with commercial partnership agreements, the Company benefits from clauses guaranteeing its interests in the various licensing agreements. It also monitors its partners, particularly with regard to the marketing and sales aspects.

# 5.7.1.4.1.5 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 is potentially exposed to this risk in the context of the marketing of Beleodaq® by its partner Acrotech Pharma LLC and has taken out specific product liability insurance to cover the safety risks associated with the marketing of its product.

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

## 5.7.1.4.2 Legal risks

# 5.7.1.4.2.1 Challenges and constraints related to the regulatory environment

Since the company's activities revolve around the development of drugs, it is subject to an increasingly restrictive regulatory environment.

Indeed, legislative and regulatory provisions defined by the French health product safety agency (ANSM), the European Commission, the EMA, the FDA and equivalent regulatory authorities in other countries, govern



research and development, preclinical and clinical studies, regulation of laboratories, and the manufacture and marketing of drugs (see section 4 of this registration document). Throughout the world, the pharmaceutical industry is confronted with a tightening 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 the approval of new therapeutic products is long and complex, and the failure rate is substantial. Moreover, regulatory requirements and procedures vary greatly from one country to another.

Even if registration of the Company's products is or will be entrusted to a partner under a licensing agreement, the uncertainties for Onxeo associated with both applying for marketing authorization and its phase of examination by the regulatory authorities carries major risks whose financial impact can 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 these risks, which could increase costs and reduce its future revenue, the Company has acquired strong expertise in clinical and regulatory fields. It also maintains active relations with its partners throughout the registration procedure.

#### 5.7.1.4.2.2 Limits on patent protection and other intellectual property rights

Onxeo regularly files patent applications in order to protect its technologies, products, preparation processes and pharmaceutical compositions. Through its patents and other intellectual 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 has the rights to three hundred and thirteen patents or patent applications, including two hundred and thirty patents granted in several countries or major jurisdictions, including 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-found prior art.

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-found prior art, 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.

Faced with these risks, the Company has a proactive Intellectual 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.



5.7.1.4.2.3 Risks on the patent portfolio associated with exploited patents falling into the public domain, or with the expiration of marketing licenses, or with the eventual emergence of generic drugs for marketed products or with the dispute of the validity of patents by a third party

At the end of their protection by 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 sales prices and/or volumes and could have a negative effect on the Company's business and financial condition.

These risks are currently not very significant to Onxeo because, firstly, the Company develops most of its product portfolio for niche markets that are not prime targets for generics and, secondly, under its Intellectual Property strategy, the Company regularly files new patent applications within existing patent families.

However, on August 21, 2018 the Company received a letter of opinion under paragraph IV which notifies that Fresenius Kabi USA, LLC submitted to the Food and Drug Administration ("FDA") in the United States an Abbreviated New Drug Application ("ANDA") asking the FDA for authorization to manufacture and sell a generic version of Beleodaq® (belinostat) for injection, 500mg, in the United States. Beleodaq® has been licensed in the United States to Spectrum Pharmaceuticals Inc., which obtained the marketing authorization and is promoting it in the second intention treatment for patients suffering from peripheral T-cell lymphoma.

The letter of notification contains "Paragraph IV" certifications that dispute the validity of two US patents (Numbers 6,888,027 and 8,835,501) held by the Company and confirm the non-infringement. Beleodaq® is protected by these 2 patents, listed in the FDA list of approved pharmaceutical products (Orange Book). Furthermore, Beleodaq® is protected from competition in the United States by an orphan drug exclusivity indication up to July 3, 2021. The Company and Spectrum have initiated patent infringement proceedings against Fresenius. These proceedings, if they turn out favorably, would prevent Fresenius from pursuing its action.

On January 17, 2019, Spectrum Pharmaceuticals signed an agreement with the Aurobindo Group and its subsidiary in the US, Acrotech Biopharma LLC, providing for the sale to Acrotech of several of its hematology / oncology products including Beleodaq®. On March 1, 2019, Spectrum Pharmaceuticals (SPPI) announced the completion of the sale of its seven hematology/oncology products approved by the FDA, including Beleodaq®, to Acrotech Biopharma LLC. The transfer terms of the obligations relating to the Beleodaq® activities between Spectrum Pharmaceuticals and Acrotech are still being finalized. On the date of publication of this document and based on the information provided to date by Spectrum, the Company does not foresee any significant impact of this transaction on the activities and results of Beleodaq® for Onxeo.



#### 5.7.1.4.3 Financial risks

#### 5.7.1.4.3.1 Risk of insufficient financial resources

The Company has posted net operating losses since the start of operations. As at December 31, 2018, the Company's cumulative book losses amounted to €12.955 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 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.

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 taking into account the extension of the equity line of credit with Nice & Green. However, the Company may need to raise additional funds ahead of time for reasons such as:

- highly interesting results that could justify the initiation of other unplanned trials to increase the value of AsiDNA™ or of platON™
- higher costs and slower progress than the Company anticipates in developing its products.
- opportunities to develop promising new products or to acquire products, technologies or other activities;

#### 5.7.1.4.3.2 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 or sales, or royalties.

Given the uncertainty concerning these triggering elements and the likely date of payments, the Company has not put in place any currency risk hedges. It is therefore possible that the €/\$ exchange rate moves adversely for the Company and that the total amount converted into euros may be significantly less than initially anticipated. As soon as payment assumptions are confirmed, the Company intends to hedge these flows in US dollars.

Regarding day-to-day operations, most revenue and payments are in Euros for which there is no currency risk to the Company.

#### 5.7.1.4.3.3 Interest rate risk

Although the company took out a debenture loan in financial year 2018, it is not exposed to interest rate risk insofar as the redemption premium of the bonds is fixed and independent of the interest rate markets.

#### 5.7.1.4.3.4 Equity risk

The Company's available cash is exclusively invested in money market funds, which involves 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 notes to the consolidated financial statements.

#### 5.7.1.5 Insurance and risk coverage

The Company has insurance cover that is 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 activities of the Company products both before and after delivery;
- o 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.
- Property damage insurance policies, which covers, in particular, the risks of fire, water damage, theft, machinery breakdown and breakage of glass, and tenants' risks, at the Company's premises in Paris, New York 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 Company's business activities and in close coordination with the development of our business activities.

# 5.7.1.6 Managing the risk management system

The Risk Committee validates and monitors action plans with the managers concerned.

# 5.7.1.7 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.

# 5.7.2 GENERAL PRINCIPLES OF INTERNAL CONTROL

#### 5.7.2.1 Internal control: definition and objectives

Internal control consists of the means, behaviors, procedures and actions adapted to the Company's particular characteristics and those of the Group as a whole that:

- Contribute to the control of its activities, its operating effectiveness and the well-organized use of its resources;
- 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;
- The reliability of financial information.

However, while supporting Company 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.

# 5.7.2.2 Reference framework used by Onxeo

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 put in place 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 using the full consolidation 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.

#### 5.7.2.3 Components of internal control

#### 5.7.2.3.1 Organization

The internal control system is based on a clear organization of responsibilities, standards, resources and procedures implemented.

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.

# 5.7.2.3.2 Reference framework and standards

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 securite du medicament et des produits de sante* (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.

#### 5.7.2.3.3 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; these last two instances are devoted to managing R&D projects.

#### 5.7.2.3.3.1 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, preclinical 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.

#### 5.7.2.3.3.2 Reports

The Senior Management of the Company has put specific reporting procedures in place for each department in the Company, under the responsibility of members of the Executive Committee (Management Board). Such reporting includes key information representative of the reality of the operation concerned and allows for tracking this latter both quantitatively and qualitatively. This key information must be verifiable and properly documented. It is to be updated each month by the people carrying out the activity concerned.

# 5.7.2.4 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 more 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 inter-company 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 Management 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 executive management. 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 report 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 executive management.

Such communication takes place via two main channels:

- The annual report and registration document and the interim financial report;
- 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 annual and interim results are also validated by the Board of Directors.

# 5.7.2.5 Persons 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.

In-house operatives of the internal control system include:

- 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 management 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.
- Risk management is the responsibility of the Risk Committee in conjunction with the Audit Committee. It 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 backed up by the outside actors, including the Auditors. The Statutory Auditors rely in particular on a review of internal control procedures relating to the preparation of accounting and financial information as part of their legal assignment of certifying or auditing the consolidated and individual financial statements of the companies of the group.

#### 5.7.3 MAIN CHANGES

The Company is pursuing its policy aimed at improving its internal control systems.

In 2018, 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.



# ONXEO'S FINANCIAL STATEMENTS

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# CONSOLIDATED STATEMENT OF FINANCIAL POSITION

ASSETS in €k	31/12/2018	31/12/2017	Note
Non-current assets			
Intangible assets	38,573	47,535	5
Property, plant and equipment	296	344	6
Long-term investments	4,005	232	7.1
Deferred tax assets	0	0	
Total non-current assets	42,874	48,111	
Current assets			
Inventories and work in progress	47	30	
Trade accounts receivable and related accounts	1,479	552	7.2
Other accounts receivable	7,597	15,103	7.3
Financial investments	0	0	
Cash and cash equivalents	11,253	14,277	7.4
Total current assets	20,376	29,962	
TOTAL ASSETS	63,250	78,073	

LIABILITIES AND SHAREHOLDERS' EQUITY (€k)	31/12/2018	31/12/2017	Note
Shareholders' equity			
Share capital	13,344	12,674	8.1
Less: treasury shares	-97	(89)	8.2
Share premium	41,824	269,060	8.3
Reserves	-270	(172,700)	8.3
Earnings	-9,399	(59,071)	
Total shareholders' equity	45,402	49,873	
Non-current liabilities			
Deferred tax liabilities	2,330	4,094	9.1
Provisions	531	550	9.2
Other financial liabilities	6,593	4,714	9.3
Total non-current liabilities	9,455	9,358	
Current liabilities			
Short-term debt	450	130	
Trade payables and related accounts	4,145	5,956	10.1
Other liabilities	3,798	12,755	10.2
Total current liabilities	8,394	18,842	
TOTAL LIABILITIES AND SHAREHOLDERS' EQUITY	63,250	78,073	



# CONSOLIDATED STATEMENT OF COMPREHENSIVE INCOME

In K€	31/12/2018	31/12/2017	Note
Daniel Company	2 240	2.042	
Recurring revenue from licensing agreements	2,310	3,042	
Non-recurring revenue from licensing agreements  Total revenue	3,817	6,463	12.1
Purchases	6,127	9,505	12.1
Personnel costs	(215)	(634) (8,217)	12.2
· · · · · · · · · · · · · · · · · · ·	(5,438)	• • •	12.2
External expenses Taxes and duties	(8,731) (346)	(17,555)	12.3
Net decrease in depreciation and amortisation	(540)	(367)	12.4
Net allocations to provisions	(340)	(1,796) 74	12.4
Other operating income	4,546	4	
Other operating income Other operating expenses	622	(203)	
	-	· ,	
Operating expenses	(9,654)	(28,694)	
Loss from recurring operating	(3,527)	(19,189)	
Other operating income and expenses	(12,117)	-47,188	
Operating result	(15,644)	-66,378	
Share of profit from equity affiliates	5,176	0	12.5
Operating loss after share of profit from equity affiliates	(10,468)	-66,378	
Income from cash and cash equivalents	15	13	
Other financial income	331	615	
Financial expenses	(1,037)	-1,119	
Net financial income (expense)	(691)	-491	13
Pre-tax loss	(11,159)	-66,868	
Tax expense	1,760	7,797	14
- Of which deferred tax	1,764	7,801	
Net loss	(9,399)	-59,071	
Earnings per share	(0.18)	(1.17)	15
Diluted earnings per share	(0.18)	(1.17)	15

In K€	31/12/2018	31/12/2017	Note
Loss for the year	(9,399)	(59,071)	
Other comprehensive income	0	0	
Translation adjustments	(2,899)	(2,528)	
Gains and losses on derecognition of assets available for sale	0	0	
Cash flow hedges	0	0	
Tax relating to comprehensive income items	0	0	
Other items that may be reclassified to profit or loss	(2,899)	(2,528)	
Actuarial gains and losses	11	7	
Other items that may not be classified to profit or loss	11	78	
Other comprehensive income for the year, net of tax	(2,888)	(2,522)	
Total comprehensive income for the year	(12,287)	(61,592)	
Total comprehensive income attributable to the			
owners of the parent company	(12,287)	(61,592)	
Minority interests			



# CONSOLIDATED STATEMENT OF CHANGES IN EQUITY

# Change in reserves and profit (loss) for the year

In K€	Share Capital	Treasury shares	Share premium	Currency translation reserve	Share- based payment	Gains and losses recorded as equity	Consolidated reserves and profit (loss) for the year	Total change	TOTAL
Equity at 1/01/2017	11,761	(97)	255,960	(770)	2,649	(102)	(175,312)	(173,535)	94,089
Total comprehensive income for the year				(2,528)		(7)	(59,071)	(61,606)	(61,606)
Capital increase Treasury shares Other movements Share-based payment Dividends	913	8	13,100		980		(68) 2,458	(68) 2,458 980	14,013 (60) 2,458 980
Equity at 31/12/2017	12,674	(89)	269,060	(3,298)	3,629	(108)	(231,992)	(231,771)	49,874
Total comprehensive income for the year				2,899		(11)	(9,399)	(6,511)	(6,511)
Capital increase Treasury shares Other movements <sup>14</sup> Share-based payment Dividends	670	(8)	1,969 (229,205)		927		(15) 227,700	(15) 227,700 927	2,639 (23) (1,505) 927
Equity at 31/12/2018	13,344	(97)	41,824	(399)	4,556	(119)	(13,705)	(9,669)	45,402

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This item includes an amount of €229,205 thousand corresponding to the offsetting of retained earnings and bonuses, in accordance with the decision of the Extraordinary General Meeting of June 19, 2018. It also includes, in the "reserves and consolidated results" section, the impact at the beginning of the 2018 financial year of the entry into force of IFRS 15, which resulted in an increase in consolidated reserves of €935 thousand.



# CONSOLIDATED NET CASH FLOW STATEMENT

K€	31/12/2018	31/12/2017
Consolidated net loss	(9,399)	(59,071)
+/- Depreciation, impairment and provisions, net (1)	9,175	40,253
(excluding provisions against working capital)		
+/- Unrealized gain and losses associated with changes in fair value		
+/- Non cash income and expenses on stock options and similar items	927	980
+/- Other calculated income and expenses	(173)	(137)
+/- Capital gains and losses on disposal		
+/- dilution gains and losses		
+/- Share of earning associates	(5,176)	
- Dividends (non-consolidated investments)		
Gross operating cash flow after cost of net debt and taxes	(4,646)	(17,973)
+ Cost of net debt	691	492
+/- Tax expenses (including deferred taxes)	(1,764)	(7,801)
Gross Operating cash flow before cost of net debt and taxes	(5,719)	(25,282)
- Taxes paid		, , ,
+/- Changes in operating WCR (including debt related to employee benefits)	(5,546)	(2,999)
NET CASH FLOW FROM OPERATING ACTIVITIES	(11,266)	(28,281)
- Expenditures on acquisition of tangible and intangible assets	(45)	(65)
+ Proceeds of disposal of tangible and intangible assets		
- Expenditures on acquisition of financial assets		(2)
+ Proceeds of disposal of financial assets		
+/- Effect on changes in scope of consolidation		
+ Dividends received (equity accounted investment)		
+/- Change in loans and advance granted		
+ Capital grants received		
+/- Other changes from investment transactions	45	
NET CASH FLOW FROM INVESTING ACTIVITIES	1	(67)
Cash flow resulting from the merger		
+ Net amount received from shareholders on capital increase		
. Paid by shareholders of the parent company	2,747	14,012
. Paid by minority interest in consolidated companies		
+ Amount received on exercise of stock options		
-/+ Purchase and Sale of treasury shares	(150)	(68)
- Dividends paid in the year	(200)	(00)
- Dividends paid to minority shareholders in consolidated companies		
'- Dividends paid to minority shareholders		
+ Amounts received on issuances of new loans	5,926	
- Reimbursements of loans (including finance leases)	(193)	(154)
- Net interest received	(193)	(154)
+/- Others flows related to financing activities	(81)	(354)
NET CASH FLOW FROM FINANCING ACTIVITIES	8,250	13,437
+/- Effects of fluctuations in foreign exchange rates	(8)	
CHANGE IN CASH AND CASH EQUIVALENTS	(3,024)	(55)
CASH AND CASH EQUIVALENTS  CASH AND CASH EQUIVALENTS at start of year	14,277	(14,966)
·	-	29,243
CASH AND CASH EQUIVALENTS at year end	11,253	14,277



# NOTE 1 - COMPANY PRESENTATION

Onxeo is a French a clinical-stage biotechnology company developing innovative oncology drugs targeting tumor DNA-binding functions through unique mechanisms of action in the sought-after field of DNA Damage Response (DDR). The Company is focused on bringing early-stage first-in-class or disruptive compounds (proprietary, acquired or in-licensed) from translational research to clinical proof-of-concept in man, which represents its know-how and added value. It conducts its programs to the most value-creating and attractive inflection points for potential partners.

The Company is based in Paris, France, with offices in Copenhagen and in New York and has about 30 employees. Onxeo is listed on Euronext in Paris, France, and on Nasdaq Copenhagen, Denmark.

The consolidated financial statements of Onxeo as at December 31, 2018 were prepared under the responsibility of the CEO and were approved by the Board of directors on 12 March 2019.

# NOTE 2 - SIGNIFICANT EVENTS AND TRANSACTIONS

#### 2.1.1. ASIDNA™

In 2018, the Group actively pursued the preclinical and clinical development of AsiDNA™ as a systemic single therapy and in combination with other treatments in various types of solid tumors and overcame several key steps:

- Presentation at the AACR (American Association for Cancer Research), in April 2018, of two preclinical studies demonstrating the unique approach AsiDNA™ has in inhibiting the repair of tumor DNA by activating those enzymes involved in DNA damage signaling and distracting them from their target. The results of one of these studies showed, in particular, that repeated, long-term administration of AsiDNA™ lead to an increase in the sensitivity of tumor cells and that no resistance was apparent following repeated treatments.
- In July 2018, new preclinical results bolstered these properties by showing a strong synergy and a reversion in tumor resistance in association with PARP inhibitors.
- The launch, in April 2018, of DRIIV (DNA Repair Inhibitor administered IntraVenously), the phase 1 AsiDNA™ clinical study into advanced solid tumors. The aim of this study is to assess AsiDNA™ tolerance and the optimum clinical dose, as well as to determine its active dose at the level of the tumor in patients with advanced solid cancer.
- In November 2018, the Company announced, on schedule, the positive interim results on the first three doses tested in the DRIIV study evaluating the tolerance to and activity of AsDNA™ when administered systemically (intravenously). A favorable safety profile was also observed, with no serious undesirable event due to the drug or any toxicity that would limit the dose.

Based on this data, and in particular the determination of active doses, the Group intends to extend the AsiDNA™ clinical program in association with the targeted indications from the first half of 2019.

AsiDNA™ has the potential to be used in a broad range of indications, to which the Group wishes to add value as part of a partnership. AsiDNA™ also has the capacity, in the short and long term, to generate a number of growth and value catalysts for the Group and its shareholders.

# 2.1.2. PLATON™

PlatON™ is a chemistry platform from which AsiDNA™ is derived and which allows it to construct new oligonucleotide-based molecules (a double-stranded DNA fragment). Throughout 2018, the Company continued to select and optimize several highly innovative compounds and is planning to enter into the preclinical phase for the most promising compound in the first half of 2019.



# 2.1.3. BELEODAQ® (BELINOSTAT)

Belinostat is a histone deacetylase inhibitor (HDACi) marketed in the US since 2014 under the name Beleodaq® as part of a conditional approval by the FDA for use in the 2nd-line treatment of patients with peripheral T cell lymphoma.

At the same time, Onxeo has been assessing belinostat in association with other compounds. These works have suggested that belinostat may potentially be better suited for use with new platON™-derived compounds.

#### 2.2. FINANCING

In June 2018, the Company announced two financing operations:

- On the one hand, Onxeo signed a royalty prefinancing agreement with SWK Holdings Corporation, a US company specialized in financing in the life sciences sector. According to the terms of the agreement, Onxeo issued bonds in an amount of \$7.5 million, fully subscribed by SWK Holdings Corporation. The terms for repaying the bonds will allow the latter to directly receive the royalties and milestone payments on the sales stemming from the marketing of Beleodaq® (belinostat) by Spectrum Pharmaceuticals, Inc. for an amount of \$13.5 million. The remaining details of the transaction have not been disclosed.
- On the other hand, on June 15, 2018, the Company set up an equity line of credit, including an incentive plan, by issuing new shares over a period of 10 months, for a maximum amount of €5.4 million together with the company Nice & Green. In accordance with the terms of the agreement, Nice & Green has undertaken, for a 10-month period, to subscribe for and exercise each month, on Onxeo's initiative, share warrants corresponding to minimum monthly financing of €500,000 up to a limit of 4,700,000 shares over the term of the contract. The shares will be issued on the basis of the average share price weighted by volumes over the first three trading days prior to each issue, less a maximum discount of 5.0%. Onxeo retains the option of suspending drawdowns or of terminating this agreement at any time. Nice & Green and Onxeo have also agreed on an incentive plan that consists of the allocation in cash, to the Company, of a share of any added value realized by Nice & Green through the sale of shares resulting from the exercise of the warrants.

#### 2.3. DISPUTE WITH SPEBIO AND SPEPHARM

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®.

In a partial arbitral award 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. Onxeo then had summons served on SpeBio for contractual liability before the Commercial Court. Onxeo then lodged a forcible joinder with the Commercial Court to add SpePharm as a co-defendant on criminal grounds, and, by a ruling dated May 3, 2016, the Paris Commercial Court granted Onxeo's forcible joinder adding SpePharm as a co-defendant and consolidating the Onxeo v. SpeBio and Onxeo v. SpePharm proceedings. In a counterclaim, SpeBio and SpePharm filed claims for damages.

On October 17, 2017, the Paris Commercial Court handed down a judgment ordering Onxeo to pay to SpeBio the sum of €8.6 million for costs sustained before the termination with interest at the statutory rate from June 30, 2014 with compound interest (in addition to €250,000 on the basis of Article 700 of the French Code of Civil Procedure) and to Spepharm the sum of €50,000 in damages (in addition to €15,000 on the basis of Article 700 of the French Code of Civil Procedure). This judgment was handed down along with provisional enforcement and, as a result, a total amount of €9.2 million was recognized under other liabilities. This amount, escrowed although not paid at December 31, 2017, has been deducted from free cash flow and recognized under assets as other receivables in the 2017 financial statements.

On October 20, 2017, Onxeo lodged an appeal against this ruling and lodged its submissions with the Court of Appeal of Paris on January 9, 2018, in order to ensure that the appeal proceedings are dealt with promptly in the interest of its shareholders. On December 7, 2018, the Court of Appeal handed down a decision ordering



Onxeo to pay SpeBio the additional sum of around €2.8 million as compensation for the damage suffered in terms of expenses incurred and loss of opportunity. The Court did, however, overturn the order that required Onxeo to pay €50,000 to SpePharm BV in damages. The amount of €2.8 million, not paid at December 31, 2018, has been recognized as other debts.

# 2.4. EVENTS TAKING PLACE AFTER DECEMBER 31, 2018

There are no post-balance sheet events likely to have a material effect on the financial statements.

# NOTE 3 - ACCOUNTING PRINCIPLES, RULES AND METHODS

#### 3.1. BASIS OF PREPARATION OF THE FINANCIAL STATEMENTS

The consolidated financial statements for the year ended 31 December 2018 were prepared in accordance with international accounting standards issued by the IASB (International Accounting Standards Board), as published by the IASB on 31 December 2018, and with international standards as adopted by the European Union as at 31 December 2018.

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 for the year ended 31 December 2018 are identical to those used in the consolidated financial statements for the year ended 31 December 2017, 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 1 January 2018 (and which had not been applied early by the Group), namely:

Standard	Name
Amendments to IFRS 2	Classification and measurement of share-based payment transactions
Amendments to IFRS 4	Applying IFRS9 financial instruments with IFRS 4 insurance contracts
IFRS 9	Financial instruments
IFRS 15	Revenue from contracts with customers
Amendments to IFRS 15	
Amendments to IAS 40	Transfers of investment property
IFRIC 22	Foreign currency transactions and anticipated counterparty

Applying these standards, amendments and interpretations had no significant effect on the consolidated financial statements of the Group, with the exception of standard IFRS 15, as described in Notes 10.2 and 12.1.

