Loose translation for information purposes only

In the event of conflict between the Spanish and the English version, the Spanish version shall prevail

REGISTRATION DOCUMENT FOR

ORYZON GENOMICS, S.A.

July 24, 2018

This registration document has been approved and recorded by the National Securities Market Commission on July 24, 2018.

The Registration Document has been prepared in accordance with the model established in Annex I to Commission Regulation (EC) No. 809/2004 of April 29, 2004, implementing Directive 2003/71/EC of the European Parliament and of the Council as regards information contained in prospectuses, as well as the format, incorporation by reference and publication of such prospectuses and dissemination of advertisements.

CONTENTS

I. RISK FACTORS

The Risk Factors set out below, as well as all information contained in this Registration Document, should be carefully reviewed before making a decision to invest in the Company. Any of these risks could have a material adverse effect on the financial condition, the business or the results of operations of ORYZON. In addition, it should be noted that such risks could affect the price of the Company's shares, which could result in a total or partial loss of the investment made.

Moreover, future risk factors that are currently unknown or that are not deemed significant by ORYZON at present might also affect the financial position, business or results of ORYZON.

1. RISK FACTORS SPECIFIC TO THE ISSUER OR ITS INDUSTRY

1.1. Risks specific to the issuer

1.1.1. Risk of not signing license agreements/not obtaining financing

The Company's business model is based on the grant of license agreements for drugs that it develops. The Company has three (3) products that can be licensed in the development phase and that are in the clinical and preclinical development phases. The Company's portfolio of projects has significantly matured since the signing in April 2014 of the Agreement with Roche, from which it has recovered the rights to develop and sell ORY-1001 in January 2018, and the company has the unrestricted legal ability to sign new agreements regarding this compound.

As of the date of registration of this document, the Company has not signed new licensing agreements regarding drugs that it has developed, and has two (2) compounds at the clinical phase: (i) ORY-1001, the most advanced compound in oncology, in Phase I/IIA studies in acute leukemia, and SCLC; and (ii) ORY-2001, a compound for neurodegenerative disorders, in Phase IIa. It also has a third compound in the preclinical phase, ORY-3001, for the treatment of non-oncological illnesses.

The Company's business model is also based on the development of drugs through Phase IIb, with the ability to choose license agreements at any of their prior phases (preclinical, Phase I, Phase IIa and Phase IIb), although in any event if financing is available, the Company could develop products for an indication that requires a lower volume of patient recruitment through Phase III or bring them to market itself.

The product licenses provide funding to the Company and allow for the development of products at different indications. The higher the funding, the higher the ability to develop products and indications thereof. The development of products requires long-term investments that are financed by contributions of capital, bank debt, refundable and non-refundable public and private grants, and income from licenses.

The expected time for licensing a product is at the intersection between the offer to license this product by the Company and the demand for that same product by multinational pharmaceutical companies or other large biotechnology companies.

Based on the phase of the business model, there may or may not be licensed products; the risk is not of whether or not licensed products simply exist, but rather the combination of this factor with whether or not funding is available. The funding should allow for continued development of the products and the day-to-day operations of the Company. Thus, the level of risk will be directly related to the available funding capacity – if a license agreement cannot be reached, the available funding at that time will determine whether or not there is a need to enter into early license agreements for other products, access additional funding through new indebtedness or

equity funding, or a redefinition, reorganization and slow-down of product development or discontinuation of operations.

1.1.2. Technical and human resources

1.1.2.1. Accidents affecting the facilities

Despite the insurance coverage obtained, if a major accident occurs at any of the Company's facilities or if there are malfunctions of equipment or other unexpected events (such as earthquake, fire, explosion, etc.), the components used by ORYZON to carry on its business might be damaged. In addition, the resumption of product development could be hindered by delays to the extent necessary to obtain any mandatory approval to rebuild all or part of the facilities.

1.1.2.2. Damage to information technology systems

ORYZON's activities heavily rely on information technology systems. If the Company's systems suffered long-term structural damage that could not be corrected within a few days, the Company could experience significant disruptions that would affect its research processes.

1.1.2.3. Highly qualified scientific personnel

ORYZON faces intense competition from other companies, academic institutions, governmental agencies and other organizations, and therefore, it might not be able to attract and retain such qualified personnel. The loss of qualified personnel or the inability to attract and retain the qualified personnel needed for the conduct of the Company's activities could have a negative impact on the business.

Although the Company has made an effort by increasing the compensation of the management team, there is a certain mismatch between large pharmaceutical companies and ORYZON in terms of remuneration capacity. In addition to the connotations of this factor regarding the Company's ability to recruit external talent, also worthy of consideration are the risks facing the Company due to the growing visibility of the ORYZON project and, as a result, of all the key members of the team.