In addition, the other standards, amendments or interpretations published respectively by the IASB and the IFRIC (International Financial Reporting Interpretations Committee) as at 31 December 2018 were not applied early by the Group:

- Adopted by the European Union but whose mandatory application is subsequent to the financial year started on 1 January 2018: IFRS 16 (Leasing Contracts), IFRIC 23 (Uncertainty on Tax Treatment published on June 7, 2017), IFRS 9 Amendment (Early Redemption Features with Negative Remuneration).
- not yet adopted by the European Union as at 31 December 2018: Amendments to IAS 19 (amendment, curtailment or wind-up), amendments to IAS 28 (long-term interests in associates), annual improvements to IFRSs (2015-2017 cycle), IFRS 3 (interests previously held in a joint venture), IFRS 11 (interests previously held in a joint operation), IAS 12 (corporate income tax consequences of payments related to financial instruments classified as equity), IAS 23 (capitalizable borrowing costs), conceptual frameworks,



amendments to IFRS 3 (business combinations), definition of an activity, amendments to IAS 1 and IAS 8 (definition of materiality).

Although IFRS 16 has not yet been applied early, the Group initiated at the end of 2018 the project to implement this standard relating to leases. When entering into a lease agreement with fixed payments, this standard requires the recording of a liability in the balance sheet corresponding to discounted future payments, with counterpart a right to use the assets amortized over the term of the contract. IFRS 16 will be applied on January 1, 2019, following the so-called "modified retrospective" transition method, which requires the recognition of a liability at the date of transition equal to the discounted residual rents, with counterpart a right of use adjusted by the amount of rents paid in advance or as expenses payable; all the impacts of the transition will be recorded against equity. The identification of contracts and the collection of data needed to calculate the liability at the transition date are being completed. The group has identified around ten contracts outstanding at the closing date falling within the scope of the standard, including contracts relating to the Group's premises as well as contracts relating to assets such as tools, equipment or vehicles. The impact on the balance sheet related to the first application of IFRS 16 will be between €1.5 and €3 million. This analysis will be continued in 2019 according to new contracts signed.

#### **Judgements and estimates of Group Management**

Preparing the financial statements requires the management to make judgements, estimates and assumptions that have an impact on the application of the accounting policies and on the amounts of the assets and liabilities, income and expenditure. Actual values may differ from estimated values.

The estimates and underlying assumptions are continuously re-examined. The impact of accounting estimate changes is recognised over the period of the change and all affected subsequent periods.

Information on the main sources of uncertainty relating to the estimates, assumptions and judgements made in applying the accounting policies, which have the most significant impact on the amounts recognised in the consolidated financial statements, concerns the following items:

- the market value of the R&D programmes acquired as part of business combinations (mergers and acquisitions) see Note 5;
- share-based payments see Note 8.3;
- provisions see Note 9.2;
- the accounts payable provisioned for at the balance sheet date pertaining to ongoing clinical trials see
   Note 10.1;
- the recognition within revenue of amounts received under licensing agreements see Note 12.1.
- Q4 2018 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 preparing the consolidated financial statements also uses estimates (see Note 16).

The financial statements have been prepared on a going concern basis. This principle has been used by the Board of Directors insofar as the Company, which had consolidated net cash of €11.3 million at 31 December 2018 and secured additional financing (extension of the current equity line) enabling it to finance its activities until the second quarter of 2020 on the basis of its financing plan.

#### 3.2. SCOPE OF CONSOLIDATION

The Group companies close their accounts on 31 December each year.

The scope of consolidation includes the following companies at 31 December 2018:

- Onxeo;
- Topotarget UK;
- Topotarget Switzerland;
- BioAlliance Pharma Switzerland;



- SpeBio;
- Onxeo US

All subsidiaries are 100% owned and fully consolidated, except SpeBio, which is a joint-venture 50% owned and consolidated using the equity method. Intra-group 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 IFRS standards 8.32 and 33, information regarding the breakdown of revenue by geographical area and product category is provided in Note 12.1. Further, in reference to this standard it is also specified that the non-current assets of the group are mainly located in France, Denmark and the United Kingdom.

The Group's main customers, representing more than 10% of revenue, are Vectans Pharma, Spectrum Pharmaceuticals and Biogen.

# 3.4. THE EFFECTS OF CHANGES IN FOREIGN EXCHANGE RATES (IAS 21)

#### 3.4.1. CONVERSION OF 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.

Assets and liabilities of those subsidiaries that have 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 recognised on the balance sheet in shareholders' equity in the item "Translation adjustments". When the foreign entity is sold, these translation adjustments are recycled to the profit and loss account as part of the gain or loss on disposal.

#### 3.4.2. RECOGNITION OF 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 underlying foreign exchange gains or losses resulting from this translation are recognised in the profit or loss for the year.

#### 3.5. INTANGIBLE ASSETS

#### **3.5.1. PATENTS**

Patents created by Onxeo are recognised in expenses or capitalised in line with the accounting treatment for research and development costs set out below.

The patents acquired for consideration by Onxeo are recognised as non-current assets and are amortised. The amortisation period generally applied by Onxeo is ten years, which corresponds to the estimated useful life.

# 3.5.2. RESEARCH AND DEVELOPMENT COSTS

Research costs are always expensed. In particular, as part of the clinical trials conducted by the Group, an estimate of the as-yet unbilled per-patient costs is determined by the management based on the study monitoring documents and recorded as expenses for the year. Development costs are capitalised 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 authorisation is obtained.

The research and development projects which were acquired (or contributed) are recognised as intangible assets at their acquisition value even in the absence of marketing authorisation.

Pursuant to IAS 38, intangible assets are classified in two categories:

- Assets with a defined useful life, whose initial value is recognised on the balance sheet, less 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 as soon as evidence of any loss of value appears, and at least on an annual basis.
- 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, goodwill corresponds to the difference between the amount of the transaction and the market value of the acquired assets and liabilities.

Goodwill is not amortised 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 impairment tests at least once a year, provided they include goodwill;
- Onxeo performs this test at the balance sheet date;
- R&D assets relating to products in development or not yet commercialised (and therefore not amortised) are subjected to impairment tests on an annual basis. Onxeo performs this test at the balance sheet date;
- R&D assets relating to commercialised (and thus amortised) products are subjected to impairment tests when new circumstances indicate that these assets might have been impaired. This would be the case where indicators show that commercialisation is slower than expected;
- In the event that a loss in the value of the above assets is identified, a provision for depreciation is recorded.

The Group considers that it is a single CGU, insofar as the projects it develops belong to the same family of products and have overlapping economic models, therefore being interdependent. This single CGU includes goodwill and R&D assets acquired as part of the merger with Topotarget (comprising Beleodaq in its indication in 1<sup>st</sup> and 2<sup>nd</sup> line PTCL, as well as potential future indications for this product) and as part of the acquisition of DNA Therapeutics (AsiDNA).

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 value in use) to their tested base. Depreciation is recognised 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. PROPERTY, PLANT AND EQUIPMENT

In accordance with IAS 16, PP&E are recognised at acquisition cost less accumulated depreciation and impairment losses. Depreciation is calculated on a straight-line basis.

The most commonly used depreciation periods are as follows:

Equipment and tooling
 Specialised equipment
 Fixtures and fittings
 Office and computer equipment
 4 years



- Furniture 5 years

PP&E 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 recognised either under financial assets at fair value through profit or loss, under loans and receivables, under investments held to maturity, or under available-for-sale financial assets. On initial recognition, financial assets are measured at fair value, plus, in the case of investments that are not recognised at fair value through profit or loss, directly attributable transaction costs.

The Group determines the classification of its financial assets on initial recognition and, in cases where it is authorised and appropriate to do so, revises this classification at each year end.

Non-current financial assets include long-term investments, in particular:

- cash OEICs (open-ended investment companies) having been pledged as collateral;
- deposits and guarantees mainly corresponding to deposits required when entering into lease agreements;
   and
- the 'cash' portion of the liquidity contract relating 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 (CIR);
- cash includes current ban account balances;
- cash equivalents include cash OEICSs and open-end investment funds, which can be accessed or disposed of very quickly to provide known cash amount with negligible risk of a change in value.

These assets are recognised based on their nature and the following policies:

#### 3.7.1. Assets at fair value through profit or loss

From the date of their initial recognition, financial assets at fair value through profit or loss include financial instruments designated as being measured at fair value through profit or loss, in the conditions applying to optional measurement at fair value through profit and loss, which can apply to items that are managed, and whose performance is measured, on the basis of fair value.

This item includes current bank accounts and cash OEICs that can be converted to cash or sold very quickly and that 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 recognised at fair value, without deducting any transaction costs that could be incurred on their sale. Realised and unrealised gains and losses associated with a change in the fair value of these assets are recognised in profit and loss under 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 traded on an active market. After initial recognition, loans and receivables are measured using the amortised cost method, applying the effective interest rate, less any impairment.

This item includes deposits and guarantees recognised under non-current assets, and commercial receivables (trade receivables and other current assets) recognised under current assets.

Trade receivables and related accounts are initially recognised at fair value. They are discounted when their due date for settlement is more than one year. They are then recognised at amortised cost, and the interest is recognised as financial income in profit or loss.

These assets may be subject to a provision for impairment if objective indications of impairment exist. The amount of 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 that have not yet been incurred), discounted at the initial effective interest rate (i.e. at the effective interest rate calculated at the date of initial recognition).



As regards commercial receivables, an impairment loss is recognised when the expected cash flows at the balance sheet date are less than the carrying amount. Analysis of the risk is carried out on a case-by-case basis, taking into account criteria such as the client's financial situation (probability of bankruptcy or significant financial difficulties), age of the receivable or existence of a dispute.

#### 3.7.3. AVAILABLE-FOR-SALE FINANCIAL ASSETS

Available-for-sale financial assets are non-derivative financial assets that are classified 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 their associated gains and losses are taken directly to equity. When an available-for-sale financial asset is derecognised or impaired, the cumulative profit or loss previously recognised through equity is taken to profit or loss.

#### 3.7.4. Inventories

Inventories are stated at the lower of cost or net realisable value. Cost is calculated in accordance with the average weighted cost method. The cost of finished goods and work in progress comprises the cost of raw materials, direct costs and general production overheads.

Impairment is calculated by comparing the recoverable amount and cost price.

#### 3.8. SHARE-BASED PAYMENTS (IFRS 2)

Equity instruments (such as share options, bonus shares and share subscription warrants) allocated by the Company are valued on the allocation date in accordance with IFRS 2 are charged as an expense in profit or loss. The valuation is performed by an external provider 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 acquisition of share options, share subscription warrants or bonus shares allocated to Group employees is subject to their presence within the company on the acquisition 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 recognised expenses are recorded in profit or loss for those plans that are not permanently acquired.

## 3.9. NON-CURRENT LIABILITIES

#### 3.9.1. EMPLOYEE BENEFIT OBLIGATIONS (IAS 19)

#### **Retirement benefit obligations**

Retirement benefit obligations are recognised 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 recognised under «other comprehensive income".

#### 3.9.2. Provisions for Litigation

A provision is recognised when the Group has an actual or implicit legal obligation to a third party, resulting from a past event, that will likely lead to an outflow of resources to that third party without receiving equivalent consideration and where such future cash outflows can be estimated reliably.



#### 3.9.3. REFUNDABLE ADVANCES

In accordance with IAS 20 concerning recognition of public subsidies and information to be provided on public aid, the advantages pertaining to loans at zero or low interest rates compared with market rates are accounted for and therefore recognised as subsidies. Refundable advances less the amount of the subsidy are recognised as financial liabilities. The interest charges are calculated using the market interest rate.

Refundable advances without a preferential rate are recognised pursuant to IAS 39 according to the "amortised cost" rule; the financial costs are calculated at the effective interest rate.

Repayable advances are recognized in "Other non-current financial debts" and "Short-term borrowings and financial debts" depending on their maturity. They are initially stated at fair value, which in most cases corresponds to their nominal value, then subsequently recognised at amortised cost.

In case of failure of the duly justified financed program with the lender, the advances received will generally remain acquired and the waiver of debt will be recorded as a subsidy on the "Other operating income" line.

#### 3.9.4. FINANCIAL LIABILITIES

Bank borrowings and debt instruments are initially recognised at fair value less directly attributable transaction costs. Subsequent to initial recognition, they are measured at amortised cost using the effective interest rate method.

Gains and losses are recorded in the profit or loss when the debt is derecognised, as well as through the amortised cost mechanism. The amortisation expense as calculated using the effective interest rate method is recognised under 'Financial income (expense), Cost of debt'.

#### 3.9.5. OTHER CURRENT LIABILITIES

Current liabilities are stated at fair value.

#### 3.9.6. OPERATING INCOME

The Group's revenue includes income from the sale of pharmaceutical products, revenue generated under licensing agreements, royalties received on sales, and revenue from services rendered.

Sales of products are recognized in revenues upon transfer of control to the customer for an amount that reflects the payment the Company expects to receive in return for those products.

The agreements by which the Group licenses to a third party access to the technology of one or more products in its portfolio generally include several components, among which an initial payment upon signature, various additional payments conditional upon the achievement of objectives of development, regulatory and commercial objectives, lump-sum payments for research and development costs and royalties on future sales of products by the partnering entity. Royalties on future sales of products correspond to a percentage of net sales made by the partnering entity.

The amounts invoiced by the Group when a new partnership agreement is signed, remunerating access to the technology, are recorded in full as revenue on the effective date of the contract, provided that the Group has no future complementary development commitments. In the event that the Group has not transferred all the rights to the partner, the initial payment is then spread over the estimated duration of the Group's involvement in future development work, which may be revised periodically taking into account the evolution of the calendar of ongoing developments. The invoicing by the Group of contractually agreed milestones for the achievement of certain predefined development and/or regulatory objectives is recognized in sales upon achievement of these objectives. Revenues related to the potential financing by the partner of the Group's research and development expenses are, first of all, recorded as deferred income and spread over the estimated duration of the Group's involvement in the future development works, which may be subject to periodic revisions. Royalties received on sales are recognised as income on the basis of the revenue generated by the partners in the period and in accordance with the contractual royalty rates. Should a partner be unable to communicate the net revenue data from royalties prior to the date of publication of the accounts, they will be measured by valuing the actual quantities for the period with the net unit sales recognised historically for the product concerned.



In the event that assets are sold, the initial payments shall be fully accounted for on the date the contract is signed.

#### 3.9.7. OPERATING SUBSIDIES

In accordance with IAS 20, public subsidies whose amounts are related to the pace of corresponding expenses are recognised less the corresponding expenses.

#### 3.9.8. OTHER OPERATING INCOME AND EXPENSES

This item includes non-recurring, non-operational and significant events.

#### 3.9.9. DEFERRED TAX

A deferred tax asset is recognised for tax loss carry forwards and unused tax credits where it is probable that there may be future taxable profits against which these tax losses and tax credits will be able to be charged.

A deferred tax liability is recognised for all taxable temporary differences and for acquired R&D fixed assets.

#### 3.9.10. RESEARCH TAX CREDIT

Research tax credits are granted to companies by the French State to encourage them to conduct technical and scientific research. Companies that 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 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 to the entity in cash by the State. 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 recognises the amount to be received as a reduction of these costs in the same financial year.

# NOTE 4 - 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 used:

# 4.1. LIQUIDITY RISK

Liquidity risk is essentially associated with the Company's financial profile, as long as it does not generate significant revenues in proportion to its expenses, notably in research and development. The net cash position at year-end, as well as the forthcoming additional financing obtained by the Company (extension of the current equity line), provides financial visibility until mid-2020. 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 organisations (including from BPI France) as part of R&D programmes, which are repayable only in the event of a duly identified commercial and technical success.

#### 4.2. MARKET RISK

Only available-for-sale financial assets (see Note 8.2) are subject to market risk. They correspond to the portion invested in Onxeo shares of the liquidity contract implemented by the company with Kepler-Cheuvreux . The value of these assets does in fact depend on the share price on the Euronext market.



#### 4.3. 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.

#### 4.4. FOREIGN EXCHANGE RISK

Although the Company performs transactions in foreign currencies, its foreign exchange risk exposure is limited. For this reason, no exchange hedging instrument has been implemented.

#### 4.5. INTEREST RATE RISK

Although the company has a bond issued during the 2018 financial year, it is not subject to interest rate risk since the bond repayment premium is fixed and independent of the interest rate markets.

#### NOTE 5 - INTANGIBLE ASSETS

Intangible assets of a net amount of €38,573 thousand as at 31 December 2018 consist primarily of R&D assets acquired within the context of the merger with Topotarget (Beleodaq) and within the context of the acquisition of DNA Therapeutics (AsiDNA) as far as a Goodwill recognised at the time of the Topotarget merger as detailed below:

In thousands €	31/12/2017	Increase	Decrease	31/12/2018
Beleodaq R&D assets	68,700			68,700
AsiDNA R&D assets	2,472			2,472
Goodwill	20,059			20,059
Other intangible assets	719		(299)	420
<b>Total Gross</b>	91,950	0	(299)	91,651
Beleodaq amortisation	(5,600)	(398)		(5,998)
Amortisation of other intangible assets	(704)	(14)	299	(419)
<b>Total Amortisations</b>	(6,304)	(412)	299	(6,417)
Beleodaq depreciation	(38,111)	(8,550)		(46,661)
<b>Total Depreciations</b>	(38,111)	(8,550)	0	(46,661)
Total	47,535	(8,962)	0	38,573

The R&D assets associated with Beleodaq were depreciated by a total amount of €398 thousand over the year as the counterpart to the revenues generated by the commercialisation of the product by the partner Spectrum Pharmaceuticals as second-line treatment to peripheral T-cell lymphoma. These assets are amortised over the duration of the product's anticipated commercialisation for this indication i.e. until 2031.

R&D assets and the single CGU comprising the goodwill were subject to value tests at 30 June and 31 December 2018, as described below.

#### 5.1. R&D ASSETS

The R&D assets acquired as part of the merger with Topotarget and the acquisition of DNA Therapeutics, specifically concerning Beleodaq® in its current PTCL (peripheral T cell lymphoma) indication as well as its potential future indications and AsiDNA™, have all been tested, whether marketed or not. The 1st- and 2nd-line PTCL indications have been regrouped in order to perform this text, with the Group believing that these cover the same pathology and share a common development plan. The value in use of these R&D assets was determined based on projected cash flow on the basis of a business plan created by the Management, a plan that represent the latter's best estimate. A discount rate of 17.6% was applied to the cash flow, taking into account the market risk and the specific risks due to Onxeo. Since the values in use obtained for Beleodaq® 1st-



and 2<sup>nd</sup>-line PTCL on the one hand and for the product's potential future indications on the other were lower than the bases tested, the R&D assets were depreciated for €8.6 million. This impairment is mainly the result of increased competitive pressure on the PTCL market. Naturally, this situation has an impact on the 2<sup>nd</sup>-line treatments segment, the first approved indication of Beleodaq® in which the product has been marketed in the US by the partner company Spectrum Pharmaceuticals. However, it is also having a forward-looking impact on the 1<sup>st</sup>-line segment, an additional indication which should be obtained at the end of the phase III study to be performed by Spectrum, whether this is in terms of the product's estimated market share or in terms of sales price.

#### 5.2. SENSITIVITY TESTS

Further, the Group has performed sensitivity tests on key parameters of the model. The table below presents the potential levels of depreciation of R&D assets related to Beleodaq®. R&D assets related to AsiDNA and goodwill have not been tested for sensitivity as the value in use is significantly higher than the book value.

In millions of eur	os Beleodaq
Change in the probability of success	
-5%	-4.6
-10%	-9.5
Change in net sales	
-5%	-1.2
-10%	-2.8
Change in discount rate	
+0,2%	-0.1
+0,5%	-0,6

#### 5.3. GOODWILL

The Group determined the recoverable value of the single CGU comprising the goodwill as being the higher value between its fair value and its 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 characterising major liquidity, the fair value of the single CGU has been assessed in reference to its market capitalisation at 31 December 2018. For its part, the value in use has been determined based on estimated 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 17.6% has been applied to the cash flow, taking into account the market risk and specific risks related to Onxeo. Since the fair value of this CGU, as its value in use, is significantly higher than the tested base (net book assets consolidated on that date), no goodwill amortisation of an amount of €20 million has been recognised.

#### 5.4. OTHER INFORMATION

Research and development costs incurred in financial year 2018 were recognised as a cost in the amount of €7,585 thousand, including €4,926 thousand for external expenses, €2,496 thousand for personnel expenses and €163 thousand euros for other expenses (regulatory taxes and amortisations).

No new significant development costs were incurred regarding the Company's registered products. Consequently, there were no development costs over the year.



# NOTE 6 - PROPERTY, PLANT AND EQUIPMENT

In thousands of €	31/12/2017	Increase	Decrease	31/12/2018
Gross value	4,261	45	(1,185)	3,121
Amortisation	(3,874)	(111)	1,185	(2,800)
Provision for depreciation	(158)	0	0	(158)
Investment subsidies	(6)		6	0
Original value of lease	222	82	0	304
Amortisation of lease	(100)	(71)	0	(171)
Net value of property, plant and equipment	344	(55)	6	296

Property, plant and equipment are mostly composed of various laboratory and research equipment, as well as Other Assets.

# NOTE 7 - OTHER ASSETS

# 7.1. FINANCIAL ASSETS

In thousands of €	31/12/2017	Increase	Decrease	Discounting	31/12/2018
Financial fixed assets (equity securities)	0	3,701			3,701
Receivable from equity investments	0				0
Deposits and guarantees	172		-45		127
Liquidity contract - Cash	50	127			177
Other	10		-10		
Net value of financial assets	232	3,829	-55		4,005

#### 7.2. TRADE ACCOUNTS RECEIVABLE

In thousands of €	31/12/2018	< 1 year	> 1 year	31/12/2017
Trade accounts receivables and related accounts, net	1,479	1,479		552

Trade accounts receivable mainly comprise receivables in respect of the partner Spectrum Pharmaceuticals and Biogen.

## 7.3. OTHER RECEIVABLES

In thousands of €	31/12/2018	< 1 year	> 1 year	31/12/2017
Personnel	0	0		0
Research tax credit	2,454	2,454		3,699
Other tax receivables	648	648		1,353
Other receivables	3,323	3,323		9,600
Prepaid expenses	1,172	1,172		481
Net amount of other receivables	7,597	7,597		15,134

The change in the 'research tax credit (CIR)' item is due to the collection of the receivable recognised as at 31 December 2017 corresponding to the 2017 research tax credit, and recognition of the research tax credit for 2018 in the amount of €2,454 thousand. This item also includes the Danish research tax credit of €42 thousand. These receivables were recovered early and were therefore all classified as less than one year.

In accordance with IAS 20, the research tax credit for FY 2018 were presented as a reduction to the expense and income items according to their nature, as follows:



In thousands of €	31/12/2018	31/12/2017
Reduction in personnel costs	480	657
Reduction in external expenses	1,925	2,964
Reduction in depreciation and amortisation	48	78
Total research tax credit	2,454	3,699

Other tax receivables mainly comprise sundry VAT credits.

The item "other receivables" mainly corresponds to accrued income from the company Vectans corresponding to the milestone payments (contractual royalties) received by Vectans from its partners, repayment of which to Onxeo was deferred to the start of 2020.

#### 7.4. CASH AND CASH EQUIVALENTS

In thousands of €	Net at 31/12/2018	Net at 31/12/2017	Change in cash and cash equivalents
Cash	11,253	14,277	(3,024)
Financial investments			
Total net cash	11,253	14,277	(3,024)

The change in net cash is a decrease of €3 million. This mainly stems from the Group's operating costs, including research and development, for a total of €20.5 million. These cash outflows were partly offset by revenue from sales of products and licensing for an amount of €2.9 million. The new financing put in place over the financial year – bond issue with SWK Holding and an equity line of credit – contributed a total of €9.1 million. The Group also cashed the 2017 CIR in the amount of €3.6 million.

Cash assets comprise euro and US dollar bank accounts opened with Neuflize-OBC, including short-term deposits in the amount of €5 million that meet the definition of cash equivalents in accordance with IAS 7.6 and IAS 7.7.

# NOTE 8 - EQUITY

#### 8.1. SHARE CAPITAL

#### 8.1.1. CHANGES IN SHARE CAPITAL

At 31 December 2018, the share capital amounted to €13,344,093.75, divided into 53,376,375 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 up at 31/12/2017		0.25	50,695,653	12,673,913.25
Capital increase – share line of credit	(1)	0.25	2,483,866	620,966.50
Capital increase – bonus shares acquired	(2)	0.25	196,856	49,214.00
Shares fully paid up at 31/12/2018		0.25	53,376,375	13,344,093.75

- (1) Capital increase resulting from the exercise of share warrants as part of the debt financing line of credit set up with Nice & Green. 2 483 866 new shares, with a par value of €0.25 each, were issued in 2018 at a unit price ranging between 1.002 and 1.1896 euros, corresponding to an increase in share capital of €621 thousand together with share premiums of €2,084 thousand.
- (2) Issuance of 196,856 vested bonus shares allocated in 2017, permanently acquired in the financial year, of a par value of €0.25 each, i.e. an amount of €49 thousand.

The share premium decreased from €269,060 thousand to €41,824 thousand as a result of charging the sums recorded for the "retained earnings" account to the "issue premiums" account, in accordance with the decision



of the combined general meeting of 16 May 2018. This decrease was partially offset by the capital increase under the equity financing line for an amount of € 2,084 thousand.

#### 8.2. TREASURY SHARES

In accordance with IAS 33, paragraph 33, treasury shares acquired under the liquidity contract signed with Kepler-Chevreux were deducted from equity in the amount of €97 thousand. Losses on share buybacks at 31 December 2018 amounting to €15 thousand were deducted from the profit or loss statement pursuant to the standard.

#### 8.3. SHARE-BASED PAYMENTS

Share subscription warrants and share options were valued using the Black & Scholes method, together with the binomial /trinomial method, to reflect different possible exercise dates. This valuation is performed by an external provider. The main assumptions taken into account are the price of the underlying share, the volatility and average maturity of the instruments in question. The 2018 expense related to share-based payments amounted to €927 thousand.

#### **8.3.1. BSA:** French share subscription warrants

The Board of Directors made two allocations of share subscription warrants to non-executive or non-salaried employees of the company as follows:

	Warrants 2018	Warrants 2018-2
Date of grant	27/07/2018	25/10/2018
Number of warrants granted	359,000	85,000
Number of warrants subscribed	274,500	85,000
Vesting	30/06/2018	30/06/2018
Exercise price (€)	1.187	1.017

The expense in respect of the financial year is €30 thousand.

#### 8.3.2. SHARE OPTIONS (SO)

The Board of Directors allocated share options to employees ("Employee SO 2017" plan) and executives ("Executive SO 2017" plan). It also made an exceptional allocation to employees and the CEO as part of a loyalty plan ("Exceptional Bonus SO 2018"). The characteristics of these plans are as follows:

	Employee SO 2018	Executive SO 2018	Exceptional bonus SO 2018
Date of grant	27/07/2018	27/07/2018	27/07/2018
Number of warrants granted	554,070	84,000	271,257
Vesting	4 years	4 years	2 years
Exercise price (€)	1.187	1.187	1.187

The expense in respect of the financial year is €58 thousand.

The Board of Directors recorded the automatic cancellation due to employee departure in 2018 of 32 200 SO 2010 options, 82 000 SO 2011 options, 97 500 SO 2012 options, 67 500 SO 2013 options, 63 850 SO 2014 options, 125 125 SO 2015 options, 111 250 SO 2016 options, 174 050 SO 2017 options and 35 757 SO 2018 options. This includes, 20 500 SO 2017 options granted to the CEO and to the members of the executive board cancelled because the performance objective target was below 100%. The impact of these cancellations is a decrease in the total cost of €12 thousand.

# 8.3.3. AGAs (BONUS SHARES)

The Board of Directors made a free-share grants to employees and the CEO as follows:



	Employee AGA 2018
Date of grant	27/07/2018
Number of warrants granted	692,948
Final acquisition	27/07/2019

The corresponding net charge for the year is €315 thousand.

The Board of Directors recorded the automatic cancellation due to employee departures in 2018 of 69 200 AGA 2017 bonus shares and 16 644 AGA 2018 bonus shares. This includes, 11 250 AGA 2017 bonus shares granted to the CEO and to the members of the executive board cancelled because the performance objective target was below 100%. The impact of these cancellations is a decrease in the total cost of €42 thousand.



### 8.3.4. SUMMARY OF BSAs (SHARE SUBSCRIPTION WARRANTS) AT DECEMBER 31, 2018

Туре	Date of authorization	Authorized BSAs	Award date	Awarded BSAs	Recipients	BSAs in circulation at 12/31/2018 adjusted (1)	BSAs exercisable at 12/31/2018 adjusted (1)	Subscription price per share in euros adjusted (1)	Expiry date
Warrants 2013	06/26/2013 Resolution 17	100,000	09/19/2013	85,000		88,490	88,490	3.85	09/19/2023
Warrants 2014	06/30/2014	244.000	09/22/2014	107,500		85,886	85,886	6.17	09/22/2024
Warrants 2014-2	Resolution 19	314,800	03/04/2015	35,500	Non-salaried, non-	19,000	19,000	6.26	03/04/2025
Warrants 2015	05/20/2015		10/27/2015	80,000	executive members of the Board	65,000	65,000	3.61	10/27/2025
Warrants 2015-2	Resolution 18	405,000	01/23/2016	90,000	)	90,000	90,000	3.33	01/23/2026
Warrants 2016			07/28/2016	260,000		160,000	106,667	3.16	07/28/2026
Warrants 2016-2	04/06/2016 Resolution 23	405,520	10/25/2016	30,000	Key company consultants	30,000	20,000	2.61	10/25/2026
Warrants 2016-3			12/21/2016	70,000	Non-salaried, non-	52,500	35,000	2.43	12/21/2026
Warrants 2017	05/24/2017 Resolution 29	470,440	07/28/2017	340,000	executive members of the Board	300,000	0	4.00	07/28/2027
BSA N&G 2018	05/24/2017 Resolution 22	4,704,340	06/15/2018	4,700,000	Nice & Green S.A.	2,216,134	2,216,134	Variable	
Warrants 2018	06/19/2018		07/27/2018	359,500	Non-salaried, non- executive members	274,500	0	1.187	07/28/2028
Warrants 2018-2	Resolution 28	360,000	10/25/2018	85,000	of the Board	85,000	0	1.017	10/25/2028
TOTAL						3,107,010	2,957,010		

<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 July 28, 2011, of November 14, 2013 and of January 22, 2015)

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## 8.3.5. Summary of share subscription options at December 31, 2018

Name of plan	Date of authorization	Number of authorized options	Award date	Number of awarded options	Recipients	Options in circulation at 12/31/2018 adjusted (1)	Options exercisable at 12/31/2018 adjusted (1)	Subscription price per share in euros adjusted (1)	Expiry date
SO Employees 2010 (1)	04/00/0040	150,500	08/25/2010	120,800	Employees	18,825	18,825	5.28	08/25/2020
SO Employees 2010 (2)	04/20/2010 Resolutions 20 and 21	150,500	12/16/2010	16,000	Employees	4,319	4,319	5.23	12/16/2020
SO Executives 2010	Nesolations 20 and 21	25,000	08/25/2010	25,000	Executives	10,791	10,791	5.28	08/25/2020
TOTAL SO 2010		175,500		161,800		33,935	33,935		
SO Employees 2011 (1)	06/29/2011	300,000	09/21/2011	218,500	Employees	39,254	39,254	3.63	09/21/2021
SO Executives 2011	Resolutions 16 and 17	210,000	09/21/2011	210,000	Executives	219,782	219,782	3.63	09/21/2021
TOTAL SO 2011		510,000		428,500		259,036	259,036		
Employee SO 2012	05/31/2012	333,000	00/12/2012	268,000	Employees	91,570	91,570	3.75	09/13/2022
SO Executives 2012	Resolutions 13 and 14	110,000	09/13/2012	110,000	Executives	103,597	103,597	3.75	09/13/2022
TOTAL SO 2012		443,000		378,000		195,167	195,167		
Employee SO 2013	06/26/2013 Resolution 15	283,000	09/19/2013	195,500	Employees	70,277	70,277	3.85	09/19/2023
TOTAL SO 2013		283,000		195,500		70,277	70,277		
Employee SO 2014	06/30/2014	24.4.000	00/22/2011	138,700	Employees	33,653	33,653	6.17	09/22/2024
SO Executives 2014	Resolution 17	314,800	09/22/2014	40,000	Executives	34,487	34,487	6.17	09/22/2024
TOTAL SO 2014		314,800		178,700		68,140	68,140		
Employee SO 2015	05/20/2015	405.000	10/27/2015	290,000	Employees	72,375	54,375	3.61	10/27/2025
SO Executives 2015	Resolution 16	405,000	10/27/2015	60,000	Executives	60,000	45,000	3.61	10/27/2025
TOTAL SO 2015		405,000		350,000		132,375	99,375		
Employee SO 2016	06/04/2016	405,520	07/28/2016	333,500	Employees	122,050	63,850	3.16	07/28/2026
SO Executives 2016	Resolution 22	405,520	07/28/2016	70,000	Executives	56,000	28,000	3.16	07/28/2026
TOTAL SO 2016		405,520		403,500		178,050	91,850		
Employee SO 2017	05/24/2017	470,440	07/28/2017	347,800	Employees	180,750	46,125	4.00	07/28/2027
SO Executives 2017	Resolution 26	470,440	07/28/2017	70,000	Executives	63,000	15,750	4.00	07/28/2027
TOTAL SO 2017		470,440		417,800		243,750	61,875		
Employee SO 2018	06/19/2018	070 000	07/27/2018	758,604	Employees	722,847	0	1.187	07/27/2028
SO Executives 2018	Resolution 27	970,000	12/16/2010	150,723	Executives	150,723	0	1.187	07/27/2028
TOTAL SO 2018		970,000		909,327		873,570	0		
TOTAL SO						2,054,300	879,655		

<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 July 28, 2011, of November 14, 2013 and of January 22, 2015)



## 8.3.6. SUMMARY OF RIGHTS TO FREE SHARES (AGA) AT DECEMBER 31, 2018

Name of plan	Date of authorization	Number of authorized free shares	Award date	Number of awarded shares	Recipients	Rights to free shares outstanding at 12/31/2018
Employee AGA 2018	06/19/2018 Resolutions 25 and 26	735,000	07/27/2018	552,170	Employees	535,526
Executive AGA 2018				140,778	Executives	140,778
TOTAL AGA 2018				692,948		676,304
TOTAL AGA				692,948		676,304



### NOTE 9 - NON-CURRENT LIABILITIES

### 9.1. DEFERRED TAX LIABILITY

This item of €2,330 thousand relates to research and development assets acquired within the context of the Topotarget merger in June 2014. The decrease in the deferred tax liability for the year is related to the recognition of an €8.6 million depreciation that reduced the Danish withholding tax value for the R&D assets in question.

### 9.2. PROVISIONS

In thousands of €	31/12/2017	Additions	Reversals		31/12/2018
			Used	Unused	
Retirement benefit obligations	468	87	59	91	404
Provision for losses and contingencies	82	190		145	127
Total non-current provision for losses and contingencies	550	277	59	236	531

### 9.2.1. RETIREMENT BENEFIT OBLIGATIONS (IAS 19 REVISED)

The provision for retirement benefit obligations amounted to €404 thousand compared with €468 thousand in 2017. This led to an increase in earnings of €53 thousand, and actuarial gains and losses of €11 thousand was recognised directly as other comprehensive income, in accordance with the standard.

The actuarial assumptions are as follows:

	31/12/2018	31/12/2017			
Collective bargaining agreement	Medical	industry			
Retirement age	Between 65 and 67 years, under the Pension Reform Act of 10 Novemb 2010				
Calculation date	31/12/2018	31/12/2017			
Mortality table	INSEE 2018	INSEE 2017			
Discount rate	1.70%	1.55%			
Rate of salary increase	2%	2%			
Employee turnover rate	By age category: - 0% from 16 to 24 - 3.70 % from 25 to 34 - 6.02 % from 35 to 44 - 0.93 % from 45 to 54 - 0.00 % above 55	By age category: - 0% from 16 to 24 - 3.61% from 25 to 34 - 6.02 % from 35 to 44 - 2.41% from 45 to 54 - 0.00% above 55			
Social security tax rate	46% for Onxeo FR				

### 9.2.2. Provisions for Litigation

Provisions for contingencies and charges in an amount of €127 thousand corresponding to disputes with former employees.

### 9.3. OTHER NON-CURRENT FINANCIAL LIABILITIES

Other non-current liabilities comprise the mandatory financing granted by SWK Holdings in the amount of €6.4 million. Since this liability was reimbursed through the royalties paid by the partner Spectrum Pharmaceuticals on future sales of Beleodaq® in the United States, the amount of which was not communicated by Spectrum, no maturity cut-off can be provided.



This item also includes the portion of repayable advances at more than one year of Bpifrance for the financing of the Company's R&D programmes, as detailed below.

In thousands of euros	31/12/2018	< 1 year	1 to 5 years	More than 5 years
AsiDNA™	485	159	326	0
TOTAL	485	159	326	0

### NOTE 10 - CURRENT LIABILITIES

### 10.1. TRADE ACCOUNTS PAYABLE AND RELATED ACCOUNTS

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 €	31/12/2018	31/12/2017
Trade accounts payable and related accounts	4,145	5,956

The increase in trade accounts payable was mainly due to the decrease in expenses following the completion of the phase III ReLive study in September 2017 and the termination of the Livatag programme.

The Company is conducting pre-clinical and clinical studies and formalising its relations with external partners assisting Onxeo in its works. As part of the clinical trials, the research expenses provisioned for at the balance sheet date were determined based on estimates of per-patient costs not yet billed, as established by the Management. These estimates are based on the information provided by the investigation centres (hospitals) under contract and the cost analyses carried out by the Management.

### 10.2. OTHER LIABILITIES

In thousands of €	31/12/2018	31/12/2017
Social security liabilities	745	2,029
Tax liabilities	162	234
Other liabilities	2,891	10,492
Total	3,798	12,755

Social security liabilities are decreasing due to departures of employees and the workforce reduction implemented at the end of 2017 as well as a reduction in end-of-year cash bonuses with a view to protecting cash.

Other liabilities at 31 December 2018 mainly comprise the amount of €2,878 thousand that the Paris Court of Appeal ordered the Company to pay in its dispute with Spebio and SpePharm. The change compared with 2017 is due to the payment, in 2018, of an amount of €9.2 million relating to the order pronounced by the Paris Commercial Court in the same dispute at the end of 2017.

Other liabilities also include licence revenue deferred to less than one year, amounting to €81 thousand. This licence revenue, collected on signing the agreements, is staggered according to the estimated date for obtaining the marketing authorisation. The amount of short-term deferred licence revenue taken to profit or loss and recognised as revenue in 2018 is detailed below:



In thousands of €	Balance at 31/12/2017	Reversal through profit and loss	reserves (1st	31/12/2018		More than 1 year
Pint Pharma	1,126	120	935	81	69	13

### NOTE 11 - FINANCIAL INSTRUMENTS

The carrying amount of financial instruments by category under IFRS 9 is detailed as follows:

	Category			Balance			
In thousands of €	in accordan ce with IFRS 9	Net at 31/12/2017	Net at 31/12/2018	Amortiz ed cost	Fair value throug h equity	Fair value through profit or loss	Fair value as per IFRS7
Loans	P&C	0	0	0	0	0	0
Derivatives at fair value	AJVPR	0	0	0	0	0	0
Trade accounts receivable and related accounts	P&C	552	1,479	1,479	0	0	1,479
Other receivables	P&C	15,134	7,597	7,597	0	0	7,597
Security deposits	P&C	172	127	127	0	0	127
Other assets available for sale	ADV	50	177	0	0	177	177
Cash and cash equivalents	AJVPR	14,277	11,253	11,253	0	0	11,253
Total Assets		30,186	20,633	20,456	0	177	20,633
Bond issues	DACA	0	6,267	6,267	0	0	6,267
Borrowings/Banks	DACA	130	133	133	0	0	133
Derivatives at fair value	PJVPR	0	154	0	0	154	154
Trade payables	DACA	5,956	4,145	4,145	0	0	4,145
Other payables/other liabilities	DACA	8,041	3,798	3,798	0	0	3,798
Total Liabilities		14,128	14,498	14,344	0	154	14,498

Financing transactions concluded during the year were treated as follows under IFRS 9:

- The bond issue with SWK Holdings has been classified as a financial liability booked at amortized cost,
- The share warrants issued in favor of Nice & Green representing derivative instruments have been reassessed at fair value through counterpart of the financial result.

### 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 through profit or loss			
Derivatives at fair value through equity	0	0	0
Financial assets available for sale	0	177	0
Money market securities available for sale	0	0	0
<b>Total Financial Assets</b>	0	177	0
Derivatives at fair value through profit or loss	0	154	0
Derivatives at fair value through equity	0	0	0
Total Financial Liabilities	0	154	0

### NOTE 12 - OPERATING INCOME AND EXPENSES

### 12.1. REVENUE

In thousands of €	31/12/2018	31/12/2017
Recurring revenue from licensing agreements	2,310	3,041
Non-recurring revenue from licensing agreements	3,817	6,463
Total revenue	6,127	9,505

Recurring revenue comes from product sales, the European named patients programme (NPP) and sales-based royalties related to license agreements with Spectrum Pharmaceuticals. The reduction compared with 2017 mainly arises from the sale of the Loramyc® and Sitavig products to Vectans Pharma at the end of July 2017.

Non-recurring revenue includes a percentage of those amounts received upon signing certain agreements over the period or over previous periods and staggered up to the scheduled market launch authorisation date. After the IFRS 15 standard was applied on 1 January, an amount of €935 thousand was reclassified as reserves, therefore reducing deferred turnover. The impact on the financial year 2018 is a reduction in non-recurring turnover of €491 thousand.

In accordance with IFRS 8.32 and 33, the table below shows the provenance of revenue by geographic area and in comparison with two Company product categories:

In thousands of €	31/12/2018	31/12/2017
Oncology products	3,270	3,130
Other products (1)	2,857	6,375
Total	6,127	9,505
Europe	582	5,194
Rest of the world	5,545	4,311
Total	6,127	9,505

<sup>(1)</sup> these products from the Lauriad technology were either sold (Loramyc and Sitavig) or licensed worldwide (Validive) during the 2017 financial year.

### 12.2. PERSONNEL COSTS

Personnel costs break down as follows:

In thousands of €	31/12/2018	31/12/2017
Salaries	3,531	5,490
Expenses	1,457	2,401
Employee benefits (IFRS 2)	927	980
Deduction of research tax credit	(477)	(654)
Deduction of operating subsidies	0	0
Total personnel costs	5,438	8,217



Headcount (employees and officers)	30	46
------------------------------------	----	----

The decrease in personnel costs is due to the workforce reduction and a reduction in end-of-year cash bonuses with a view to protecting cash flowbonus share.

### 12.3. EXTERNAL EXPENSES

External expenses mainly comprise the following items:

In thousands of €	31/12/2018	31/12/2017
R&D expenses	4,926	15,363
Deduction of operating subsidies	0	0
Deduction of research tax credit	(1,912)	(2,954)
General and administrative expenses	5,716	5,123
Total	8,731	17,555

The change in R&D costs is consistent with the evolution of the company's programmes and, in particular, the termination of the Livatag® programme.

The increase in general and administrative expenses is mainly due to non-recurring costs, in particular fees related to implementing the royalty monetisation contract with SWK Holdings and the rehabilitation of space freed up at the headquarters by the Company at the end of 2018 (savings anticipated from 2019).

### 12.4. DEPRECIATION AND AMORTISATION EXPENSE

As explained in Note 5, an amortisation charge for part of the research and development programmes acquired under the merger was recognised in the amount of €398 thousand. Other depreciation and amortisation expenses/reversals mainly comprise depreciation of the Company's property, plant and equipment.

### 12.5. RESULTS OF EQUITY AFFILIATES

At 31/12/2018, only the company SpeBio are accounted for using the equity method.

The table below presents the key data on the financial statements of the company SpeBio for the 2018 financial year, accounted for using the equity method:

In thousands of €	31/12/2018
Total assets	10,660
Total liabilities	3,257
Equity	7,403
Revenue	2,868
Net result	2,537
Share of SpeBio in net results	5,176

### 12.6. OTHER INCOME AND OPERATIONAL EXPENSES

This post, for an amount of €12,117 thousand at 31 December 2018, mainly consists of the provision for depreciation of R&D assets for an amount of €8,550 thousand (see Note 5), as well as the amount the Company was ordered to pay in the context of the appeal made in the dispute with the companies SpeBio and SpePharm for an amount of €2 868 thousand.

As of December 31, 2017, the Company had recognized a provision for depreciation of R&D assets of €38.1 million and an amount of €9.2 million corresponding to the conviction imposed to Onxeo by the Paris Commercial Court in the litigation with SpeBio and SpePharm.



### NOTE 13 - NET FINANCIAL INCOME (EXPENSE)

In thousands of €	Cash	Non Cash	31/12/2018	31/12/2017
Income from cash and cash equivalents	300	46	346	626
Cost of gross financial debt	(381)	(656)	(1,037)	(1,118)
Cost of net financial debt	(81)	(610)	(691)	(492)
Other financial income and expenses	0	0	0	0
Financial income	(81)	(610)	(691)	(492)

Cash income mainly comprises currency gains in the amount of €105 thousand, as well as interest from short-term investments.

The financial costs mainly comprise interest expense related to the royalty pre-financing agreement with SWK Holdings Corporation.

### NOTF 14 - TAX

The tax income of €1,764 thousand recognised in the financial year corresponds to the decrease in the deferred tax liability as a result of the depreciation of the R&D assets acquired as part of the merger with Topotarget, as explained in Note 5. The added value from the merger recognised on these assets benefits from a tax deferral in accordance with Danish tax rules, which explains how deferred tax was determined.

At 31 December 2018, the Onxeo Group had French tax loss carry-forwards of €271 million.

No deferred tax asset was recognised insofar as the Company is unable to recover these tax losses in the short term.

### NOTE 15 - EARNINGS PER SHARE

### 15.1. NET EARNINGS PER SHARE

In thousands of €	31/12/2018	31/12/2017
Net profit/(loss) attributable to holders of ordinary shares	(9,399)	(59,071)
Number of ordinary shares	53,376,375	50,695,653
Number of treasury shares	111,095	77,752
Net Earnings per share	(0.18)	(1.17)

Basic earnings per share is calculated by dividing the net profit (or loss) attributable to holders of ordinary shares (the numerator) by the weighted average number of outstanding ordinary shares (the denominator) for the period.

In thousands of €	31/12/2018	31/12/2017
Net profit/(loss) attributable to holders of ordinary shares	(9,399)	(59,071)
Number of ordinary shares	53,376,375	50,695,653
Effect of dilution (1)	-	-
Number of shares adjusted for diluted net profit (loss)	53,376,375	50,695,653
Diluted earnings	(0.18)	(1.17)

(1) Conversion into shares of all of the share options, bonus shares and share subscription warrants attributed at the balance sheet date would lead to 6 197 114 extra shares being created, of which 3 980 980 in addition to the warrants allocated to Nice & Green as part of the equity line of credit; the impact of dilution is not presented due to the net loss.

To calculate diluted earnings per share, the average number of outstanding shares is adjusted to take into account the conversion of all potentially dilutive ordinary shares, notably due to share 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 Onxeo ordinary shares is adjusted by:

- any dividend or other item in respect of potentially dilutive ordinary shares that have been deducted in order to obtain the profit (or loss) attributable to the holders of ordinary shares;
- interest recognised in the period in respect of potentially dilutive ordinary shares;
- any other changes in income or expense that would result from the conversion of the potentially dilutive ordinary shares.

### NOTE 16 - OFF-BALANCE-SHEET COMMITMENTS

# 16.1. OFF-BALANCE-SHEET COMMITMENTS RELATED TO THE COMPANY'S OPERATIONAL ACTIVITIES

### Operating leases (IAS 17)

The company has entered into real estate lease contracts for its registered office at 49, Boulevard du Général Martial Valin, Paris (15<sup>th</sup> arrondissement), and for the registered office 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 years	> 5 years
436	1,708	999

### 16.2. OFF-BALANCE-SHEET COMMITMENTS RELATED TO THE COMPANY'S FINANCING

None.

# 16.3. OTHER COMMITMENTS LINKED TO COMPANIES INCLUDED IN THE SCOPE OF CONSOLIDATION

None.