The Company has mitigated the risk described in the preceding paragraph by adopting measures including a stock option plan available to all non-executive officers of ORYZON, who exercised their corresponding rights during 2016 and 2017. There are currently no rights to participate in such plan. Furthermore, the Company has reached a level of maturity and of functional compartmentalization that helps it to partly counter this generic risk, as ORYZON does not have a single "key person." Mr. Carlos Manuel Buesa Arjol and Ms. Tamara Maes also have an LTI until December 31, 2019, which if applicable is payable in 2020 if the targets established therein are reached.

1.1.3. International expansion

ORYZON plans to intensify its commercial presence in the USA by boosting several of its activities, including interaction with U.S. regulatory authorities such as the FDA, the development of clinical trials, interaction and communication with investors, and development of the business. The Company will need considerable financial resources in order to carry out these activities at an appropriate level of intensity.

Furthermore, the Company's business plan provides for the possibility of engaging in corporate transactions, especially at the international level, with other biopharmaceutical companies that have strategic and/or complementary intellectual property or technologies. If such corporate transactions are approved, a significant amount of funds will be required, entailing a substantial

cash outflow, an increase in financial debt, the implementation of capital increases or a combination of all such strategies.

1.1.4. Country risk

Due to the intensification of political events in the Autonomous Community of Catalonia during the fourth quarter of 2017, several measures to mitigate the risks of such instability were established, such as the transfer of the registered office to Madrid, at Carrera de San Jerónimo 15, 28014, the relocation of its computer backup systems and the geographic diversification of financial resources and key suppliers to mitigate the risk of geographic concentration. Laboratory facilities are located at Calle Sant Ferran, 74, Cornellà de Llobregat (Barcelona).

1.2. Risks specific to the industry

1.2.1. Heavily regulated industry

The biotechnology sector is subject to exhaustive regulation in all jurisdictions in which it has a presence, as well as to regulatory uncertainties. Any change in the laws and regulations that govern such sector might adversely affect ORYZON's business, financial condition and income statement, as well as the planning, implementation and financing of R&D activities and any financial and tax aid that it receives.

The development of compounds in the pharmaceutical industry poses uncertainties inherent in R&D activities, because in order to move from the preclinical development phase to the first clinical phase and, once at this stage, to move through successive clinical phases, the submission of dossiers is required for review by the competent authorities. Such authorities are partly responsible for the decision as to whether or not a phase has been successfully completed, based on technical and safety standards.

In addition, changes in regulations and the requirements imposed by domestic and international regulators in connection with obtaining certain data in clinical trials could have a material impact on the expectations as to investment timeframes, and ultimately on the viability of the Company's products. ORYZON reduces these risks by: (i) performing a comparison among clinical designs of similar products for the different indications in question (benchmarking); (ii) seeking external advice from private specialists and companies specializing in regulatory issues; and (iii) engaging in an open and constructive dialogue with regulatory agencies, including the use of binding consultation mechanisms.

1.2.2. Company dependence on third parties for the development of its products

ORYZON's mission primarily consists of the development of therapeutic products. The Company has been carrying out this activity through alliances with partners and, more recently, independently, with its own means and those of subcontracted third parties. Thus, ORYZON's pipeline of business opportunities may include both co-developed and self-developed products.

Clinical testing is supported by clinical research organizations, which handle the implementation, monitoring and operational control and quality of the clinical test, and are unique for each clinical test, which entails a risk of concentration. The Company mitigates this risk of concentration by directly subcontracting activities like analytics and imaging studies.

Even if the Company manages to move its various projects through to a stage in which they are ready to be licensed, there is a risk that it may not find or may take long to find third parties with whom to execute the relevant license agreements on terms satisfactory to the Company.

1.2.3. Company dependence on the results of clinical tests

The therapeutic products developed by the Company are subject to specific risks of failure inherent in the development of therapeutic products. Both co-developed and self-developed products require preclinical studies and clinical trials on healthy volunteers and/or patients as well as regulatory approvals of varying scope and difficulty.

One way to mitigate the risk inherent in these projects is to increase the number of projects in order to offset the pipeline success and achievement percentage, through the diversification of targets and molecules and of the indications in which each molecule is tested. The Company has made a strong pitch for the ORY-2001 project for the treatment of neurodegenerative diseases in various Phase IIa clinical trials of ORY-2001 for multiple sclerosis (SATEEN) and Alzheimer's (ETHERAL). Furthermore, basic research is leading to advances in understanding of the action mechanism of ORY-2001 and its potential impact on other neurodegenerative as well as psychiatric disorders, for which reason the Company will evaluate expanding the development of this product in new clinical trials based on its financial capacity and the competitive landscape for the various indications.