### NOTE 17 - REMUNERATION OF CORPORATE OFFICERS

The table below summarises the remuneration accounted for as at 31 December 2018 for Judith Greciet (CEO), a non-salaried corporate officer, as well as for members of the Board of Directors.

In thousands of €	31/12/2018	31/12/2017
Short-term benefits (fixed/variable/exceptional)	394	387
Post-employment benefits	102	82
Long-term benefits	0	0
Share-based payments	461	350
Benefits in kind	3	3
Severance pay	0	0
Directors' fees	203	210
Fees (related party agreement))	0	0
Total	1,164	1,031

Onxeo has established a method of remuneration of its directors through fees..

Corporate officers' retirement benefits amounted to €102 245.



### NOTE 18 - 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 14.5% of the capital, and as a board member, is considered to exert a significant influence on the company.
- No transactions were made with Financière de la Montagne in the year 2018.
- The Chairman of the Board of Directors, as one of the main directors presenting the financial statements.
- No transactions were effected with the Chairman of the Board of Directors in 2018.

### NOTE 19 - INTRA-GROUP TRANSACTIONS

The transactions effected between the parent company and the other companies of the group are summarised in gross values in the following table:

In thousands of euros	31/12/2018	31/12/2017
Assets	76,906	75,783
Liabilities	4,827	3,534
Income	36	26
Expenses	1,289	198

### NOTE 20 - STATUTORY AUDITORS' FEES

The fees paid by Onxeo to its statutory auditors in 2018 and 2017 are as follows:

	Grant Thornton			Ernst & Young					
In thousands of €	Amo	ount	9	6		Amo	unt	%	5
	2018	2017	2018	2017		2018	2017	2018	2017
Audit, statutory audit,	certification,	review of fin	ancial staten	nents under F	ren	ch and IFRS s	standards		
Issuer	81	75	100%	97%		78	80	84%	89%
Fully consolidated subsidiary									
Services other than certification of the accounts		2		3%		15	10	16%	11%
Sub-total	81	77		100%		93	90	100%	100%
Other services rendered by the networks to the fully consolidated subsidiary									
Sub-total									
Total	81	77	100%	100%		93	90	100%	100%



# 6.2 STATUTORY AUDITORS' REPORTS ON THE CONSOLIDATED FINANCIAL STATEMENTS (FRENCH ONLY)

This is a translation into English of the statutory auditors' report on the consolidated financial statements of the Company issued in French and it is provided solely for the convenience of English- speaking users.

This statutory auditors' report includes information required by European regulation and French law, such as information about the appointment of the statutory auditors or verification of the information concerning the Group presented in the management report.

This report should be read in conjunction with, and construed in accordance with, French law and professional auditing standards applicable in France.

### **GRANT THORNTON**

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Commissaire aux Comptes Membre de la compagnie régionale de Versailles

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344 366 315 R.C.S. Nanterre

Commissaire aux Comptes Membre de la compagnie régionale de Versailles

#### Onxeo

Year ended December 31, 2018

Statutory auditors' report on the consolidated financial statements

To the Annual General Meeting of Onxeo,

### **Opinion**

In compliance with the engagement entrusted to us by your Annual General Meetings, we have audited the accompanying consolidated financial statements of Onxeo for the year ended December 31, 2018.

In our opinion, the consolidated financial statements give a true and fair view of the assets and liabilities and of the financial position of the Group as at December 31, 2018 and of the results of its operations for the year then ended in accordance with International Financial Reporting Standards as adopted by the European Union.

The audit opinion expressed above is consistent with our report to the Audit Committee.

### **Basis for Opinion**

### **Audit Framework**

We conducted our audit in accordance with professional standards applicable in France. We believe that the audit evidence we have obtained is sufficient and appropriate to provide a basis for our opinion.

Our responsibilities under those standards are further described in the *Statutory Auditors' Responsibilities for the Audit of the Consolidated Financial Statements* section of our report.



### Independence

We conducted our audit engagement in compliance with independence rules applicable to us, for the period from January 1, 2018 to the date of our report and specifically we did not provide any prohibited non-audit services referred to in Article 5(1) of Regulation (EU) No 537/2014 or in the French Code of Ethics (Code de déontologie) for statutory auditors.

### **Emphasis of matter**

We draw attention to the following matter described in Notes 3.9.6, 10.2 and 12.1 to the consolidated financial statements relating to the impact of the first application in 2018 of IFRS 15 on revenue recognition. Our opinion is not modified in respect of this matter

### Justification of Assessments - Key Audit Matters

In accordance with the requirements of Articles L.823-9 and R.823-7 of the French Commercial Code (Code de commerce) relating to the justification of our assessments, we inform you of the key audit matters relating to risks of material misstatement that, in our professional judgment, were of most significance in our audit of the consolidated financial statements of the current period, as well as how we addressed those risks.

These matters were addressed in the context of our audit of the consolidated financial statements as a whole, and in forming our opinion thereon, and we do not provide a separate opinion on specific items of the consolidated financial statements.

# Revenue recognition related to license agreements (Cf. Notes 2.2, 3.1, 3.9.6, and 12.1 to the consolidated financial statements)

### Risk identified Our response

.

Revenues are made notably from license agreements signed with partners. Such agreements result in the cash-in of initial payments, then cashins conditioned to technical, commercial or regulatory objectives by partners.

On the other hand, the Company benefits from royalties corresponding to a percentage of net sales achieved by the partners.

Finally, revenues also include sales of assets and other non-recurring items, as presented in Note 3.9.6to the consolidated financial statements.

From an accounting standpoint, initial payments at signature date are spread out from signature to expected date of marketing authorization. Further payments conditioned to contractual objectives are fully recorded when objectives are met. Royalties on net sales are booked depending on actual sales made by partners, applying contractual rates.

Our audit procedures consisted in examining all on going agreements. Our controls consisted in:

- analyzing the contractual clauses and accounting method applicable to initial payments, further conditioned payments and royalties on net sales;
- analyzing accounting treatments related to such agreements in accordance with the new IFRS standard, IFRS 15, in application starting January 1, 2018;
- assessing the assumptions used for revenue recognition, notably the expected dates of marketing authorization and research costs to be incurred after signing. Within that framework, we held meetings in particular with the Finance department and the R&D teams, and examined internal historical data and the documents submitted by the partners;



Contracts accounting relies on several key assumptions determined by management, notably:

- estimate of the marketing authorization date and research costs to be incurred by the group after signing the contract;
- estimate of the net sales made by partners and computation of the corresponding royalties.

We considered that revenue recognition from license agreements was a key audit matter.

- reconciling the partners' net sales at closing in order to verify the calculation of the royalties based on these sales;
- in the case of asset's intellectual property right sale, investigate on the conditions of the intellectual property right effective transfer of the products to the partners for the molecule sales;

# Intangible assets related to R&D and Goodwill valuation (Cf. Notes 3.5 and 5 to the consolidated financial statements)

### **Risk identified**

As at December 31, 2018, the net book value of the fixed assets related to research and development (R&D) and to goodwill amounts to M€ 38,6. Such assets are mainly made up of:

- (i) intangible assets related to R&D originating, on the one hand, from research work performed by Danish company TopoTarget and brought to Onxeo in the context of a merger dated August 5, 2014, for M€ 63,1 and, on the other hand, from the acquisition of the DNA Therapeutics on February 29, 2016 for M€ 2,5;
- (ii) goodwill accounted for following the aforementioned merger with TopoTarget for an amount of M€ 20,1.

Notes 3.5.4, 5.1, 5.2 and 5.3 to the consolidated financial statements describe the terms and conditions of the impairment tests performed on intangible assets relating to R&D and those relating to the single Cash Generating Unit, including inter alia the intangible assets relating to R&D assets and goodwill:

- the CGU, when they include goodwill, and assets related to R&D not commercialized yet (and consequently not amortized yet) are subject to an impairment test at least once a year. The Group performs such test at closing;
- R&D assets related to commercialized (and therefore amortized) products are subject to an impairment test, when new circumstances indicate that such assets may have suffered an impairment.

### Our response

Our audit procedures regarding intangible assets relating to R&D and goodwill, consisted of controls on (i) the business plan prepared by the Group's management and including various operational assumptions and the chances of success in the projected cash-flows and (ii) the financial model used to determine the recoverable value of each of the assets tested by your Company.

We also examined the terms and conditions of the impairment tests performed, examined the main estimates and assumptions used and compared such data with projected information prepared by your Company's management to (i) prepare the business plans based on internal information and on information provided by partners of the Group's license contrats and (ii) the financial model used to determine the recoverable value of each of the assets. We focused our attention on the following elements:

- the main operational assumptions included in the business plan: we examined estimates and assumptions used and compared such data with projected information provided by partners of your Company's license contracts;
- chance of success: we assessed, with the assistance of our financial valuation expert, the various chances of success used by your Company and compared them with the practices observed in the biotechnology sector;



Impairment tests have been performed using the discounted cash flow method in order to determine the value in use of the assets. Impairment tests performed at December 31, 2018, were satisfactory. However, impairment tests done at June 30, 2018 mid-year closing led to accounting for a depreciation of M€ 8,6.

We considered that determining the recoverable value of intangible assets relating to R&D and goodwill is a key audit matter due to (i) the significance of the assets in the Group's consolidated financial statements, (ii) the necessary estimates to determine projected cash flows and (iii) the estimates and assumptions, namely regarding the chances of success and the discount rate, used to determine the recoverable value

 discount rates used: we assessed the relevance of the rates used, with the support of our financial valuation experts.
 Sensitivity tests were therefore performed by Group Management and reviewed by us.

### Share-based payments (Cf. Notes 3.8 and 8.3 to the consolidated financial statements)

### **Risk identified**

Note 8.3 "Share-based payments" to the consolidated financial statements sets out share purchase warrants (BSA) plans, stock option plans, and free-share plans for the benefit of employees, senior executives and board members.

As at December 31, 2018, the personnel expenses related to these plans amounts to 927 thousand euros. As indicated in Notes 3.8 "Share-based payments (IFRS 2)" and 8.3 "Share-based payments" to the consolidated financial statements, the fair value of these plans was determined by an external service provider using the Black & Scholes and binomial/trinomial method.

We considered that the valuation of these plans was a key audit matter due to the sensitivity of their fair value to the assumptions used.

### Our response

Our audit procedures namely consisted in:

- reviewing the minutes of the meetings of the Board of Directors and the plans' bylaws, in order to examine the correct accounting for the new plans granted during the financial year, as well as the inclusion in the calculation assumptions of the plans, the specific conditions attached to these plans;
- analyzing the valuation performed by the external service provider and the factors justifying the key assumptions used to determine the fair value of these plans;
- studying the main assumptions used (presence conditions, performance conditions, etc.) and assessing the correct execution of these assumptions in the financial model. We included an actuarial expert in our audit team to assist us in this work;
- examining the amortization period of these plans and the related personnel expenses.



# Valuation of costs incurred for the performance of clinical trials (Cf. Notes 3.5.2 and 5.4 to the consolidated financial statements)

### Risk identified

.

As set out in Note 3.5.2 to the consolidated financial statement, in the context of the development of its products, your Company performs clinical trials in collaboration with research centers.

The costs incurred for such trials are recognized as expenses according to the state of completion of the medical treatments. At closing, an estimate of the costs not yet invoiced by third-parties per patient is determined by management and recorded as expenses for the year. These cost estimates are determined by management based on the information provided by the investigation centers (hospitals) under contract and cost analyzes performed by your Company.

Given the importance of the research and development expenses and their methods of estimate at closing, we considered their valuation to be a key audit matter.

### Our response

Our audit procedures namely consisted in taking into account valuation and the factors justifying the key assumptions used by management to determine the amount of the provisions. In this context, we:

- took note of the internal control procedures set up by the Group to identify and estimate the costs to be recorded at closing;
- assessed the significant contracts entered into with clinical trial centers, as well as the elements established by management to justify the cost per patient of the medical treatments carried out;
- analyzed the previous year accruals with the actual amounts to review the consistency of management's past estimates;
- examined the consistency of the stage or completion of medical treatments per patient and the calculation of the related expenses, in the light of the information provided by research centers or the analysis carried out by management on the basis of historical data.
- analyzed the expenses recognized in the subsequent period to assess that there is no discrepancy with the estimates made.

### Specific verifications

We have also performed, in accordance with professional standards applicable in France, the specific verifications required by laws and regulations of the information pertaining to the Group presented in the Board of Directors' management report.

We have no matters to report as to its fair presentation and its consistency with the consolidated financial statements.



### Report on Other Legal and Regulatory Requirements 15

### **Appointment of the Statutory Auditors**

We were appointed as statutory auditors of Onxeo by your annual general meeting held on February 25, 1997 for GRANT THORNTON and on November 7, 2005 for ERNST & YOUNG Audit.

As at December 31, 2018, Grant Thornton was in the 22<sup>nd</sup> year of total uninterrupted engagement (including 14 years since Onxeo is listed on a regulated market) and ERNST & YOUNG Audit in the 14<sup>th</sup> year.

# Responsibilities of Management and Those Charged with Governance for the Consolidated Financial Statements

Management is responsible for the preparation and fair presentation of the consolidated financial statements in accordance with International Financial Reporting Standards as adopted by the European Union and for such internal control as management determines is necessary to enable the preparation of consolidated financial statements that are free from material misstatement, whether due to fraud or error.

In preparing the consolidated financial statements, management is responsible for assessing the Company's ability to continue as a going concern, disclosing, as applicable, matters related to going concern and using the going concern basis of accounting unless it is expected to liquidate the Company or to cease operations.

The Audit Committee is responsible for monitoring the financial reporting process and the effectiveness of internal control and risks management systems and where applicable, its internal audit, regarding the accounting and financial reporting procedures.

The consolidated financial statements were approved by the Board of Directors.

### Statutory Auditors' Responsibilities for the Audit of the Consolidated Financial Statements

### Objectives and audit approach

Our role is to issue a report on the consolidated financial statements. Our objective is to obtain reasonable assurance about whether the consolidated financial statements as a whole are free from material misstatement. Reasonable assurance is a high level of assurance, but is not a guarantee that an audit conducted in accordance with professional standards will always detect a material misstatement when it exists. Misstatements can arise from fraud or error and are considered material if, individually or in the aggregate, they could reasonably be expected to influence the economic decisions of users taken on the basis of these consolidated financial statements.

As specified in Article L.823-10-1 of the French Commercial Code (*Code de commerce*), our statutory audit does not include assurance on the viability of the Company or the quality of management of the affairs of the Company.

As part of an audit conducted in accordance with professional standards applicable in France, the statutory auditor exercises professional judgment throughout the audit and furthermore:



- ▶ Identifies and assesses the risks of material misstatement of the consolidated financial statements, whether due to fraud or error, designs and performs audit procedures responsive to those risks, and obtains audit evidence considered to be sufficient and appropriate to provide a basis for his opinion. The risk of not detecting a material misstatement resulting from fraud is higher than for one resulting from error, as fraud may involve collusion, forgery, intentional omissions, misrepresentations, or the override of internal control.
- Obtains an understanding of internal control relevant to the audit in order to design audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the internal control.
- Evaluates the appropriateness of accounting policies used and the reasonableness of accounting estimates and related disclosures made by management in the consolidated financial statements.
- Assesses the appropriateness of management's use of the going concern basis of accounting and, based on the audit evidence obtained, whether a material uncertainty exists related to events or conditions that may cast significant doubt on the Company's ability to continue as a going concern. This assessment is based on the audit evidence obtained up to the date of his audit report. However, future events or conditions may cause the Company to cease to continue as a going concern. If the statutory auditor concludes that a material uncertainty exists, there is a requirement to draw attention in the audit report to the related disclosures in the consolidated financial statements or, if such disclosures are not provided or inadequate, to modify the opinion expressed therein.
- Evaluates the overall presentation of the consolidated financial statements and assesses whether these statements represent the underlying transactions and events in a manner that achieves fair presentation.
- Obtains sufficient appropriate audit evidence regarding the financial information of the entities or business activities within the Group to express an opinion on the consolidated financial statements. The statutory auditor is responsible for the direction, supervision and performance of the audit of the consolidated financial statements and for the opinion expressed on these consolidated financial statements.

### **Report to the Audit Committee**

We submit to the Audit Committee a report which includes in particular a description of the scope of the audit and the audit program implemented, as well as the results of our audit. We also report, if any, significant deficiencies in internal control regarding the accounting and financial reporting procedures that we have identified.

Our report to the Audit Committee includes the risks of material misstatement that, in our professional judgment, were of most significance in the audit of the consolidated financial statements of the current period and which are therefore the key audit matters that we are required to describe in this report.

We also provide the Audit Committee with the declaration provided for in Article 6 of Regulation (EU) N° 537/2014, confirming our independence within the meaning of the rules applicable in France such as they are set in particular by Articles L.822-10 to L.822-14 of the French Commercial Code (Code de commerce) and in the French Code of Ethics (code de déontologie) for statutory auditors. Where appropriate, we discuss with the Audit Committee the risks that may reasonably be thought to bear on our independence, and the related safeguards.



Neuilly-Sur-Seine and Paris-La Défense, April 5, 2019

- The Statutory Auditors French original signed by

GRANT THORNTON
French Member of Grant Thornton International

**ERNST & YOUNG Audit** 

Samuel Clochard

Franck Sebag



## 6.3 ANNUAL FINANCIAL STATEMENTS

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# **BALANCE SHEET**

## 1. ASSETS

		Amortization &		
In € thousands	Gross	Depreciation / Impairment	Net 2018	Net 2017
SUBSCRIBED UNCALLED SHARE CAPITAL		Impairment		
INTANGIBLE FIXED ASSETS				
Incorporation expenses				
Development costs	65 089	47 392	17 697	25,760
Concessions, patents and similar rights	181	181		
Goodwill	4 450		4 450	4 450
Other intangible assets	238	238		14
Advances and prepayments on intangible assets				
Total intangible fixed assets	69 959	47 811	22 147	30 224
TANGIBLE FIXED ASSETS				
Land				
Buildings				
Plant & equipment	1 298	1 224	75	48
Other tangible assets	1 823	1 735	88	181
Tangible assets in progress				
Advances and prepayments				
Total tangible fixed assets	3 121	2 959	162	228
LONG-TERM INVESTMENTS				
Holdings valued by the equity method				
Other equity holdings	48 630	43 080	5 550	6 011
Receivables from investments				
Other long-term securities	97		97	89
Other financial fixed assets	297		297	215
Total long-term investments	49 024	43 080	5 944	6 316
NON-CURRENT ASSETS	122 104	93 850	28 254	36 768
INVENTORIES				
Raw materials and supplies				
Work in progress - goods				
Work in progress - services				
Semi-finished and finished goods				
Merchandise	47		47	30
Total stocks	47		47	30
ACCOUNTS RECEIVABLE				
Prepayments to suppliers				
Trade receivables	1 009	152	856	730
Other receivables	33 068	23 387	9 681	15 527
Subscribed, called, unpaid share capital				
Total receivables	34 077	23 540	10 537	16 258
LIQUID ASSETS				
Securities including treasury shares:				
Liquid assets	11 182		11 182	13 965
Total liquid assets	11 182		11 182	13 965
CURRENT ASSETS	45 306	23 540	21 767	30 252
Prepaid expenses	1 172		1 172	482
Issuing costs to be spread over several years				
Loan redemption premiums				
Unrealized foreign exchange losses	7		7	57
GRAND TOTAL	168 589	117 390	51 199	67 559



# 2. LIABILITIES

€ thousands	Net 2018	Net 2017
NET EQUITY		
Share capital Of which paid: 13 344	13 344	12 674
Issue, merger and acquisition premiums	28 524	255 760
Excess of restated assets over historical cost		
Legal reserve		
Reserves required by the articles of incorporation or by contract		
Regulated reserves		
Other reserves	179	72
Retained earnings		(162 781
NET INCOME for the period (profit or loss)	(12 955)	(66 425
Total net equity	29 092	39 301
Capital grants		(
Regulated provisions		
SHAREHOLDERS' EQUITY	29 092	39 307
Proceeds from issue of preference shares		
Advances with specific conditions attached	485	4 714
OTHER SHAREHOLDERS' EQUITY	485	4 714
Contingency provisions	7	57
Loss provisions	127	82
PROVISIONS FOR LIABILITIES AND CHARGES	134	139
FINANCIAL LIABILITIES		
Convertible bonds		
Other bonds	5 926	
Bank debts and debts with credit institutions	4	g
Other debt	222	
Total financial liabilities	6 152	ġ
OPERATING LIABILITIES		
Customer prepayments		
Trade payables	5 156	6 129
Accrued taxes and personnel costs	924	2 269
Total operating liabilities	6 080	8 398
OTUED LIA DILITIES		
OTHER LIABILITIES	10	
Payables on fixed assets and related accounts	19	13.690
Other debts  Total other financial liabilities	6 796 <b>6 814</b>	12 686
Total other illiancial liabilities	0 014	12 699
ACCRUALS		
Deferred revenue	411	1 244
TOTAL LIABILITIES	19 458	22 350
Unrealized foreign exchange gains	2 031	1 049
GRAND TOTAL	51 199	67 559



# **INCOME STATEMENT**

## 1. INCOME STATEMENT (PART 1)

In € thousands	France	Export	Net 2018	Net 2017
Sale of goods	526	·	526	697
Production goods sold				
Production services sold	23		23	198
NET SALES	549		549	895
Production left in stock				
Capitalized production				
Operating grants				2
Excess depreciation and recovery on pr	ovisions charged i	n prior years	2 930	1 018
Royalties from licensing and other inco	me.		5 186	8 393
TOTAL OPERATING INCOME			8 664	10 308
EXTERNAL EXPENSES				
Purchases of goods for resale (including	g customs duties)		(7)	218
Change in inventories				184
Purchases of raw materials and supplie	S		222	233
Change in inventories				
Other purchases and external expenses	5		10 565	20 467
Total external expenses			10 780	21 101
TAXES OTHER THAN ON INCOME			325	366
PERSONNEL COSTS				
Wages and salaries			3 202	5 182
Payroll charges			1 450	2 396
Total personnel costs			4 652	7 578
OPERATING ALLOWANCES  Amortization on fixed assets			404	1 761
Provisions on fixed assets			404	1 /61
Provisions on current assets			42	751
Provisions for contingencies and losses			42	/31
Total operating allowances			446	2 670
iotal operating anowances			770	2070
OTHER OPERATING EXPENSES			261	203
TOTAL OPERATING EXPENSES			16 463	31 918
OPERATING INCOME/(LOSS)			(7 800)	(21 611)



# 2. INCOME STATEMENT (PART 2)

€ thousands	Net 2018	Net 2017
OPERATING INCOME/(LOSS)	(7 800)	(21 611
IOINT TRANSACTIONS		
Allocated gain or transferred loss		
Sustained loss or transferred gain		
FINANCIAL INCOME		
Financial income from investments	149	2
Financial income from other securities and from fixed asset securities	15	1
Other interest and similar income	63	1
Provision reversals and expense transfers	66	
Foreign exchange gains	105	59
Net gains on sales of marketable securities		
TOTAL FINANCIAL INCOME	398	65
FINANCIAL EXPENSES		
Amortization, depreciation and provisions		
Interest and similar expenses	794	34
Foreign exchange losses	(1)	94
Net losses on sales of marketable securities		
TOTAL FINANCIAL EXPENSES	793	1 28
FINANCIAL INCOME	(395)	(638
LOSS BEFORE EXCEPTIONAL ITEMS AND TAX	(8 195)	(22 249
EXCEPTIONAL INCOME		
Exceptional income on operating transactions	4 154	
Exceptional income on capital transactions	62	8
Provision reversals and expense transfers	145	5
Exceptional income	4 361	14
EXCEPTIONAL EXPENSES		
Exceptional expenses on operating transactions	11 291	47,78
Exceptional expenses on capital transactions	77	15
Exceptional provisions and expense transfers	190	6
Exceptional expenses	11 558	48 00
EXCEPTIONAL ITEMS	(7 197)	(47 863
Foundation of the desire		
Employee profit sharing	(2.426)	/2.60-
Corporate income tax	(2 436)	(3 687
TOTAL EARNINGS	13 422	11 10
TOTAL COSTS	26 378	77 52



## ACCOUNTING METHODS AND RULES

Onxeo ("the Company") is a clinical trial biotechnology company that develops new drugs aimed at fighting cancer by targeting the functions of tumor DNA using the only mechanisms of their kind in the heavily researched field of DNA Damage Response (DDR). The Company focuses on developing innovative first-in-class or disruptive compounds (internal, acquired or licensed) from translational research to proof of clinical concept in humans, one of the most value-creating and attractive points of inflection for potential partners.

Onxeo's separate financial statements for the year ended December 31, 2018 were prepared under the responsibility of the CEO and approved by the Board of Directors on March 12, 2019.

### 1. ACCOUNTING POLICIES

The financial statements for the financial year ended December 31, 2018 were prepared and presented in accordance with the provisions of the French Commercial Code, the French General Accounting Plan and Regulation ANC 2016-07 of November 4, 2016 in accordance with the principle of prudence and independence of financial years.

The financial statements were prepared on a going concern basis based on the Company's cash flow forecasts. These latter incorporate an extension of the current share financing line which allows for financing the business until Q2 2020.

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. Goodwill is tested at least once per annum at the balance sheet date. Those assets pertaining to acquired but as-yet non-marketed (and, as such, not-yet amortized) molecules are also tested an annual basis at the balance sheet date and as soon as an indicator of impairment is identified. By way of example, slower-than-expected marketing may constitute evidence of impairment.

### 1.2. TANGIBLE FIXED 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 PP&E is calculated on a straight-line basis. Depreciable lives and depreciation methods are generally as follows:

Equipment and tooling 5 years

Specialized equipment
 Fixtures and fittings
 Office and computer equipment
 Furniture
 5 years
 4 years
 5 years

### 1.3. FINANCIAL FIXED 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 their value in use is less than their book value. The value in use of the shares is established on the basis of net assets at the balance sheet date. Profitability prospects must be judged by the Management so as to confirm the determination of the net carrying value of the participating shares.

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 the 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 impairment 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. LIQUID ASSETS

All liquid assets held in cash or banks are valued at their nominal value.

### 1.8. PROVISIONS FOR RISKS 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



### 1.9.1. LICENCES 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 entered into by the Company, research costs still being borne by Onxeo, are initially recognized in deferred income 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. This duration corresponds, in general, to the estimated time required to obtain marketing authorization for the product in question, this estimate being reviewed by the Management each year. 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.

The Company also benefits from royalties corresponding to a percentage of the net sales actually achieved over the period, at a contractual rate. Generally speaking, the royalties are calculated on the basis of a monthly or quarterly report transmitted by the partners. At the balance sheet date, in the event that the report for the latest period is not received, the royalties shall be valued on the basis of the actual quantities sold on the basis of a net historic sales price.

In the event that assets are sold, the initial payments shall be fully accounted for on the date the contract is signed.

### **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 the event that the project fails (this to be duly justified to the lending body), the advances cashed generally will not be repaid and will be recognized in the profit and loss account.

### SIGNIFICANT DEVELOPMENTS DURING THE YEAR

### 2.1. R&D PROGRAMS

### 2.1.1. **ASIDNA**<sup>TM</sup>

In 2018, the Company actively pursued the preclinical and clinical development of AsiDNA™ as a systemic single therapy and in combination with other treatments in various types of solid tumors and overcame several key steps:

- The presentation to the AACR (American Association for Cancer Research), in April 2018, of two preclinical studies demonstrating the unique approach AsiDNA™ has in inhibiting the repair of tumor DNA by activating those enzymes involved in DNA damage signaling and distracting them from their target. The results of one of these studies showed, in particular, that repeated, long-term administering of AsiDNA™ lead to an increase in the sensitivity of tumor cells and that no resistance was apparent following repeated treatments.
- In July 2018, new preclinical results bolstered these properties by showing a strong synergy and a reversion in tumor resistance in association with PARP inhibitors.
- The launch, in April 2018, of DRIIV (DNA Repair Inhibitor administered IntraVenously), the phase 1 AsiDNA™ clinical study into advanced solid tumors. The aim of this study is to assess AsiDNA™ tolerance and the optimum clinical dose, as well as to determine its active dose at the level of the tumor in patients with advanced solid cancer.
- In November 2018, the Company announced, on schedule, the positive interim results on the first three doses tested in the DRIIV study evaluating the tolerance to and activity of AsDNA™ when administered



systemically (intravenously). A favorable safety profile was also observed, with no serious undesirable event due to the drug or any toxicity that would limit the dose.

Based on this data, and in particular the determination of active doses, the Company intends to extend the AsiDNA™ clinical program in association with the targeted indications from the first half of 2019.

AsiDNA™ has the potential to be used in a broad range of indications, to which the Group wishes to add value as part of a partnership. AsiDNA™ also has the capacity, in the short and long term, to generate a number of growth and value catalysts for the Company and its shareholders.

### 2.1.2. **PLATON™**

PlatON™ is the Company's patented oligonucleotide platform from which AsiDNA™ is derived, whose aim is to construct new oligonucleotide-based molecules (a double-stranded DNA fragment). Throughout 2018, the Company continued to select and optimize several highly innovative compounds and is planning to enter into the preclinical phase for the most promising compound in the first half of 2019.

### 2.1.3. BELEODAQ® (BELINOSTAT)

Belinostat is a histone deacetylase inhibitor (HDACi) marketed in the US since 2014 under the name Beleodaq® as part of a conditional approval by the FDA for use in the 2nd-line treatment of patients with peripheral T cell lymphoma. The Company's US partner, Spectrum Pharmaceuticals (SPPI), is preparing the first-line phase III clinical study for the treatment of peripheral T cell lymphoma.

At the same time, Onxeo has been assessing belinostat in association with other compounds. These works have suggested that belinostat may potentially be better suited for use with new platON™-derived compounds.

### 2.2. FINANCING

In June 2018, the Company announced two financing operations:

- On the one hand, Onxeo signed a royalty prefinancing agreement with SWK Holdings Corporation, a US company specialized in financing in the life sciences sector. According to the terms of the agreement, Onxeo issued bonds in an amount of \$7.5 million, fully subscribed by SWK Holdings Corporation. The terms for repaying the bonds will allow the latter to directly receive the royalties and milestone payments on the sales stemming from the marketing of Beleodaq® (belinostat) by Spectrum Pharmaceuticals, Inc. for an amount of \$13.5 million. The remaining details of the transaction have not been disclosed.
- On the other hand, on June 15, 2018, the Company set up an equity line of credit, including an incentive plan, by issuing new shares over a period of 10 months, for a maximum amount of €5.4 million together with the company Nice & Green. In accordance with the terms of the agreement, Nice & Green has undertaken, for a 10-month period, to subscribe for and exercise each month, on Onxeo's initiative, share warrants corresponding to minimum monthly financing of €500,000 up to a limit of 4,700,000 shares over the term of the contract. The shares will be issued on the basis of the average share price weighted by volumes over the first three trading days prior to each issue, less a maximum discount of 5.0%. Onxeo retains the option of suspending drawdowns or of terminating this agreement at any time. Nice & Green and Onxeo have also agreed on an incentive plan that consists of the allocation in cash, to the Company, of a share of any added value realized by Nice & Green through the sale of shares resulting from the exercise of the warrants.

### 2.3. DISPUTE WITH SPEBIO AND SPEPHARM

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®.

In a partial arbitral award 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. Onxeo then had summons served on SpeBio for contractual liability before the Commercial Court. Onxeo then lodged a forcible joinder with the



Commercial Court to add SpePharm as a co-defendant on criminal grounds, and, by a ruling dated May 3, 2016, the Paris Commercial Court granted Onxeo's forcible joinder adding SpePharm as a co-defendant and consolidating the Onxeo v. SpeBio and Onxeo v. SpePharm proceedings. In a counterclaim, SpeBio and SpePharm filed claims for damages.

On 17 October 2017, the Paris Commercial Court handed down a judgment ordering Onxeo to pay to SpeBio the sum of €8.6 million for costs sustained prior to termination with interest at the statutory rate from June 30, 2014 with compound interest (in addition to €250 000 on the basis of Article 700 of the French Code of Civil Procedure) and to SpePharm the sum of €50 000 in damages (in addition to €15 000 on the basis of Article 700 of the French Code of Civil Procedure). This judgment was handed down along with provisional enforcement and, as a result, a total amount of €9.2 million was paid by Onxeo at the start of 2018.

On October 20, 2017, Onxeo lodged an appeal against this ruling and lodged its submissions with the Court of Appeal of Paris on January 9, 2018, in order to ensure that the appeal proceedings are dealt with promptly in the interest of its shareholders. On December 7, 2018, the Court of Appeal handed down a decision ordering Onxeo to pay SpeBio the additional sum of around €2.8 million as compensation for the damage suffered in terms of expenses incurred and loss of opportunity. The Court did, however, overturn the order that required Onxeo to pay €50,000 to SpePharm BV in damages. The amount of €2.8 million, not paid at December 31, 2018, has been recognized as other debts.

### 2.4. EVENTS SUBSEQUENT TO DECEMBER 31, 2018

There are no post-balance sheet events likely to have a material effect on the accounts.



### NOTES TO THE BALANCE SHEET

### 3.1. INTANGIBLE ASSETS

In € thousands	12/31/2017	Increase	Decrease	12/31/2018
Beleodaq® R&D assets	61,830			61,830
AsiDNA™ R&D assets	3,259			3,259
Goodwill	4,450			4,450
Other intangible assets	719		300	419
TOTAL Gross	70,258	0	300	69,958
Amortization Beleodaq®	-5,120	-279		-5,399
Amortization AsiDNA™	0	0		0
Amortization of other intangible assets	-704	-14	-299	-419
TOTAL Amortization	-5,824	-293	-299	-5,818
Beleodaq® impairment	-34,210	-7,783		-41,993
TOTAL Impairment	-34,210	-7,783	0	-41,993
Total	30,224	-8,076	1	22,147

Gross intangible assets amounted to €69,958,000 as at December 31, 2018, and consist mainly of:

- €65 089 in Development Costs, allocated to Beleodaq® (belinostat) in the amount of €61,830,000 and to AsiDNA™ in the amount of €3,259,000 in connection with the merger-absorption operation of Topotarget in 2014 and the acquisition of DNA Therapeutics in 2016 respectively.
- Goodwill of €4 450 representing the difference between the acquisition value of Topotarget and the net assets contributed.

Intangible assets also include patents and brands acquired by the Company for a gross amount of €181 and software for a gross amount of €238.

Depreciation amounted to €5,818,000, of which €5,399,000 resulted from the amortization of assets associated with the product Beleodaq® for its 2<sup>nd</sup>-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 marketing 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, 2018, as follows:

### • Recoverable amount of intangible assets

Every year, goodwill is subjected to an impairment test. This test is performed at least once per year at the closing date. 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, 2018, the Company 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, 2018. 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 Company. As the recoverable amount thus obtained, net of disposal costs, was higher than the book value of the goodwill, no impairment appeared necessary.



### R&D assets

The R&D assets acquired as part of the merger with Topotarget and the acquisition of DNA Therapeutics, specifically concerning Beleodaq® in its current PTCL (peripheral T cell lymphoma) indication as well as its potential future indications and AsiDNA™, have all been tested, whether marketed or not. The 1st- and 2nd-line PTCL indications have been regrouped in order to perform this text, with the Group believing that these cover the same pathology and share a common development plan. The value in use of these R&D assets was determined based on projected cash flow on the basis of a business plan created by the Management, a plan that represents the latter's best estimate. A discount rate of 17.6% has been applied to the cash flow, taking into account the market risk and specific risks related to Onxeo.

Since the values in use obtained for Beleodaq® 1st- and 2nd-line PTCL, on the one hand, and for the product's potential future indications on the other were lower than the bases tested, the R&D assets were impaired for €7,783K. This loss in value is mainly the result of increased competitive pressure on the PTCL market. Naturally, this situation has an impact on the 2nd-line, treatments segment, the first approved indication of Beleodaq® in which the product has been marketed in the US by the partner company Spectrum Pharmaceuticals. However, it is also having a forward-looking impact on the 1st-line segment, an additional indication which should be obtained at the end of the phase III study to be performed by Spectrum, whether this is in terms of the product's estimated market share or in terms of sales price.

It should be noted that the R&D assets relating to Beleodaq®, which were acquired through the merger with Topotarget, are partly held by the subsidiary Topotarget UK. The above value test had an impact on the value of this subsidiary's assets and, as a result, a provision for impairment of the participating interests held by Onxeo was accounted for, as indicated in paragraph 3.3 below.

The Group performed sensitivity tests on the model's key parameters. The table below presents the potential impairment levels of R&D assets linked to Beleodaq®. The R&D assets and goodwill did not undergo a sensitivity test insofar as the value in use is significantly higher than the book value.

The Company has also performed sensitivity tests on the model's key parameters, the results of which are summarized below:

In € thousands	Beleodaq®
Change in probability of success/PTCL 1L	
-5%	-4.1
-10%	-8.6
Change in net sales	
-5%	-1.0
-10%	-2.5
Change in discount rate	
+0.2%	-0.1
+0.5%	-0.5

### 3.2. TANGIBLE FIXED 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 financial year 2018, acquisitions amounted to €45K. The item was also depreciated by €1 185K, corresponding to an asset update to the disposal of fully amortized assets and, as a result, improvement works being carried out on the Paris headquarters and moving the premises of the Danish site.

### 3.3. FINANCIAL FIXED ASSETS

Financial assets correspond primarily to interests held by Onxeo in its subsidiaries.

Changes in this item mainly correspond to provisioning for 2018 for the impairment of the subsidiary Topotarget UK's interests for the amount of €481,000, which was recorded as an extraordinary expense. This change is due



to the loss in the value of the R&D assets due to Beleodaq®, which is explained above, part of which are held by the subsidiary.

The amount of treasury shares held as part of the liquidity agreement at December 31, 2018 was €97K, corresponding to 111,095 shares recognized in 'Other long-term securities". Cash not invested within the framework of the agreement amounted to €177,000.

### 3.4. TRADE RECEIVABLES

Net accounts receivable amounted to €856K at December 31, 2018, €212,000 of which due from other companies of the Group. Trade accounts receivable due from outside the Group mainly comprise:

- receivables owed by the partner Spectrum Pharmaceuticals and correspond to rebilling of R&D expenses and fees on sales due by this partner for an amount of €443,000.
- receivables from sales of Beleodaq® as part of a managed access program also known as the named patient program – for Beleodaq®, for an amount of €178,000.

### 3.5. OTHER RECEIVABLES

Other net receivables amount to €9 681 at December 31, 2018, and mainly consist of the following:

- Research Tax Credits in France and Denmark 2018: €2,454K
- Single Accrued income from the company Vectans corresponding to the milestone payments received by Vectans from its partners, repayment of which to Onxeo was deferred to the start of 2020: €1,791K
- Net value of subsidiaries' current accounts: €4,638K
- Deductible VAT: €453K
- VAT refund requested: €157K

#### 3.6. CASH

At December 31, 2018, cash amounted to €11 182K, corresponding to cash and cash equivalents, including short-term deposits in the amount of €5,183,000.

The change in net cash was a decrease of €2,783,000. This mainly stems from the Company's operating costs, including research and development, for a total of €7.8 million. These cash outflows were partly offset by the income from the sales of products and licensing agreement for an amount of €1.9 million. The new financing implemented over the course of the financial year—bond issue with SWK Holding and equity credit line—contributed a total of €9.1 million. The Group also collected the CIR 2017 receivable in the amount off €3.6 million.

### 3.7. PREPAID EXPENSES

Prepaid expenses at December 31, 2018 amounted to €1 172K and mainly correspond to subcontracted services and fees.

### 3.8. SHAREHOLDERS' EQUITY

At December 31, 2018, share capital amounted to €13 344 divided into 53,376,375 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 12/31/2017		0.25	50,695,653	12,673,913.25
Capital increase – share line of credit	(1)	0.25	2,483,866	620,966.50
AGA capital increase acquired	(2)	0.25	196,856	49,214.00
Shares fully paid at 12/31/2018		0.25	53,376,375	13,344,093.75

- (3) Capital increase resulting from the exercise of share warrants as part of the equity line of credit set up with Nice & Green. 2,483,866 new shares with a par value of €0.25 each were issued in 2018 at a unit price ranging from €1.002 to €1.1896, corresponding to an increase in share capital of €621,000, together with a share premium of €2,084,000.
- (4) Issuance of 196,856 vested bonus shares awarded in 2017, permanently acquired in the financial year, of a par value of €0.25 each, i.e. an amount of €49,000.

The issue premium, contribution, merger item reduced by €255 760K to 28 524 thousand euros mainly due to of the charging of the Credit retained earnings of €229,205K on issue, contribution and merger premiums in accordance with the decision of the Combined Ordinary and Extraordinary General Meeting of May 16, 2018. This decrease was partially offset by the capital increase as part of a share line of credit for an amount of €2,084K

### 3.9. OTHER SHAREHOLDERS' EQUITY

Other equity capital corresponds to an advance from Bpi France of €562,000 paid in 2010 under the AsiDNA™ program, repayable in the event of commercial success. The balance of €485,000 at December 31, 2018 is to be repaid over the period 2019 to 2021.

### 3.10. OTHER BONDS

In June 2018, the Company issued bonds to the company SWK Holdings in June 2018 for an initial amount of \$7.5 million. Repayment of this debt, for a total amount of \$13.5 million, will be made through royalties on sales of Beleodaq® paid by the US partner Spectrum Pharmaceuticals. The remaining capital owed as at December 31, 2018 amounted to €5,926,000, with accrued interest totaling €222,000.

### 3.11. PROVISIONS FOR RISKS AND LOSSES

Provisions for contingencies and losses amounted to €134K, mainly corresponding to exchange rate risk and litigation provisions.

### 3.12. TRADE DEBTS

Trade payables fell from €6 129K at December 31, 2017 to €5 156K at December 31, 2018 due to the change in R&D activities.

The Company is conducting preclinical and clinical studies and formalizing its relations with external partners assisting Onxeo in its works. As part of the clinical trials, the research expenses provisioned for at the balance sheet date were determined based on estimates of per-patient costs not yet billed, as established by the Management. These estimates are based on the information provided by the investigation centers (hospitals) under contract and the cost analyses carried out by the Management.

### 3.13. ACCRUED TAXES AND PERSONNEL COSTS

The decrease in tax and social security charges, from €2 269K to €924K is the result of the workforce reduction, particularly the plan implemented by the company at the end of 2017.

### 3.14. OTHER DEBTS

This item of €6 796K corresponds to the subsidiary Topotarget UK's current account credit for an amount of €3,917K and the charge relating to the sentence pronounced by the Paris Court of Appeal in the context of the dispute with SpeBio and SpePharm for an amount of €2,878K.

### 3.15. DEFERRED REVENUE



Deferred income for an amount of €411K mainly consists of license revenue deferred for less than one year with Pint Pharma, whose recognition in profit or loss staggered over several financial years based the estimated date of obtaining the marketing authorization and whose balance at December 31, 2018 was €616,000.

### 4. NOTES ON THE INCOME STATEMENT

### 4.1. REVENUE

Revenue for the financial year 2018 amounted to €549K and came from sales of products as part of a managed access program – also known as the named patient program – for Beleodaq® for €526K, and from various services for €23K.

### 4.2. ROYALTIES FROM LICENSING AND OTHER INCOME.

This item of an amount of €5 186K includes a portion of the amounts received on signing the marketing licensing agreements for an amount of €616,000, staggered over time, royalties on the sales of partners under license for an amount of €1,697,000, as well as non-recurring license revenue of €2,720,000 received as part of the agreement with the company Vectans Pharma.

### 4.3. OPERATING EXPENSES

Operating expenses sharply decreased from €31 918K in 2017 to €16 463K in 2018.

The major changes of the year are:

- A €9,902,000 decrease in external expenses, due to the change in the R&D programs and, in particular, the conclusion of the phase III ReLive clinical trial in 2017.
- A €2,925K decrease in salaries, benefits and social security charges due to the workforce reduction social security contributions.
- A €1,357K decrease in amortizations of intangible assets, due to the impairment of R&D assets as a result of the value tests carried out over the year (see note 3.1);

The research and development costs in 2018 amounted to €7.54 million.

The employment competitiveness tax credit for 2018 amounted to €21K and was recognized as a reduction of operating expenses. It was assigned exclusively to the Company's research and development effort.

### 4.4. FINANCIAL PROFIT (LOSS)

Financial income mainly includes foreign exchange gains in the amount of €105K Group current account interest for €149K, and income generated by short-term investments for €15K. Interest-bearing accounts generated profits of €63K.

Financial expenses include interest relating to current account advances for a total amount of €204K, and an amount of €588K corresponding to interest on the SWK bond issue.

### 4.5. EXCEPTIONAL ITEMS

The negative extraordinary result of €(7 197)K mainly corresponds to:

- The impairment of the acquired R&D assets in the amount of €7,783K as a result of the value tests conducted over the year (see note 3.1);
- The allowance for provisions for impairment of the Topotarget UK account for €481K.
- The amount of €2,868,000 which the Company was ordered to pay in the context of the appeal in its dispute with the companies SpeBio and SpePharm; and
- Exceptional income for the previous year of €4,037,000 corresponding to the advance paid by Bpifrance for the Livatag® program as part of the NICE consortium. Since Bpifrance acknowledges the program's commercial failure following the negative results of ReLive phase III, Onxeo was fully released from its repayment obligations in accordance with the contract.



#### 4.6. CORPORATE INCOME TAX

Corporate income tax is income of (€(2 436)K), corresponding to the French and Danish research tax credits.

Onxeo had a tax loss carried forward amounting to €271 million at December 31, 2018.

# 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:

- Collective bargaining agreement: Medical industry
- Retirement age: From 65 years, in accordance with the Pension Reform Act of November 10, 2010
- Calculation date: 31/12/2018Mortality table: INSEE 2018
- Discount rate: 1.70 %
- Rate of salary increase: (Salary growth rate + inflation) 2%
- Employee turnover rate: By age category:
- Social security tax rate: 46 %

At December 31, 2018, retirement benefit obligations amounted to €404,000.

#### 5.2. LEASING COMMITMENTS

Leasing commitments amount to €121.5K at December 31, 2018.

# REMUNERATION OF CORPORATE OFFICERS

Remuneration of corporate officers amounted to €1,031,000, including the retirement benefits of the Chief Executive Officer for an amount of €102,000.

# 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 12.67% of the capital and as a board member, is considered to exert a significant influence on the company.

No transactions were made with Financière de la Montagne in the year 2018.

- The Chairman of the Board of Directors, as one of the main executives presenting the financial statements.

No transactions were made with the Chairman of the Board of Directors in the year 2018.

# 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 at December 31, 2018:

In € thousands	31/12/2018	12/31/2017
Assets	76,906	75,783



Liabilities	4,827	3,534
Products	36	26
Expenses	1,289	198

The amount of the assets mainly corresponds to the current account of the subsidiary Topotarget Switzerland and to participating shares, the amount of the liabilities corresponding to that of the subsidiary Topotarget UK's current account. The increase in expenses is due to the billing of the US subsidiary's management costs.