ORYZON continues to advance with the clinical development of ORY-1001 in acute leukemia and SCLC. Various Phase IIa clinical trials are expected to commence in the coming months for LMA (ALICA) and SCLC (CLEPSIDRA).

ORYZON also has a third molecule called ORY-3001, which was designed as a preclinical candidate in the middle of 2016 and which has provided preclinical data on effectiveness in sickle-cell anemia. The other products in the pipeline are at an earlier stage and it is more difficult to make forecasts regarding the completion of preclinical studies. Furthermore, the decision to begin the regulatory preclinical phase and the clinical studies will depend both on the success of the internal program and on an assessment of the status of the development programs of competitors. The Company has begun a scouting process with a view to the potential inclusion of more epigenetic projects that supplement the pipeline.

1.2.4. Elimination or reduction of tax incentives and/or grants

1.2.4.1. Grants

The financing of R&D activities depends in part on governmental agencies and on the existence of budget allocations that, in certain cases, are decided on a yearly rather than a multi-year basis. Some of the sources of funds used by the Company come in the form of grants, reimbursable aid and loans provided by governmental agencies; R&D activities also depend in part on private funding. The elimination or reduction of grants may cause ORYZON to have to commit additional funds to its R&D activities, which might adversely affect the Company's financial condition, income statement and balance sheet. In order to mitigate this risk, the Company looks to other sources of funds, preferably by requesting financing through international programs that by their nature are less exposed to sharp reductions in budget allocations.

1.2.4.2. Tax deductions

Spanish law provides that certain R&D expenses may qualify as deductions from corporate income tax. Since fiscal year 2013, an election can be made for the tax monetization of such deductions upon satisfying a number of requirements (including the loss of 20% of the deduction, reinvestment of the amounts monetized, maintenance of average staff headcount, etc.). Along these lines, ORYZON could choose to monetize deductions from corporate income tax for R&D. In addition, the current tax benefits for biotechnology companies stem from present and past regulations that may be modified and/or repealed.

1.2.5. Competition in the biotechnology sector

The entry of new competitors into ORYZON's sector of the market may affect the strategy contemplated for growth.

Fast-paced evolution and intense competition are distinctive features of the biotechnology sector and its multiple business models. The competitors of ORYZON include, among others, classical pharmaceutical companies focusing on chemical development, biopharmaceutical companies and biotechnology companies that pursue the same aims as ORYZON, as well as those that develop new technological platforms. Many of ORYZON's competitors have better financial, technological and marketing resources than those available to the Company. In addition, some of ORYZON's competitors have already entered into alliances with large, well-established companies that finance and support their programs, some of which may compete with the Company's programs in the future. In this industry, the first product to reach the market in response to a particular clinical need often gains a significant competitive edge over competitor products introduced later. Additionally, there is a risk that competitors may successfully introduce products based on different technological approaches, such as antibodies, cellular therapy technologies, genic therapy or others that, due to their greater effectiveness or lower cost or simply because they have reached the market earlier, may reduce the commercial potential of the products that ORYZON has developed or is developing.

This type of generic risk, affecting all players in the industry, can only be mitigated through adequate and exhaustive technological, scientific and business surveillance, intended to provide the Company's management with useful real-time information. For such purpose, a competitive intelligence scan is continuously carried out at three (3) levels:

- Scientific scouting through reading of the main scientific journals in the Company's relevant areas of activity and attendance at subject-specific conferences and scientific meetings.
- Analysis of the relevant industrial property map in the Company's various areas of development.
- Analysis of the agreements entered into among various biotechnology and pharmaceutical companies as indicators of trends and regrouping in the industry.

The purpose of this scan is to detect those threats that may jeopardize the commercial or technological future of projects under way and to highlight industry developments, especially those carried out by competitors, in order to make such decisions as may be appropriate: halt, modify or accelerate a project, enter into alliances with competitors, etc.

Moreover, the Company tries to minimize its market access risk vis-à-vis competitor developments by weaving a fabric of alliances with various larger companies that may serve as safe harbors in adverse scenarios. In this regard, the Company's business model is based on maintaining strategic alliances with pharmaceutical groups and/or domestic and international biotechnology companies of the same or a smaller or larger size with a view to the development of joint projects.

1.2.6. Risks relating to intellectual and industrial property

The industrial property dimension of biomarkers, the technology for application of DNA chips, the development of pharmacological inhibitors and, in general, all applications of the technological platform used by the pharmaceutical industry are highly complex and matrix-dependent. In certain cases, it is difficult to ascertain the owner of certain technology, and litigation to clarify ownership is not infrequent in the industry.