# **APPENDICES**

# **ASSETS**

In € thousands	Amount at start of <b>2018</b>	Increases	Decreases	Amount at end of 2018
Formation costs and research and development costs	65,089			65,089
Other intangible assets	5,168		299	4,869
TOTAL INTANGIBLE FIXED ASSETS	70,258		299	69,959
Land				
Construction on own land				
Buildings on non-freehold land				
Facilities, fixtures and fittings				
Plant & equipment	1,255	44		1,298
Facilities, fixtures and fittings	2,232		772	1,460
Transport equipment				
Office and computer equipment, furniture	775	1	413	363
Recoverable packaging & other				
Tangible fixed assets in course of construction				
Advances and prepayments				
TOTAL TANGIBLE FIXED ASSETS	4,261	45	1,185	3,121
Holdings valued by the equity method				,
Other equity holdings	48,630			48,630
Other long-term securities	89	8		97
Loans and other financial assets	215	82		297
TOTAL LONG-TERM INVESTMENTS	48,934	89		49,024
GRAND TOTAL	123,454	134	1,484	122,104

# **DEPRECIATION TABLE**

In € thousands	Amount at start of <b>2018</b>	Increases	Decreases	Amount at end of 2018
Formation costs and research and development costs	5,120	279		5,399
Other intangible assets	704	14	299	419
TOTAL INTANGIBLE FIXED ASSETS	5,824	293		5,918
Land				
Construction on own land				
Buildings on non-freehold land				
Facilities, fixtures and fittings				
Plant & equipment	1,049	17		1,065
Fixtures and fittings	2,099	64	772	1,392
Transport equipment				
Office, IT, equipment and furniture	726	30	413	344
Recoverable packaging & other				
TOTAL TANGIBLE FIXED ASSETS	3,874	111	1,185	2,801
GRAND TOTAL	9,698	404	1,484	10,102



# **PROVISIONS**

In € thousands		Increases: in		Decreases:		
	Amount at	allowances in the	Hand double a Abra		Davasala	Amount at
	start 2018	year	Used during the period	Unused during the period	Reversals during the year	period end 2018
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%						
Provisions for construction and equipment loans						
Other regulated provisions						
TOTAL REGULATED PROVISIONS						
Provisions for risks and losses						
Provisions for litigation						
Provisions for customer warranties						
Provisions for future market losses						
Provisions for fines and penalties						
Provisions for foreign exchange losses	57	2			51	7
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	82	190			145	127
TOTAL PROV. FOR CONTINGENCIES AND LOSSES	139	191			196	134
Provisions for impairment						
On intangible fixed assets	34,210	7,783				41,993
On tangible fixed assets	158					158
On long-term investments in equity securities						
On long-term investments in equity capital	42,619	481			20	43,080
On other long-term investments						
On stocks and work in progress						
On trade receivables	150	2				152
Other provisions for impairment	26,251	42			2,906	23,387
OTAL PROVISIONS FOR MPAIRMENT	103,389	8,308			2,926	108,772
GRAND TOTAL	103,528	8,499			3,122	108,905
of which operating allowances and re	worsals	42			2,907	
of which financial allowances and rev		44			66	
of which exceptional allowances and reversals	CIJUIJ	8,454			145	



5 926

# **RECEIVABLES**

In € thousands	Gross amount	1 year at most	More than 1 year
Receivables from investments			,
Loans (1) (2)			
Other financial fixed assets	297		297
Total fixed assets	297		297
Doubtful or contentious receivables	140	140	
Other trade receivables	868	868	
Receivables representing loaned securities			
Personnel	11	11	
Social security and other employee benefit charges			
Corporate income tax	2,454	2,454	
Value added tax	610	610	
Taxes other than on income			
Other	39	39	
Group and shareholders (2)	28,026	28,026	
Miscellaneous receivables	1,929	1,929	
Total current assets	34,077	34,077	
Prepaid expenses	1,172	1,172	
TOTAL RECEIVABLES	35,546	35,249	215297
(1) Amount of loans granted during the period			
(1) Amount of repayments obtained during the period			
(2) Shareholders' loans and advances (natural persons)			

# **PAYABLES**

(1) Loans contracted during the year

(2) Amount of loans and debts payable to shareholders

(1) Loans repaid during the year

In € thousands	Gross amount	1 year at most	Between 1 and 5 years	More than 5 years
Convertible bonds (1)				
Other bonds (1*)	5,926	5,926		
Bank debts < 1 year	4	4		
Bank debts > 1 year				
Other debt (1) (2)	222	222		
Trade payables	5,156	5,156		
Personnel	350	350		
Social security and other employee benefit charges	406	406		
Corporate income tax				
Value added tax	43	43		
Secured obligations				
Taxes other than on income	126	126		
Payables on fixed assets and related accounts	19	19		
Group and shareholders (2)				
Other debts	6,796	6,796		
Debt representing borrowed securities				
Deferred revenue	411	411		
TOTAL PAYABLES	19,458	19,458		

<sup>\*</sup> Other bond issues are mainly composed of the loan granted by SWK Holdings. Since its repayment is connected with royalties paid by the partner Spectrum, it is not possible to indicate with certainty the breakdown of the repayment over time.



# **ACCRUED INCOME**

In € thousands	2018	2017
Financial fixed assets		
Receivables from investments		
Other financial fixed assets		
Total long-term investments		
Receivables		
Trade receivables	467	330
Other receivables	1,967	636
Total receivables	2,434	966
Liquid assets		
Marketable securities		
Liquid assets	19	
Total liquid assets	19	
TOTAL	2,453	966

# **ACCRUED EXPENSES**

In € thousands	2018	2017
Financial debts		
Convertible bonds		
Other bonds	222	
Bank debts and debts with credit institutions		
Other debt		
Customer prepayments		
Total financial liabilities	222	
Operating liabilities		
Trade payables	4,481	5,558
Accrued taxes and personnel costs	652	1,669
Total operating liabilities	5 133	7 227
Other payables		
Payables on fixed assets and related accounts	19	13
Other debts	2,878	9,152
Total operating liabilities	2,897	9,165
TOTAL	8,252	16,391



# TABLE OF CHANGES IN SHAREHOLDERS' EQUITY

In € thousands	01/01/2018	Capital increase	Capital reduction	Effect on 2017 result	Other changes	2018 result	31/12/2018
Share capital	12,674	621			49		13,344
Issue, merger and acquisition premiums	255,760	2,084			(229,320)		28,524
Excess of restated assets over historical cost							
Legal reserve							
Reserves required by the articles of incorporation or by contract							
Regulated reserves							
Other reserves	72				107		179
Retained earnings	(162,781)			(66,425)	229,205		
Period Earnings	(66,425)			66,425		(12, 955)	(12,955)
Capital grants	6				(6)		
Regulated provisions							
Dividends paid							
	39,307	2,705			35	(12,955)	29,092

# **LEASING**

LEASED ASSETS	Initial cost	Amortization ar	Net value	
(In € thousands)		for the period	Cumulative	
Land				
Buildings				
Plant & equipment	198	40	90	108
Other tangible assets	107	19	27	80
Tangible assets in				
progress				
TOTAL	304	58	116	188

LEASE	Royalti	es paid		Amounts outstanding			
COMMITMENTS (In € thousands)	for the period	Cumulative	< 1 year	From 1 to 5 years	> 5 years	Total	purchase price
Land							
Buildings							
Technical installations	50	100	44	83		127	1
Other tang. fixed assets	27	108	25	12		37	
Tangible assets in progress							
TOTAL	77	208	68	95		164	1



# **AVERAGE HEADCOUNT**

Category	Average h	eadcount	Average available headcount		Total	
	2018	2017	2018	2017	2017	2018
Executives	30	40			30	40
Supervisors						
Staff and Technicians	9	9			9	9
Total	39	49			39	49

# **RELATED COMPANIES AND HOLDINGS**

In € thousands	Amount c	oncerning
	related companies	with which the company has an equity investment
Financial fixed assets		
Advances and prepayments on intangible assets		
Investments	48,630	
Receivables from investments		
Loans		
Total long-term investments		
Receivables		
Prepayments to suppliers		
Trade receivables	212	
Other receivables	28,029	
Subscribed, called, unpaid share capital		
Total receivables	76,871	
Convertible bonds		
Other bonds		
Bank debts and debts with credit institutions		
Other debt		
Customer prepayments		
Trade payables		
Other debts	5,156	
Total payables	5,156	
Financial income		
Income from investments		
Other financial income	(36)	
Financial expenses	205	
Others		
Total financial income	241	

# TABLE OF SUBSIDIARIES AND EQUITY INTERESTS (IN EUROS)

Company	Share	% share of capital	Book value o hel		Loans and advances made by	Result (profit or loss for the last
Company	Capital	held (as %)	Gross	Net	the Company and not yet repaid	financial year)
Bioalliance Pharma Switzerland	89	100	32		227	(10)
		Erreur!				
Spebio	40	Signet non défini.50	20	20	1,475	7,286
Topotarget Switzerland	608	100	9,918		25,283	912
Topotarget UK LTD	1,527	100	38,659	5 530	(3,917)	464
Onxeo US	1	100	1		1,041	463
Total	2,278		48,630	5,550	24,109	9,115



# RESULTS OF THE LAST FIVE FINANCIAL YEARS (IN EUROS)

In euros	2014	2015	2016	2017	2018
Capital at the end of the financial year					
Share capital	10,136,051	10,138,021	11,760,851	12,673,913	13,344,094
Number of common shares outstanding	40,544,204	40,552,083	47,043,404	50,695,653	53,376,375
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 of the financial year					
Net sales, excluding VAT	456,774	810,343	556,854	894,784	548,504
Net loss before tax, profit-sharing, depreciation, amortization and provisions	8,842,926	-23,266,312	-45,158,403	-30,432,231	-9,632,677
Corporate income tax	878,352	-3,718,068	-3,954,873	-3,686,612	-2,436,446
Employee profit sharing for the period					
Net loss after tax, profit-sharing, depreciation, amortization and provisions	8,521,759	-25,163,280	-21,236,246	-66,424572	-12,955,412
Distributions					
Earnings per share					
Net loss after tax, profit-sharing, depreciation, amortization and provisions	0.20	-0.48	-0.88	-0.53	-0.13
Net loss after tax, profit-sharing, depreciation, amortization and provisions	0.21	-0.62	-0.45	-1.31	-0.24
Dividend allocated to each share					
Personnel					
Average headcount during the period	59	53	52	49	39
Gross payroll for the period	8,023,027	5,447,799	4,613,673	5,181,976	3,202,473
Amounts paid for employee benefits	2,392,857	2,063,410	2,070,805	2,395,768	1,449,962



# 6.4 STATUTORY AUDITORS' REPORTS ON THE ANNUAL FINANCIAL STATEMENTS

This is a translation into English of the statutory auditors' report on the financial statements of the Company issued in French and it is provided solely for the convenience of English-speaking users.

This statutory auditors' report includes information required by European regulation and French law, such as information about the appointment of the statutory auditors or verification of the management report and other documents provided to the shareholders.

This report should be read in conjunction with, and construed in accordance with, French law and professional auditing standards applicable in France.

#### **GRANT THORNTON**

French Member of Grant Thornton International 29, rue du Pont – CS 20070 92200 Neuilly-sur-Seine cedex S.A. au capital de € 2.297.184 632 013 843 R.C.S. Nanterre

Commissaire aux Comptes Membre de la compagnie régionale de Versailles

#### **ERNST & YOUNG Audit**

Tour First TSA 14444 92037 Paris-La Défense cedex S.A.S. à capital variable 344 366 315 R.C.S. Nanterre

Commissaire aux Comptes Membre de la compagnie régionale de Versailles

#### Onxeo

Year ended December 31, 2018

Statutory auditors' report on the financial statements

To the Annual General Meeting of Onxeo,

# Opinion

In compliance with the engagement entrusted to us by your Annual General Meetings, we have audited the accompanying financial statements of Onxeo for the year ended December 31, 2018.

In our opinion, the financial statements give a true and fair view of the assets and liabilities and of the financial position of the Company as at December 31, 2018 and of the results of its operations for the year then ended in accordance with French accounting principles.

The audit opinion expressed above is consistent with our report to the Audit Committee.

# **Basis for Opinion**

### Audit Framework

We conducted our audit in accordance with professional standards applicable in France. We believe that the audit evidence we have obtained is sufficient and appropriate to provide a basis for our opinion.

Our responsibilities under those standards are further described in the *Statutory Auditors' Responsibilities for the Audit of the Financial Statements* section of our report.



#### Independence

We conducted our audit engagement in compliance with independence rules applicable to us, for the period from January 1, 2018 to the date of our report and specifically we did not provide any prohibited non-audit services referred to in Article 5(1) of Regulation (EU) No 537/2014 or in the French Code of Ethics (Code de déontologie) for statutory auditors.

# Justification of Assessments - Key Audit Matters

In accordance with the requirements of Articles L.823-9 and R.823-7 of the French Commercial Code (Code de commerce) relating to the justification of our assessments, we inform you of the key audit matters relating to risks of material misstatement that, in our professional judgment, were of most significance in our audit of the financial statements of the current period, as well as how we addressed those risks.

These matters were addressed in the context of our audit of the financial statements as a whole, and in forming our opinion thereon, and we do not provide a separate opinion on specific items of the financial statements.

Revenue recognition relating to license agreements (Cf. Notes 1.9.1, 2.2, 4.1 and 4.2 to the financial statements)

#### **Risk identified**

Revenues are made notably from license agreements signed with partners. Such agreements result in the cash-in of initial payments, then cashins conditioned to technical, commercial or regulatory objectives by partners.

Moreover, these agreements usually include royalties on partners' net sales that correspond to a percentage of given net sales.

Operating income booked in the December 31, 2018 accounts come from income related to various license agreements on going, as well as non-recurring income from asset sales achieved by your Company.

From an accounting standpoint, initial payments at signature date are spread over the period from signature to expected date of marketing authorization. Further payments conditioned to contractual objectives are fully recorded in other income when objectives are met. Royalties on net sales are booked depending on actual sales made by partners, applying royalties' contractual rates.

Contracts accounting relies on several key assumptions determined by management, notably:

 estimate of the marketing authorization dates and research costs to be incurred after signing the contract;

### Our response

Our audit procedures consisted of examining all on going agreements or terminated over the period. Our controls consisted in:

- analyzing the contractual clauses and accounting method applicable to initial payments, further conditioned payments and royalties on net sales;
- assessing the assumptions used for revenue recognition, notably the expected dates of marketing authorization and research costs to be incurred after signing. Within that framework, we held meetings in particular with the Finance department and the R&D teams, and examined both historical data and the documents submitted by the partners;
- reconciling the partners' net sales at closing in order to verify the calculation of the royalties.
- In the case of asset's intellectual property right sale, investigate on the conditions of the intellectual property right effective transfer of the products to the partners for the molecule sales.



- estimate of the net sales made by partners and computation of the corresponding royalties.

We considered that revenue recognition relating to license agreements was a key audit matter of the audit.

■ Intangible assets related to R&D and "Goodwill valuation" (Cf. Notes 1.1, 2.1 and 3.1 to the financial statements)

#### Risk identified

The net book value of the fixed assets related to research and development (R&D) and to goodwill amount to M€ 22,1 as at December 31, 2018, . Such assets are mainly made up of:

- intangible assets related to R&D (i) originating, on the one hand, from research work performed by Danish company;TopoTarget and brought to Onxeo in the context of a merger dated August 5, 2014, for M€ 14,3 and (ii) on the other hand, from the acquisition of the DNA Therapeutics on February 29, 2016 for M€ 3,3;
- goodwill accounted for following the aforementioned merger with TopoTarget for an amount of M€ 4,45.

Note 3.1, Paragraph "R&D assets" to the financial statements describes the terms and conditions of the impairment tests performed on intangible assets relating to R&D and those relating to goodwill ("fonds commercial"):

- goodwill and R&D assets not commercialized yet (and consequently not amortized yet) are subject to an impairment test at least once a year. The Company performs such test at closing;
- R&D assets related to commercialized (and therefore amortized) products are subject to an impairment test, when new circumstances indicate that such assets may have suffered an impairment. They have been tested at 2018 year-end.

Impairment tests have been performed using the discounted cash flow method in order to determine the value in use of the assets.

#### Our response

Our audit procedures regarding intangible assets relating to R&D and goodwill, consisted of controls on (i) the business plan prepared by your Company's management and including various operational assumptions and the chances of success in the projected cash-flows and (ii) the financial model used to determine the recoverable value of each of the assets used by your Company. We focused our attention on the following:

- the main operational assumptions included in the business plan: we examined estimates and assumptions used and compared such data with projected information provided by partners of your Company's license contracts;
- chance of success: we assessed the various chances of success used and compared them with the practices observed in the biotechnology sector;
- discount rates used: we assessed the relevance of the rates used, with the support of our financial valuation experts. Sensitivity tests were therefore performed;
- arithmetical computations: we examined the calculations made by your Company's management in the business plan and the financial model.



Impairment tests performed as at December 31, 2018, were satisfactory. However, these tests performed as at June 30, 2018, led to accounting for a depreciation of M€ 7,8.

We considered that determining the recoverable value of intangible assets relating to R&D and goodwill (fonds commercial) is a key audit matter due to (i) the significance of the assets in the company's annual financial statements, (ii) the necessary estimates to determine projected cash flows and (iii) the estimates and assumptions, namely regarding the chances of success and the discount rate, used to determine the recoverable value.

# ■ Valuation of investments in subsidiaries (Cf. Notes 1.3 and 3.3 to the financial statements)

#### **Risk identified**

As at December 31, 2018, investments in subsidiaries are recorded in the balance sheet at a net book value of € 5.550, i.e. 11% of the total assets. As mentioned in Note 1.3 "Financial assets" to the financial statements, when the value in use of the investments is less than their book value, a depreciation is recognized for the amount of the difference. The value in use of the investments is determined on the basis of net assets or adjusted net assets at closing.

The profitability forecast requires the exercise of management's judgment to confirm the valuation made of the net book value of the investments.

Given the weight of these investments and the significant impact that a decrease in the profitability forecasts would have on their value in use, we considered the valuation of investments in subsidiaries to be a key audit matter.

#### Our response

Our assessment of the valuation of investments in subsidiaries is based on the process set up by the Company to determine the value in use of these investments. Our work consisted in:

- reviewing the methodology used by management to assess the recoverable amount of each equity security;
- analyzing, for the valuations based on historical items that the retained equity is consistent with the accounts of the entities and that the adjustments on equity, when applicable, are based on conclusive documentation;
- assessing these valuation results based on historical financial data in relation to the valuation works performed on R&D assets and goodwill on projected financial data.

# ■ Valuation of costs incurred for the performance of clinical trials (Cf. Notes 1.1 and 3.12 to the financial statements)

# Risk identified Our response

As set out in Note 3.12 to the financial statements, in the context of the development of its products your Company performs clinical trials in collaboration with research centers.

Our audit procedures consisted namely in taking into account the valuation and factors justifying the key assumptions used by management to determine the amount of the provisions. In this context, we:



The costs incurred for such trials are recognized as expenses according to the state of completion of the medical treatments. At closing, an estimate of the costs not yet invoiced by third-parties per patient is determined by management and recorded as expenses for the year. These cost estimates are determined by management based on the information provided by the investigation centers (hospitals) under contracts and cost analyzes performed by your Company.

Given the importance of the research and development expenses and their methods of estimate at closing, we considered their valuation to be a key audit matter.

- took note of the internal control procedures set up by to identify and estimate the costs to be recorded at yearend;
- assessed the significant contracts entered into with clinical trial centers, as well as the elements established by management to justify the cost per patient of the medical treatments carried out;
- analyzed previous year accruals to review the consistency of management's past estimates;
- examined the consistency of the stage or completion of medical treatments per patient and the calculation of the related expenses, in the light of the information provided by research centers or the analysis carried out by management on the basis of historical data.
- analyzed the expenses recognized in the subsequent period to assess that there is no discrepancy with the estimates made.

# Specific verifications

We have also performed, in accordance with professional standards applicable in France, the specific verifications required by laws and regulations.

■ Information given in the Management Report and in the Other Documents with respect to the financial position and the financial statements provided to the Shareholders

We have no matters to report as to the fair presentation and the consistency with the financial statements of the information given in the Board of Directors' management report and in the other documents with respect to the financial position and the financial statements provided to the Shareholders.

We attest that the information relating to payment terms referred to in Article D. 441-4 of the French Commercial Code (Code de commerce) is fairly presented and consistent with the financial statements.

# Information relating to Corporate Governance

We attest that the section of the Board of directors' management report devoted to corporate governance sets out the information required by Articles L. 225-37-3 and L. 225-37-4 of the French Commercial Code (Code de commerce).

Concerning the information given in accordance with the requirements of Article L. 225-37-3 of the French Commercial Code (Code de commerce) relating to remunerations and benefits received by the directors and any other commitments made in their favor, we have verified its consistency with the financial statements, or with the underlying information used to prepare these financial statements and, where applicable, with the information obtained by your Company from controlling and controlled companies. Based on these procedures, we attest the accuracy and fair presentation of this information.



With respect to the information relating to items that your Company considered likely to have an impact in the event of a takeover bid or exchange offer, provided pursuant to Article L. 225-37-5 of the French Commercial Code (Code de commerce), we have agreed this information to the source documents communicated to us. Based on these procedures, we have no observations to make on this information.

#### Other information

In accordance with French law, we have verified that the required information concerning the purchase of investments and controlling interests and the identity of the shareholders and holders of the voting rights has been properly disclosed in the management report.

# Report on Other Legal and Regulatory Requirements

# Appointment of the Statutory Auditors

We were appointed as statutory auditors of Onxeo by your Annual General Meeting held on February 25, 1997 for Grant Thornton and on November 7, 2005 for ERNST & YOUNG Audit.

As at December 31, 2018, Grant Thornton was in the 22<sup>nd</sup> year of total uninterrupted engagement (including 14 years since Onxeo is listed on a regulated market) and ERNST & YOUNG Audit in the 14<sup>th</sup> year.

# Responsibilities of Management and Those Charged with Governance for the Financial Statements

Management is responsible for the preparation and fair presentation of the financial statements in accordance with French accounting principles and for such internal control as management determines is necessary to enable the preparation of financial statements that are free from material misstatement, whether due to fraud or error.

In preparing the financial statements, management is responsible for assessing the Company's ability to continue as a going concern, disclosing, as applicable, matters related to going concern and using the going concern basis of accounting unless it is expected to liquidate the Company or to cease operations.

The Audit Committee is responsible for monitoring the financial reporting process and the effectiveness of internal control and risks management systems and where applicable, its internal audit, regarding the accounting and financial reporting procedures.

The financial statements were approved by the Board of Directors.

# Statutory Auditors' Responsibilities for the Audit of the Financial Statements

#### Objectives and audit approach

Our role is to issue a report on the financial statements. Our objective is to obtain reasonable assurance about whether the financial statements as a whole are free from material misstatement. Reasonable assurance is a high level of assurance, but is not a guarantee that an audit conducted in accordance with professional standards will always detect a material misstatement when it exists. Misstatements can arise from fraud or error and are considered material if, individually or in the aggregate, they could reasonably be expected to influence the economic decisions of users taken on the basis of these financial statements.

As specified in Article L.823-10-1 of the French Commercial Code (*Code de commerce*), our statutory audit does not include assurance on the viability of the Company or the quality of management of the affairs of the Company.



As part of an audit conducted in accordance with professional standards applicable in France, the statutory auditor exercises professional judgment throughout the audit and furthermore:

- Identifies and assesses the risks of material misstatement of the financial statements, whether due to fraud or error, designs and performs audit procedures responsive to those risks, and obtains audit evidence considered to be sufficient and appropriate to provide a basis for his opinion. The risk of not detecting a material misstatement resulting from fraud is higher than for one resulting from error, as fraud may involve collusion, forgery, intentional omissions, misrepresentations, or the override of internal control.
- ▶ Obtains an understanding of internal control relevant to the audit in order to design audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the internal control.
- Evaluates the appropriateness of accounting policies used and the reasonableness of accounting estimates and related disclosures made by management in the financial statements.
- Assesses the appropriateness of management's use of the going concern basis of accounting and, based on the audit evidence obtained, whether a material uncertainty exists related to events or conditions that may cast significant doubt on the Company's ability to continue as a going concern. This assessment is based on the audit evidence obtained up to the date of his audit report. However, future events or conditions may cause the Company to cease to continue as a going concern. If the statutory auditor concludes that a material uncertainty exists, there is a requirement to draw attention in the audit report to the related disclosures in the financial statements or, if such disclosures are not provided or inadequate, to modify the opinion expressed therein.
- ▶ Evaluates the overall presentation of the financial statements and assesses whether these statements represent the underlying transactions and events in a manner that achieves fair presentation.

# Report to the Audit Committee

We submit to the Audit Committee a report which includes in particular a description of the scope of the audit and the audit program implemented, as well as the results of our audit. We also report, if any, significant deficiencies in internal control regarding the accounting and financial reporting procedures that we have identified.

Our report to the Audit Committee includes the risks of material misstatement that, in our professional judgment, were of most significance in the audit of the financial statements of the current period and which are therefore the key audit matters that we are required to describe in this report.

We also provide the Audit Committee with the declaration provided for in Article 6 of Regulation (EU) N° 537/2014, confirming our independence within the meaning of the rules applicable in France such as they are set in particular by Articles L.822-10 to L.822-14 of the French Commercial Code (Code de commerce) and in the French Code of Ethics (Code de déontologie) for statutory auditors. Where appropriate, we discuss with the Audit Committee the risks that may reasonably be thought to bear on our independence, and the related safeguards.

Neuilly Sur Seine and Paris-La Défense, April 5, 2019

The Statutory Auditors French original signed by



# GRANT THORNTON French Member of Grant Thornton International

**ERNST & YOUNG Audit** 

Samuel Clochard

Franck Sebag



# 6.5 OTHER FINANCIAL INFORMATION

# Date of latest financial information

12 March 2019: Publication of the press release on the audited 2018 annual financial statements approved by the Board of Directors on March 12, 2019.

# 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.



# 6.6 STATUTORY AUDITORS' SPECIAL REPORT ON REGULATED AGREEMENTS AND COMMITMENTS

This is a translation into English of a report issued in French and it is provided solely for the convenience of English-speaking users.

This report should be read in conjunction with, and construed in accordance with, French law and professional standards applicable in France.

#### **GRANT THORNTON**

French Member of Grant Thornton International
29, rue du Pont
92200 Neuilly-sur-Seine cedex
S.A. au capital de € 2.297.184
632 013 843 R.C.S. Nanterre

Commissaire aux Comptes Membre de la compagnie régionale de Versailles

#### **ERNST & YOUNG Audit**

Tour First TSA 14444 92037 Paris-La Défense cedex S.A.S. à capital variable 344 366 315 R.C.S. Nanterre

Commissaire aux Comptes Membre de la compagnie régionale de Versailles

#### Onxeo

Annual General Meeting held to approve the financial statements for the year ended December 31, 2018

#### Statutory auditors' report on related party agreements and commitments

To the Annual General Meeting of Onxeo,

In our capacity as statutory auditors of your Company, we hereby present to you our report on related party agreements and commitments.

We are required to inform you, on the basis of the information provided to us, of the terms and conditions of those agreements and commitments indicated to us, or that we may have identified in the performance of our engagement, as well as the reasons justifying why they benefit the Company. We are not required to give our opinion as to whether they are beneficial or appropriate or to ascertain the existence of other agreements and commitments. It is your responsibility, in accordance with Article R. 225-31 of the French Commercial Code (Code de commerce), to assess the relevance of these agreements and commitments prior to their approval.

We are also required, where applicable, to inform you in accordance with Article R. 225-31 of the French Commercial Code (*Code de commerce*) of the continuation of the implementation, during the year ended December 31, 2018, of the agreements and commitments previously approved by the Annual General Meeting.

We performed those procedures which we deemed necessary in compliance with professional guidance issued by the French Institute of Statutory Auditors (Compagnie nationale des commissaires aux comptes) relating to this type of engagement.

# Agreements and commitments submitted for approval to the Annual General Meeting

We hereby inform you that we have not been notified of any agreements or commitments authorized and concluded during the year ended December 31, 2018 to be submitted to the Annual General Meeting for approval in accordance with Article L. 225-38 of the French Commercial Code (Code de commerce).



# Agreements and commitments previously approved by the Annual General Meeting

We hereby inform you that we have not been notified of any agreements or commitments previously approved by the Annual General Meeting, whose implementation continued during the year ended December 31, 2018.

Neuilly-Sur-Seine and Paris-La Défense, April 5, 2019

The Statutory Auditors French original signed by

GRANT THORNTON

French Member of Grant Thornton International

**ERNST & YOUNG Audit** 

Samuel Clochard

Franck Sebag



# SUPPLEMENTARY FINANCIAL 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 2018, Onxeo had many meetings with institutional investors in France and also in Europe and the United States, as well as with individual investors in France.

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 among the financial community.

# 2019 AGENDA

- March 12, 2019; Consolidated financial statements for 2018
- April 26, 2019; General Shareholders' Meeting (May 22, 2019 in case of 2<sup>nd</sup> notice)
- July 25, 2019; 1<sup>st</sup> half 2019 consolidated results

# 7.1.2 ONXEO'S SHARE CAPITAL

As at December 31, 2018, the Company's share capital consisted of 87.9% bearer shares and 12.1% registered shares.

In accordance with the provisions of Article L. 233-13 of the French Commercial Code, please find below the identity of the shareholders with interests 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 of December 31, 2018.

	Sha	res	Voting rights		
Shareholders	Number of shares	% of share capital	Number of voting rights	% of voting rights	
Financière de la Montagne	7,723,379	14.47%	7,723,379	14.50%	
Others	45,652,996	85.53%	45,541,901	85.50%	
Total as of 31/12/2018	53,376,375	100.00%	53,265,280	100.00%	

The shareholder structure remained stable during FY 2018, with the percentage held by institutional investors slightly down, accounting for approximately 40% of the shareholder base.



The Company has not been notified of the existence of a shareholders' agreement.

In 2018, the Company received no notifications regarding the crossing of thresholds.

# 7.1.3 CHANGE IN THE SECURITY AND OTHER INFORMATION CONCERNING THE SHARE CAPITAL

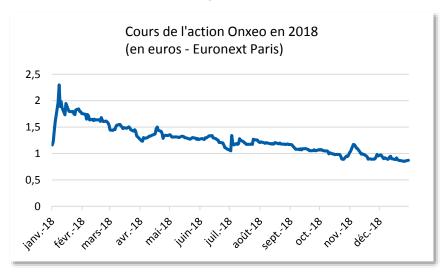
The Company's shares have been listed on Compartment C of the Euronext Paris stock market since January 27, 2017. According to Euronext regulations, market segment changes are made annually based on the market cap of the final 60 days of the year. Compartment C includes listed companies with less than €150 million in market cap.

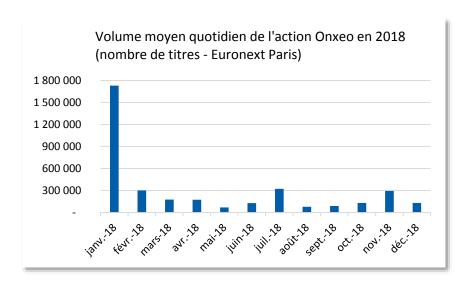
During FY 2018, the share hit its lowest price of €0.836 on December 27, 2018, closing at €0.872 on December 31, 2018. The highest price of €2.490 was reached on January 10, 2018.

Furthermore, the share has had a secondary listing on the NASDAQ OMX in Copenhagen since August 1, 2014.

# 7.1.3.1 Change in share price and trading volumes

The tables below show the changes in the share price and trading volumes for the period from January 2, 2018 to December 31, 2018 on the Euronext Paris Exchange.







# 7.1.3.2 Stock exchange data

	12/31/2018
Market capitalization at the end of the period (millions of euros)	46.54
Share price (in euros)	
Highest (closing)	2.300
• Lowest (closing)	0.850
At end of period (closing)	0.872

### 7.1.3.3 Dividends

#### **ONXEO** shares

Number of shares	Dividend paid for the period
13,536,072	-
17,659,715	-
17,659,715	-
20,682,992	-
40,544,204	-
40,552,083	-
47,043,404	-
50,695,653	-
53,376,375	-
	13,536,072 17,659,715 17,659,715 20,682,992 40,544,204 40,552,083 47,043,404 50,695,653

# 7.2 SUPPLEMENTARY INFORMATION ABOUT THE GROUP

## 7.2.1 HISTORY

1997. Founding of the company on March 5, 1997.

**1999-2005** The Company financed the development of its first projects, notably its first clinical trials of products based on two patented technologies - 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 on Euronext Paris on December 7, 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 1) for severe and chronic cancer pain and clonidine Lauriad® (phase 2) in the treatment of oral mucositis, and a new chemical entity, the anti-invasive biotherapy AMEP® (phase 1), designed for the treatment of invasive melanoma. Positive phase 3 results obtained in December 2009.

**2010.** MA issued for Loramyc<sup>®</sup> in the USA in April 2010, under the brand name Oravig<sup>®</sup>. Marketing launch of Oravig<sup>®</sup> 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<sup>®</sup> 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 3 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 financing round for the Livatag® development program and to strengthen the Group's orphan drugs portfolio.

**2012**. Clinical programs: start of the Livatag® phase 3 trial, widening in Europe of the phase II Validive® trial and ANSM approval for the AMEP® phase 1/2 clinical trial protocol. Signature of licensing agreements: with the Teva Pharmaceutical Industries Limited group 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 3 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. Obtaining of the Sitavig® MA in the United States. Capital increase of €8.7 million, notably intended for the acceleration and completion of the Validive® phase 2 trial.

**2014.** Merger with Bioalliance Pharma and Topotarget in summer 2014, to create Onxeo, which benefits from dual listing on the regulated market of Euronext Paris on Nasdaq in Copenhagen. Beleodaq®: US marketing authorization in the treatment of peripheral T-cell lymphoma and marketing launch by the US partner Spectrum Pharmaceuticals. Validive: positive preliminary results for the phase 2 trial into the treatment of severe oral mucositis. Obtaining of the "Fast Track" status granted by the FDA. Livatag®: Granting of "Fast Track" status by the FDA for the second-line treatment of hepatocellular carcinoma after treatment with Sorafenib. Achieved capital increase of €40.7 million to finance the continuation of the Group's development program.

**2015.** Livatag®: Progress of the "ReLive" phase 3 trial in primitive lung cancer, with the opening of 4 new centers. Filing of a new patent application based on a specific composition of Livatag® nanoparticles that would allow for the extension of the product's industrial protection until 2036. Initiation of a preclinical development program in view of testing Livatag® and Beleodaq® in association with other anti-cancer products. Beleodaq®: Publication in December 2015 of the positive phase 1 results of Beleodaq® (belinostat) in association with the CHOP¹6 standard protocol in 1st-line PTCL treatment. Validive®: Presentation of positive final results for the Validive® phase 2 study in the treatment of severe oral mucositis as part of several international congresses.

**2016.** Acquisition of DNA Therapeutics and of a new product: AsiDNA™. Launch of the AsiDNA™ preclinical development program. Announcement of the issuance by the US Patent Office of a key patent on AsiDNA™, extending its protection through to 2031. AsiDNA™ showed a synergistic effect in combination with PARP inhibitors, without restrictions related to the tumor's genetic profile. Continuation of the "ReLive" phase 3 study with Livatag®. Promising preclinical program results for Beleodaq® in combination with control point inhibitors. Exclusive license agreement with Pint Pharma for the marketing of Beleodaq® in South America in the field of PTCL. Onxeo raises €12.5 million from American and European investors.

**2017.** Appointment of two experienced directors to boost preclinical and clinical development. Launch of a managed access program for belinostat in Europe for patients suffering from peripheral T-cell lymphoma (PTCL) Raising of €15 million from American and European investors. Positive preclinical proof of concept results demonstrating the activity of AsiDNA™ systemically Sale of two non-strategic historical products, Loramyc® and Sitavig®, to Vectans Pharma. Negative results of the phase 3 Livatag® trial, ReLive, in advanced hepatocellular carcinoma and decision not to continue the development program without partnership. Signature of a global licensing agreement for Validive® with Monopar Therapeutics. Obtaining of convincing preclinical data for use of the two innovative molecules, AsiDNA™ and belinostat in combination Presentation of platON™, a chemical oligonucleotides platform based on the "decoy" mechanism First instance ruling of the Commercial Court of Paris within the framework of the proceedings against SpeBio/SpePharm Setting-up of a scientific committee composed of international experts, specialists in DNA targeting

The CHOP protocol is a multidrug chemotherapy (MDT) recommended for the treatment of lymphoma and typically consists of the following drugs: cyclophosphamide, hydroxydaunomycin (doxorubicin), vincristine (Oncovin®) and prednisolone (steroid).



**2018.** EPO Intent-to-Grant Notice for key AsiDNA™ patent Presentation of two studies highlighting potential of AsiDNA™ as anti-cancer treatment at 2018 AACR Annual Meeting Initiation of DRIIV Phase 1 Clinical Trial of AsiDNA™ for treatment of advanced solid tumors Securing of \$7.5 Million of non-dilutive capital from SWK Holdings Corporation through sale of rights related to future Beleodaq® royalties Implementation of an equity line of credit including an incentive plan with Nice & Green New preclinical results on Onxeo's AsiDNA™, first-in-class DNA repair inhibitor, point to strong synergy and reversion of tumor resistance when combined to PARP inhibitors Positive interim results from Phase 1 Study of AsiDNA™, a first-In-class DNA Damage Response Inhibitor Decision from the Paris Court of Appeal in the lawsuit against SpeBio/SpePharm Notice of intent to issue by the EPO of a patent protecting AsiDNA™ in association with any PARP inhibitor.

#### 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 form**

Onxeo is a French *société anonyme* whose securities are traded on the regulated market of Euronext Paris and also have a secondary listing on the Copenhagen Nasdaq market and is governed by the French Commercial Code and its implementing 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: March 5, 1997.

Incorporation expiry date: March 5, 2096.

## Registration

The company is registered in the Paris commercial and companies register under number: 410,910,095. APE/NAF code: 219Z. 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 Association, 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 the Registration Document; and
- The historical financial information on the Company for each of the two financial years prior to the publication of the Registration Document.

The 'regulated' financial information is available on Onxeo's website at the following address: www.onxeo.com

# **Corporate object**

Under the terms of Article 2 of the Company's Articles of Association, the corporate object 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 lasts twelve (12) months from January 1 to December 31.

# **Distribution of profits**

Each share confers a right to the Company's profits and assets and to the surplus from liquidation in proportion to the fraction of the number and nominal value of existing shares that it represents.

Each time there is a need to have several shares, whether or not they are preference shares, or securities in order to exercise any right whatsoever, the shareholders or the holders of securities shall be personally responsible for combining the number of shares or of securities necessary.

On the profits of the financial year, minus, as the case may be previous years, a withdrawal has to be made of at least five per cent (5%) allocated to the formation of a "legal reserve" fund. This withdrawal ceases being mandatory when the amount of the reserve fund has reached one tenth of the share capital.

The distributable profit is constituted by the profit of the financial year minus previous losses and the withdrawal referred to above and is added to from retained earnings.

If the year's financial statements, as approved by the General Meeting, show distributable profits as defined by law, the General Meeting will decide to recognize them under one or several reserve accounts for which it will determine the appropriation and use in the form of dividends.



However, in the event of a capital reduction, no distribution may be made to the shareholders should the share capital subsequently fall below the amount of capital plus reserves prevented from being distributed by the law or the Articles of Association.

General meeting may decide to distribute amounts debited from discretionary reserve funds in order to enable or complete a dividend or in the form of an exceptional dividend.

After confirming the existence of reserves it has, the General Meeting may decide to distribute sums withdrawn from those reserves. In such case, only the resolution explicitly on the reserve items from which such withdrawals are made will be implemented. However, dividends are deducted by priority from the distributable profit of the financial year.

The methods of paying dividends are set by the General Meeting, or, failing that, by the Board of Directors.

However, any dividends payable must be paid out no later than nine months after the end of the financial year.

The General Shareholders' Meeting approving the financial statements can grant to each shareholder, for all or part of the distributable dividend, the choice of payment in cash or in the form of shares.

Similarly, the Ordinary General Shareholders' Meeting deliberating under the terms of Article L. 232-12 of the French Commercial Code, can allocate to each shareholder an interim dividend, and for all or part of the interim dividend the choice between payment in cash or in the form of shares.

# **Dividend limitation period**

The dividend limitation period is five years from their date of issue, subsequent to which they are paid to the Public Treasury.

#### Amendment terms of shareholders' rights

Shareholders' rights as provided in the Articles of Association of the Company may only be amended by the Extraordinary General Shareholders' Meeting 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 C on the Euronext Paris regulated market and have also had a secondary listing on the Nasdaq Copenhagen market since August 1, 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 second 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 Association do not contain any provisions stipulating double voting rights for shareholders or limiting the voting rights attached to shares. The General Meeting of May 20, 2015 rejected the establishment of a legal double voting right and confirmed the statutory rule according to which a share is given one vote only.

# 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.

In 2017, the Company received no notifications regarding the crossing of thresholds.

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

The significant contracts are presented in section 7.2.2.2 below.

Transactions with related companies are described in Note 18 to the consolidated financial statements, presented in section 6.2 of the 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 120 m<sup>2</sup> in Copenhagen in Denmark.

### Elements that could have an impact on a public tender offer

In accordance with Article L 225-100-3 of the French Commercial Code, we set out below the elements that could have an impact on a takeover bid:

- The capital structure of the Company has no characteristics that are likely to have an impact on a 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 French 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 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 Association, the members of the Board of Directors are appointed for a term of four years by the Ordinary General Meeting. In case of vacancy by death or resignation of one or more board seats, the Board of Directors may, between Annual General Meetings, make appointments on an interim basis that are subject to ratification by the next Annual General Meeting. The Company's Articles of Association may be amended only by an Extraordinary General Shareholders' Meeting;
- the Board of Directors benefits from delegations that are described in the paragraph "Authorized capital, but not issued/receivables" below; and
- The Company has concluded certain agreements explicitly containing a clause with regard to change in control. These are in particular collaboration and licensing agreements concerning the New Entities that include a clause requiring prior approval by the contracting party in the event of a change in control of the Company;

To date, there has been no agreement providing for indemnities for members of the Senior Management or employees if they resign or are dismissed without just and serious cause, or if their employment ends due to a takeover bid.

# Third-party information, statements by experts and declarations of interest None.

# 7.2.2.2 Sizeable contracts

On June 6, 2016, Onxeo, SWK Funding and SELARL Robin de Malet Fiduciaire entered into a trust guarantee and management contract. Under that contract, allocation assets in the form of a trust guarantee was created in order to transfer full title to the receivables placed in trust on the Beleodaq® product in favor of SWK Funding.

The contract provides that Onxeo issues bonds for an amount of \$7.5M subscribed in full by SWK Funding, which will directly collect the payments on the feels and the future sales arising from the marketing of Beleodaq® due by Spectrum to Onxeo.



# 7.2.2.3 Supplementary information about the capital

On December 31, 2018, the Company's share capital amounted to €13,344,933.75 divided into 53,376,375 shares each of a par value of €0.25, all of the same class and fully paid up.

On June 15, 2018, the Company set up an equity line of credit, including an incentive plan, by issuing new shares over a period of 10 months, for a maximum amount of €5.4 million together with the company Nice & Green, acting by delegation of the Board of Directors and in accordance with the 22<sup>nd</sup> resolution of the Extraordinary General Shareholders' Meeting of May 24, 2017 (capital increase with the cancellation of the preferential right of subscription for one category of persons as part of an equity line of credit up within the limit of 10% of capital).

In accordance with the terms of the agreement, Nice & Green, in its capacity as a specialized investor, this investment not intended to be a permanent stake in the Company's capital, has undertaken, for a 10-month period, to subscribe for and exercise each month, on Onxeo's initiative, share warrants corresponding to minimum monthly financing of €500,000 up to a limit of 4,700,000 shares over the term of the contract. The shares will be issued on the basis of the average share price weighted by volumes over the first three trading days prior to each issue, less a maximum discount of 5.0%. In the event that this line of credit is used up in full<sup>17</sup>, any shareholder that held 1.00% of Onxeo's capital before it was set up would see its holding drop to 0.92% of the capital<sup>18</sup>. Onxeo retains the option of suspending drawdowns or of terminating this agreement at any time. Nice & Green and Onxeo have also agreed on an incentive plan that consists of the allocation in cash, to the Company, of a share of any added value realized by Nice & Green through the sale of shares resulting from the exercise of the warrants.

During fiscal 2018, the Company's share capital was increased several times, mainly in the context of the aforementioned line of credit:

- In June 2018, a capital increase of a nominal amount of €10 000 by the issue of 40 000 new shares with a par value of €0.25 each, in the context of the equity line of credit set up on 15 June 2018.
- In July 2018, a capital increase of a nominal amount of €166,001.50 by the issue of 664 006 new shares with a par value of €0.25 each, in the context of the equity line of credit set up on June 15, 2018, as well as a capital increase of a nominal amount of €49,214 by the issue of 196,856 new shares with a par value of €0.25 each as a result of the permanent acquisition of bonus shares awarded by the Board of Directors on June 15, and July 28, 2017;
- In August 2018, a capital increase of a nominal amount of €215,995.50 by the issue of 863,982 new shares with a par value of €0.25 each, in the context of the equity line of credit set up on June 15, 2018;
- In September 2018, a capital increase of a nominal amount of €153,969.50 by the issue of 615,878 new shares with a par value of €0.25 each, in the context of the equity line of credit set up on June 15, 2018;
- In September 2018, a capital increase of a nominal amount of €25,000.50 by the issue of 100,000 new shares with a par value of €0.25 each, in the context of the equity line of credit set up on June 15, 2018;
- In November 2018, a capital increase of a nominal amount of €50,000.50 by the issue of 200,000 new shares with a par value of €0.25 each, in the context of the equity line of credit set up on June 15, 2018.

The table below details the new share issues that took place during financial year 2018 in the context of the equity line of credit set up on June 15, 2018.

Issue date	Number of shares	Exercise price (€)
06/22/2018	40,000	1.1896
07/02/2018	50,000	1.0508
07/04/2018	100,000	1.0266
07/11/2018	100,000	1.1221
07/12/2018	100,000	1.1161
07/19/2018	64,006	1.1467

<sup>&</sup>lt;sup>17</sup> In this case, 4,700,000 new shares would be issued.

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<sup>&</sup>lt;sup>18</sup> On the basis of the 50,695,653 shares comprised in Onxeo's capital at December 31, 2017.



Issue date	Number of shares	Exercise price (€)
07/23/2018	100,000	1.1182
07/27/2018	150,000	1.1288
08/03/2018	100,000	1.1580
08/07/2018	220,000	1.1504
08/10/2018	43,982	1.1362
08/17/2018	200,000	1.1199
08/29/2018	300,000	1.1166
09/03/2018	126,332	1.1165
09/14/2018	350,000	1.0197
09/17/2018	139,546	1.0255
10/10/2018	100,000	1.0016
11/06/2018	200,000	1.0257
Total 2018	2,483,866	1,0892 <sup>(1)</sup>

As of the date of the Registration Document, share capital amounts to €13,704,097 divided into 54,816,388 shares each of a nominal value of €0.25. 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 Company purchase 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 purchased

We wish to remind you that, 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 for a period of eighteen months by the Company's Ordinary and Extraordinary General Shareholders' Meeting of April 26, 2017 under the terms of its fourteenth resolution, then renewed for a period of eighteen months by the Company's Ordinary General Shareholders' Meeting of May 16, 2018 under the terms of its twelfth resolution.

During the year ended December 31, 2018, the Board of Directors successively implemented the program authorized by the shareholders' meeting of April 26, 2017 and then, from May 17, 2018, the program authorized by the shareholders' meeting of May 16, 2018, identical to the previous.

The objectives pursued by this buyback program, in decreasing order of priority, concern the following situations:

- increasing the liquidity of the company's shares on the market 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 Article L. 225-177 et seq. of the French Commercial Code;
- award of bonus shares to employees and corporate officers under the provisions of Articles L. 225-197-1 *et seq.* of the French Commercial Code;
- to award 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 Article L. 3332-18 et seq. 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;



- cancellation of shares bought back within the limits set by law.

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 contract

In accordance with the provisions of Article L 225-211 of the Commercial Code, we hereby indicate the methods of the share buyback program carried out during the past financial year.

During the 2018 financial year, this share buyback program was exclusively used within the scope of a liquidity agreement 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 December 22, 2003, on January 2, 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 Financial Markets Authority.

With effect from November 30, 2018 following the balance sheet date, Onxeo terminated the liquidity agreement with CM-CIC Securities. At that date, the liquidity account contained 82,704 shares and €46,423 in cash. The trading expenses for this contract amounted to €27,000 a year.

Onxeo entrusted Kepler-Cheuvreux with implementing a liquidity agreement relating to its ordinary shares, with effect from December 3, 2018 for a term of twelve months, tacitly renewable. This contract is compliant with the deontology charter of the French Association of Financial Markets ("AMAFI"). In order to implement this contract, 87,612 shares and €196,423 in cash have been granted to the liquidity account. The trading expenses for this contract amount to €25,000 a year.

Under the share buyback program, the Company, between the opening date and the closing date of the last financial year, made the following purchases and sales of its own shares:

	Number of shares purchased	Number of shares sold	Average purchase price	Average selling price	Number of shares registered in the Company's name	Percentage of capital
Outright buyback agreement	0	0	0	0	0	0
Liquidity contract						
January 2018	53,318	87,857	1.8259	1.8020	48,121	0.09%
February 2018	72,267	41,451	1.6511	1.6759	78,937	0.16%
March 2018	62,283	39,233	1.4719	1.4873	101,987	0.20%
April 2018	84,516	89,387	1.3499	1.3561	97,116	0.19%
May 2018	39,127	37,167	1.3023	1.3100	99,076	0.20%
June 2018	41,786	52,286	1.2486	1.2613	88,576	0.17%
July 2018	42,691	59,340	1.1850	1.2050	71,927	0.14%
August 2018	49,090	36,351	1.1878	1.1948	84,666	0.16%
September 2018	15,123	21,105	1.0926	1.0976	78,684	0.15%
October 2018	75,646	81,261	0.9968	1.0041	73,069	0.14%
November 2018	78,114	63,571	0.9955	1.0178	87,612	0.16%
December 2018	137,187	113,704	0.8980	0.9030	111,095	0.21%
<b>Total 2018</b>	838,760	722,713	1.0962 (1)	1.2408 (1)		

(1) Weighted average calculated over the year



The company held 11,095 treasury bearer shares at December 31, 2018, with a par value of €27,773.75 and a book value of €96,874.84 measured at the purchase price of the shares.

# 7.2.2.3.2.2 Shares held by the company (excluding liquidity contract)

At December 31, 2018 the company no longer held any own shares. The 4,908 treasury shares registered as at November 30, 2018, of a total nominal value of €1,227 and a total book value of €5,300.64 were contributed in full under the new liquidity contract entered into with Kepler Cheuvreux.

All purchases and shares made by the Company on its sales since their admission to trading on the regulated market of Euronext Paris were made under the liquidity contract.

#### 7.2.2.3.3 Potential share capital

The Company has authorized the capital increases, not effected at the date of this Registration Document, which could result from the warrants, stock options and free shares described in chapter 5 of the Registration Document.



# 7.2.2.3.4 Summary of valid delegations regarding capital increases granted by the General Meeting to the Board of Directors

In accordance with the provisions of Article L. 225-37-4 of the French Commercial Code, we hereby report the currently valid delegations granted by the General Shareholders' Meeting to the Board of Directors in respect of capital increases and the use made of these delegations during the year ended December 31, 2018.

	Duration of validity/expiry date	Maximum (nominal value)	Use made of the delegation				
Delegations of authority granted by the general meeting of May 24, 2017							
Delegation of authority granted to the Board of Directors to increase the share capital immediately or in the future through the issuance of common shares or any securities giving access to the capital without preferential subscription rights (16 <sup>th</sup> resolution).	26 months/July 24, 2019 This delegation of authority was replaced the one granted by the General Meeting of June 19, 2018 under its 13 <sup>th</sup> resolution	€ 5,880,425 (23,521,700 shares)	The Board did not use this delegation of authority				
Delegation of authority granted to the Board of Directors for a capital increase through the issue of common shares or of any securities giving access to the capital without preferential subscription rights of shareholders and a public takeover bid (17 <sup>th</sup> resolution).	26 months/July 24, 2019 This delegation of authority was replaced the one granted by the General Meeting of June 19, 2018 under its 14 <sup>th</sup> resolution	€ 5,880,425 (23,521,700 shares)	The Board did not use this delegation of authority				
Delegation of authority granted to the board of directors with a view to issuing shares or any securities giving access to the capital immediately or in the future with removal of shareholders' preferential subscription rights through an offer to qualified investors or a restricted circle of investors within the meaning of paragraph II of Article L. 411-2 of the French Monetary and Financial Code (18 <sup>th</sup> resolution).	26 months/July 24, 2019 This delegation of authority was replaced the one granted by the General Meeting of June 19, 2018 under its 15 <sup>th</sup> resolution	€ 2,352,170 (9,408,680 shares)	The Board did not use this delegation of authority				

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Delegation of authority granted to the Board of Directors to increase the amount of each share issue with or without preferential subscription rights that would be decided under the 16 <sup>th</sup> to 18 <sup>th</sup> resolutions above (19 <sup>th</sup> resolution).	26 months/July 24, 2019 This delegation of authority was replaced the one granted by the General Meeting of June 19, 2018 under its 16 <sup>th</sup> resolution	15% of the initial issue	The Board did not use this delegation of authority
Authorization granted to the Board of Directors in the event of share issuance or shares of any securities giving access to the capital without shareholders' preferential subscription rights, to set the issue price within the limit of 10% of the share capital and within those set by the General Meeting by virtue of the delegations of authority decided under the 17 <sup>th</sup> and 18 <sup>th</sup> resolutions above (20 <sup>th</sup> resolution).	26 months/July 24, 2019 This delegation of authority was replaced the one granted by the General Meeting of June 19, 2018 under its 17 <sup>th</sup> resolution	Within the limit of 10% of the share capital.	The Board did not use this delegation of authority
Delegation of authority granted to the Board of Directors to increase the share capital by issuing ordinary shares or any securities giving access to the share capital, without preferential subscription rights in favor of a category of persons (21st resolution).	18 months / November 24, 2018 This delegation of authority was replaced the one granted by the General Meeting of June 19, 2018 under its 18 <sup>th</sup> resolution and by the authorization granted by the General Meeting of June 19, 2018 under its 19 <sup>th</sup> resolution	€ 2,352,170 (9,408,680 shares) Amounts not cumulative with those stated above	The Board did not use this delegation of authority
Delegation of authority granted to the Board of Directors to increase the share capital by issuing ordinary shares or any securities giving access to the share capital, without preferential	18 months / November 24, 2018 This delegation of authority was replaced	€ 1,176,085	By decision dated June 15, 2018, the Chief Executive Officer, acting by delegation of the Board of Directors of May 16, 2018, decided to issue 4 700 000 warrants in favor of Nice & Green for a global price of 100 euros,



subscription rights in favor of a category of persons within the framework of an equity line of credit (22 <sup>nd</sup> resolution).	the one granted by the General Meeting of June 19, 2018 under its 20 <sup>th</sup> resolution		giving the right to subscribe to a maximum number of 4,700,000 shares at an issue price equal to 95% of the average share price weighted by volumes over the 3 trading days prior to the date on which the Company receives an exercise notice. The exercise price of a warrant may not be less than the par value of one of the Company's shares, not may it be less than 1 euro.
Delegation of authority to the Board of Directors to increase the share capital within a limit of 10% of the capital in remuneration of contributions in kind of any equity securities or securities giving access to the capital of third-party companies not within the context of a share exchange offer (23 <sup>rd</sup> resolution).	26 months/July 24, 2019 This delegation of authority was replaced the one granted by the General Meeting of June 19, 2018 under its 21 <sup>th</sup> resolution	10% of the share capital	The Board did not use this delegation of authority
Authorization for the Board to grant share subscription options or share purchase options (26 <sup>th</sup> resolution).	38 months / July 24, 2020	470,400 shares representing a maximum nominal amount of €117, 610	The Board did not use this delegation of authority
Authorization is given to the Board to award bonus shares—existing or to be issued (27 <sup>th</sup> resolution).	38 months / July 24, 2020	470,400 shares representing a maximum nominal amount of €117, 610	The Board did not use this delegation of authority
Delegation of authority granted to the Board of Directors to issue a maximum number of 470,440 warrants in favor of the members of the Board Of Directors in office as at the warrant award date who are neither employees nor executives of the Company or of any of its subsidiaries and persons bound by a service agreement or a consultancy agreement to the Company or one of its subsidiaries (29 <sup>th</sup> resolution).	18 months / November 24, 2018	470,400 shares representing a maximum nominal amount of €117, 610	The Board did not use this delegation of authority

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Delegations granted by the General Meeting of June 19, 2018			
Delegation of authority granted to the Board of Directors to increase the share capital immediately or in the future through the issuance of common shares or any securities giving access to the capital without preferential subscription rights (13 <sup>th</sup> resolution).	26 months / August 19, 2020	€6,336,750 (25.347.000 shares)	The Board did not use this delegation of authority
Delegation of authority granted to the Board of Directors for a capital increase through the issue of common shares or of any securities giving access to the capital without preferential subscription rights of shareholders and a public takeover bid (14 <sup>th</sup> resolution).	26 months / August 19, 2020	€6,336,750 (25.347.000 shares)	The Board did not use this delegation of authority
Delegation of authority granted to the board of directors with a view to issuing shares or any securities giving access to the capital immediately or in the future with removal of shareholders' preferential subscription rights through an offer to qualified investors or a restricted circle of investors within the meaning of paragraph II of Article L. 411-2 of the French Monetary and Financial Code (15 <sup>th</sup> resolution).	_	€6,336,750 (10.139.000 shares)	The Board did not use this delegation of authority
Delegation of authority granted to the Board of Directors to increase the amount of each share issue with or without preferential subscription rights that would be decided under the 14 <sup>th</sup> to 15 <sup>th</sup> resolutions above (16 <sup>th</sup> resolution).	26 months/August 19, 2020	15% of the initial issue	The Board did not use this delegation of authority
Authorization granted to the Board of Directors in the event of share issuance or shares of any securities giving access to the capital without shareholders' preferential subscription rights, to set the issue price within the limit of 10% of the share capital and within those set by the General Meeting by virtue of the delegations of authority decided under the 14 <sup>th</sup> and 15 <sup>th</sup> resolutions above (17 <sup>th</sup> resolution).	26 months/August 19, 2020	Within the limit of 10% of the share capital.	The Board did not use this delegation of authority
Delegation of authority granted to the Board of Directors to increase the share capital by issuing ordinary shares or any securities giving access to the share capital, without preferential	18 months / December 19, 2019	€6,336,750 (10.139.000 shares)	The Board did not use this delegation of authority

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subscription rights in favor of a first category of persons ( $18^{\text{th}}$ resolution).		Amounts not cumulative with those stated above	
Delegation of authority granted to the Board of Directors to increase the share capital by issuing ordinary shares or any securities giving access to the share capital, without preferential subscription rights in favor of a second category of persons (19th resolution).	18 months / December 19, 2019	€6,336,750 (10.139.000 shares) Amounts not cumulative with those stated above	The Board did not use this delegation of authority
Delegation of authority granted to the Board of Directors to increase the share capital by issuing common shares or any securities giving access to the share capital, without preferential subscription rights in favor of a category of persons in the context of an equity or bond line of credit (20 <sup>th</sup> resolution).	18 months / December 19, 2019	€3,000,000 (12.000.000 shares)	The Board did not use this delegation of authority
Delegation of authority granted to the Board of Directors to increase the share capital by issuing common shares or any securities giving access to the share capital, without preferential subscription rights in favor of a category of persons in the context of an equity or bond line of credit (21 <sup>th</sup> resolution).	18 months / December 19, 2019	€1,267,250 (5.069.000 shares) Amounts not cumulative with those stated above	The Board did not use this delegation of authority
Delegation of authority to the Board of Directors to increase the share capital within a limit of 10% of the capital in remuneration of contributions in kind of any equity securities or securities giving access to the capital of third-party companies not within the context of a share exchange offer (22 <sup>rd</sup> resolution).	26 months/August 19, 2020	10% of the share capital	The Board did not use this delegation of authority
Authorization for the Board to award bonus shares - existing or to be issued as replacement for the payment in cash of part of the variable remuneration of the interested parties in the financial year 2017 (25 <sup>th</sup> resolution).		300,000 shares representing a maximum nominal amount of €75,000	The Board of Directors meeting of July 27, 2018 awarded bonus shares in favor of employees and the Chief Executive Officer. Cf. section 4 above.
Authorization is given to the Board to award bonus shares—existing or to be issued (26 <sup>th</sup> resolution).	38 months / August 19, 2021	(435,000 shares) 435,000 shares representing a maximum nominal amount of €108,750	The Board of Directors meeting of July 27, 2018 awarded bonus shares in favor of employees and the Chief Executive Officer. Cf. section 4 above.

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Authorization for the Board to grant share subscription options or share purchase options (27 <sup>th</sup> resolution).	38 months / August 19, 2021	970,000 options representing a maximum nominal amount of €227,500	The Board of Directors meeting of July 27, 2018 awarded bonus shares in favor of employees and the Chief Executive Officer. Cf. section 4 above.  Each option grant the right to subscribe to one share of the Company of a nominal value of €0.25 at the price of €4
Delegation of authority granted to the Board of Directors to issue a maximum number of 360.000 warrants in favor of the members of the Board Of Directors in office as at the warrant award date who are neither employees nor executives of the Company or of any of its subsidiaries and persons bound by a service agreement or a consultancy agreement to the Company or one of its subsidiaries (28 <sup>th</sup> resolution).	18 months / December 19, 2019	360,000 warrants representing a maximum nominal amount of €90,000	The Board of Directors meeting of July 27, 2018 decided to issue 274,500 warrants in favor of the Company's directors at the price of €1.187. Each option grant the right to subscribe for one share of the Company of a nominal value of €0.25 at the price of €4. The Board of Directors meeting of October 25, 2018 decided to issue 85,000 warrants in favor of the Company's directors at the price of €0.10. Each option grant the right to subscribe to one share of the Company of a nominal value of €0.25 at the price of €1.017.

The complete text of the resolutions of the company's general meetings may be viewed on the website of *Bulletin d'Annonces Légales Obligatoires*: http://www.journal-officiel.gouv.fr/balo.

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# 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 the General Shareholders' Meeting.

#### **Statutory auditors**

#### **Grant Thornton**

French member of Grant Thornton International 29, rue du Pont 92200 Neuilly-Sur-Seine

Represented by Mr. Samuel Clochard, members of the Compagnie des commissaires aux comptes of Paris.

The appointment of Ernst & Young was renewed at the General Meeting held on April 6, 2016 for a period of six financial years. This appointment expires at the close of the shareholders' meeting deciding on the financial statements for the period ending December 31, 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 Versailles Institute of Statutory Auditors.

The appointment of Ernst & Young was renewed at the General Meeting held on April 26, 2017 for a period of six financial years. This appointment expires at the close of the General Meeting deciding on the financial statements for the period ending December 31, 2022.

During the period covered by the historical financial information, no legal controller of the Company resigned or was set aside.

#### 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 January 1 and December 31, 2018 is provided in Note 20 to the consolidated financial statements provided in section 6.1 of the Registration Document.



# 8. PERSONS RESPONSIBLE

# 8.1 PERSON RESPONSIBLE FOR THE REFERENCE DOCUMENT

Judith GRECIET Director, Chief Executive Officer

# 8.2 CERTIFIED STATEMENT OF 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.

The financial information presented in this document has been included in reports of the statutory auditors.

Done on April 5, 2019, at Paris, France

Judith Greciet - Chief Executive Officer

#### 8.3 PERSON RESPONSIBLE FOR THE FINANCIAL INFORMATION

Mr. Nicolas Fellmann - Administrative and Finance Director

Address: 49 boulevard Valin – 75015 Paris – France – Tel.: +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 is incorporated by reference in the Registration Document:

- the consolidated financial statements and the associated statutory auditors' report provided in paragraphs
   6.1 and 6.2 of the registration document for the year 2016 submitted to the AMF on April 26, 2018 under number D.18-0389.
- the consolidated financial statements and the associated statutory auditors' report provided in paragraphs 6.1 and 6.2 of the registration document for the year 2016 submitted to the AMF on April 24, 2017 under number D.17-0423.

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# CROSS-REFERENCE TABLE: ANNUAL REPORT

In order to enhance the readability of the Registration Document, the cross-reference table below enables information in this Registration Document to be identified which constitutes the annual financial report that listed companies are required to publish in accordance with Article L. 451-1-2 of the French Monetary and Financial Code and Article 222-3 of the AMF General Regulation.

ANNUAL FINANCIAL REPORT	SECTIONS
1. Certificate of person responsible	8.2
2. Financial statements — French standards	6.3
3. Consolidated financial statements — IFRS standards	6.1
4. Annual management report	See table below
5. Corporate governance report	See table below
6. Report on the amount of auditors' fees	7.2.2.4.2
7. Statutory auditors' reports on the annual financial statements in accordance with French and IFRS standards	6.2 6.4
ANNUAL MANAGEMENT REPORT	SECTIONS
1. The company's situation and work in progress during this financial year	2
2. Examination of the financial statements — Allocation of earnings— Reminder of dividends distributed—Non-tax-deductible expenses	3.1.1
3. Information on supplier payment terms	3.1.1.6
4. Main risks and uncertainties to which the Company is exposed	5.7.1.4
5. Foreseeable developments and future prospects	2.3
6. Significant post-balance sheet events	2.2
7. Information on capital - treasury shares - cross-equity interests	7.2.2.3
8. Employee participation in the capital	None
9. Transactions in the Company's shares made by officers or members of the Board of Directors	5.6
10. Risk management and internal control procedures	5.7.1
	5.7.2
11.  Information on the agreements entered into between a director or a significant shareholder and a subsidiary of the Group	5.1.2.7
12. Table of the financial results for the last five financial years	6.3



# 10. CROSS-REFERENCE TABLE: REFERENCE 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 April 29, 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	Reference
	Alliex For Le Regulation no. 003/ 2004	document
		Paragraph(s)
l. 	Persons responsible	8.1
II.	Statutory Auditors	1.2.3 7.2.2.4
III.	Selected financial data	
1.	Selected historical financial data	1.3
2.	Selected financial data for interim periods and comparative data covering the same periods of the preceding financial year	N/A
IV.	Risk factors	5.7.1.4
V.	Details of issuer	
1.	Corporate history and development	7.2.1
	1.1. Registered name and trade name	7.2.2.1
	1.2. Issuer location and company registration number	7.2.2.1
	1.3. Date of incorporation and term of the issuer	7.2.2.1
	1.4. Registered office and legal form of the issuer, legislation	7.2.2.1
	governing its activities, country of origin, address and telephone number	
	1.5. Significant events in the development of the issuer's activity	2.1
		7.2.1
2.	Investments	2.3
		3.2.5
VI.	Business overview	4.4
1.	Main activities	1.1
	1.1. Type of operations carried out by the issuer and its main activities	1.1
	1.2. Important new product or service launched on the market	4.2
2.	Main markets	4.2
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
5.	Basis of any declaration by the issuer concerning its competitive position	4.2
VII.	Organization chart	2.1.1
VIII.	Property, plant and equipment	7.2.2.1
	Environmental impact	2.4.2
IX.	Examination of the financial situation and operating income	3.1
Χ.	Cash and capital	3.2
XI.	Research and development, patents and licenses	4 4.1.4
XII.	Information on trends	2.3
XIII.	Profit forecasts or estimate	N/A



XIV.	Administrative, management and supervisory bodies and general management	
1.	Information on activities, absence of any conviction and terms of office	5.1.2 5.1.2.1
2.	Information on conflicts of interest, agreements concluded with third parties and restriction on the sale of shares	5.1.2.2 5.1.2.6
	tillid parties and restriction on the sale of shares	5.1.2.7
XV.	Remuneration and benefits of the persons referred to in point XIV.1	5.1.2.4 5.2.2
XVI.	Functioning of the administrative and management bodies	
1.	Expiry date of the current term of office of members of the administrative, management and supervisory bodies	5.1.2.1
2.	Information on service contracts involving members of the administrative, management and supervisory bodies of the issuer or	5.1.2.7
3.	of any of its subsidiaries Information on the issuer's audit committee and remuneration	5.1.1.3
	committee	
4.	Compliance with the corporate governance regime in force	5 7.2.2.1
XVII.	Employees	
1.	Number of employees at the end of the period covered by the historical financial data or average number during each financial year of this period and distribution of employees	2.4.1
2.	Holdings and stock options: for each of the persons referred to in	2.4.1.1.4
	point XIV.1, information on the participations that he or she holds in the issuer's share capital and any option existing over its shares	5.2.2
3.	Agreement providing for employee participation in the issuer's capital	7.2.2.1
XVIII	Main shareholders	7.1.2
	Double voting right	7.2.2.1
	Jointly-held shares and thresholds	7.2.2.1
XIX	Agreement which could lead to a change in control  Transactions with related companies	7.2.2.1 7.2.2.1
ΛIΛ	Transactions with related companies	6.1 note 19
XX.	Financial data on the issuer's assets and liabilities, financial situation and operating income	
1.	Historical financial information	6
2.	Pro-forma financial data and description of the effect of the restructuring	N/A
3.	Annual financial statements (individual company and consolidated financial statements)	6.1 6.3
4.	Verification of historical financial data	
	4.1. Declaration certifying that the historical financial data has been	6.2
	verified	6.4
	4.2 Other information contained in the registration decument and	8.2 6.5
	4.2. Other information contained in the registration document and verified by the statutory auditors	6.6
	4.3. When financial data appearing in the registration document is not derived from financial statements verified by the issuer, state its source and stipulate that it is not verified	N/A
5.	Date of latest financial data verified	6.5
6.	Interim and other financial data	6.5
7.	Dividend distribution policy	6.5)
8.	Legal and arbitration proceedings	6.1
		6.3
9.	Significant change in the financial or commercial situation since the end of the last financial year	2.2



XXI.	Supplementary information	
1.	Share capital	7.1.2 7.2.2.3
	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	
	1.2. Shares not evidencing capital	N/A
	1.3. Number, book value and nominal value of shares held by the issuer or its subsidiaries	7.2.2.3
	1.4. Securities that are convertible or exchangeable or come with subscription warrants	7.2.2.3
	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
	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
	1.7. History of the share capital for the period covered by the historical financial data	7.1
2.	Memorandum and Articles of Association	7.2.2.1 5.1.2.2
XXII.	Sizeable contracts	7.2.2.2
XXIII	Third-party information, statements by experts and declarations of interest	7.2.2.1
XXIV	Publicly available documents	7.2.2.1
XXV.	Information on holdings	3.1.1.5 2.1.1



# 11. CROSS-REFERENCE TABLE: CORPORATE GOVERNANCE REPORT

Element of the Corporate Governance Report	Position in the Registration Document
List of all terms of office and functions performed by each corporate officer	Paragraph 5.1.2.1
List of agreements entered into between a director or a shareholder of the Company and a subsidiary of the Company	Note 7 of the annual statements
Table summarizing currently valid authorizations granted by the General Shareholders' Meeting	Paragraph 7.2.2.3.4
Decision on the operating methods of the senior management	Paragraph 5.1.1.1
Total remuneration and benefits to corporate officers	Paragraphs 5.1.2.4 and 5.2.2
Board of Directors' Report on the principles and criteria relating to the remuneration of the Chairman and of the CEO	Paragraph 5.4
Composition and conditions for preparing and organizing works of the Board of Directors	Paragraph 5.1.1
Description of the diversity policy applied to Board members	Paragraph 5.1.1.1
Limitations which the Board of Directors makes to the powers of the CEO	Paragraph 5.2.1
Reference to a governance code	Paragraph 5
Special terms of shareholder participation in the General Meetings	Paragraph 7.2.2.1
Elements likely to have an impact in case of a public offering	Paragraph 7.2.2.1



# 12. GLOSSARY

WORDS	DEFINITIONS
ANSM	Agence Nationale de Sécurité du Médicament (French drug agency)
MA	Marketing Authorization
Quality Assurance	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.
GCP (Good Clinical Practice)	The set of measures ensuring the quality of clinical trials.
GMP	An aspect of pharmaceutical quality assurance that ensures drugs are manufactured and
(Good Manufacturing	controlled in a consistent manner according to quality standards suitable for the drug's
Practice)	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 Center).
CRO	Contract Research Organization.
DDR (DNA Damage Response)	DNA Damage Response: general term designating the numerous cell responses to damage caused to DNA.
DSMB	Data Safety and Management 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 - the US Agency for drug registration.
ICH	International Conference of Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use.
IFRS	International Financial Reporting Standards – International accounting standards as adopted by the European community.
IND	Investigational New Drug – Request for authorization 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 well-being 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.



WORDS	DEFINITIONS
In vivo ISO 9000 (9001, 9002,	Manipulation taking place in the body of a human or animal.  Quality system: A system designed to ensure quality in design, development, production,
9003)	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.
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 1	This phase corresponds to the initial clinical trials. It must evaluate drug tolerance in a small number of volunteer subjects and enable initial studies on the administration of the drug in the human body.
Phase 2	This phase is often divided into two sub-phases. The objective of Phase 2a is to study the effects of the drug on a small number of volunteer patients and to complete pharmacokinetic studies. The objective of Phase 2b 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 3	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.
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.
Homologous recombination	In the widest sense of the term, homologous recombination is the mechanism which causes the exchange between DNA molecules. The homologous recombination is initiated by a DNA double-strand break.
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.
Tracking	All the information and measures taken to monitor and rapidly retrace each stage of a process.
Dose-limiting toxicity	Dosestabligibeneditugi per autich abkhattyripistrapptatio. Marsutesei maker acess, sprieceoldetine
(DLT)	equipmentective dosterial iaktivityt nesassaniyabellally enthalast beenteal (Zabien in it lagned outlong) s and set specifications.
Validation	

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