ORYZON has built a strong position in its patent portfolio, currently holding thirty-two (32) patent families, twenty-seven (27) of which regard the LSD1 inhibitor and the remaining five (5) of which regard other epigenetic targets, with some of them having been granted in the USA and other countries. The freedom-to-operate searches performed by the Company have not shown that the Company infringes third-party patents or rights. However, ORYZON cannot assure that its pending patents will be granted or that its present or future patents will not be subject to challenges or nullification claims by third parties, or that the Company will not be subject to litigation by third parties holding patents already granted or applied for and of whose existence the Company is unaware. A resolution of any such litigation contrary to the interests of ORYZON could have serious adverse effects on its business.

In order to counter risks in this scenario, ORYZON has long had in place an in-house industrial property division, and it is one of the few Spanish biotechnology companies that has supported the in-house establishment of an area this key in the development of this business. The Company prepares industrial property maps for the technology developments on which it is working, in order to be able to identify and minimize such risks. In particular, an attempt is made, to the extent possible, to seek alternatives that provide freedom to operate. The Company also outsources part of this work to well-known patent-specialist offices in Europe and the USA. The Company has also adopted a policy of acquiring use licenses for technologies that are critical to its developments and of never taking any inappropriate action in connection with the use of third-party technology.

1.2.7. Liability

ORYZON's activities are exposed to civil liability risks inherent in the research into, preclinical and clinical development, production, commercialization and use of human therapeutic products, even if the products are sold by third-party licensees.

In accordance with applicable law, the Company has obtained civil liability insurance in connection with all the clinical tests it performs. Although the Company has ensured prudent levels of coverage under such insurance, it cannot assure that the present or future insurance coverage is adequate or that the activities or financial condition of ORYZON may not be affected by a product liability suit or other type of claim.

1.3. Financial and market risks

1.3.1. Financial risks

The pursuit of the Company's goals means that financial resources will be allocated, among other purposes, to R&D activities and to pharmaceutical development (both in-house and outsourced), to structural fixed costs (salaries and equipment), as well as to regulatory, legal and financial services. The Company also maintains a high level of outsourcing through a group of CROs that gives ORYZON flexibility in managing expenses and investments, allowing the Company to limit or avoid expenses if necessary. As the Company's products are in different stages of clinical and preclinical development and the outcome for each of them is dependent on technical uncertainties, it is not possible to accurately determine the investment needed to complete the various stages successfully. In order to minimize this risk, the Company reviews the average level of such investments in the industry on an international scale in order to make the best possible estimates, and compartmentalizes and segments the development of its programs as much as possible in order to establish intermediate points for evaluation and for technical and financial adjustment.

As the Company continues to expand, the ability to manage growth might become an increasingly greater challenge. If the increase in income is not at least proportional to the increase in the costs associated with such growth, operating and profit margins may be reduced.

As of the date hereof, and provided that no supervening events occur, the Company has the cash required to meet expenses and investments in the short and the medium term. ORYZON has various projects supported by grants or reimbursable governmental aid that partially pay for costs relating to personnel and to outsourced R&D studies, among other costs.

However, ORYZON's future capital needs depend on the evolution of its research activities, on the date when the required governmental approvals are granted, if at all, and on other potential restrictions beyond the Company's control. Thus, it is possible that if any of these factors proves to be negative, the Company's foreseeable income might not be sufficient to pay for the operations; in that case, fresh funds would be needed, which would come from bank borrowings or from new capital increases or from other external sources of funds.

In this regard, if the capital increases must be implemented at adverse market times, the equity interests held by ORYZON's shareholders might be diluted if such increases are implemented with an exclusion of preemptive rights, and if such dilution is not offset by an increase in the value of the Company.

In addition, in certain unfavorable scenarios, future collaboration agreements on new products might be executed under conditions of stress, and diminished bargaining power might give rise to giving greater financial rights than those the Company believes to be standard in the market.

Finally, in the event that the Company is unable to obtain additional funds under acceptable conditions in the future, it might be forced to delay, limit, reduce or even discontinue the development of its products or the sale thereof.

1.3.2. Competitors with greater resources

The Company has a smaller structure than its international competitors, which means that the capabilities of competitors can erode the competitive advantage available to ORYZON and, ultimately, the potential of the programs. In order to partially mitigate this threat, the Company maintains a competitive cost structure and focuses on a greater use of public funds as a source of financial support for the development of molecules, clinical trials and other development work required in order to file for regulatory approvals. If the Company fails to maintain its competitive position, its business, financial condition and income statement might be adversely affected to a significant degree.

1.3.3. Exchange rate and interest rate risk

Part of ORYZON's business plan rests on the internationalization of the Company and on the implementation of programs and activities outside the euro zone; consequently, part of its business will be carried out in foreign currencies, with the associated risk related to changes in the rate of the relevant currency against the euro.

At present, ORYZON has not entered into any instruments to hedge exchange rate risks. Although significant variations in the value of the U.S. dollar against the euro would only affect transactions signed with suppliers, they could have a significant impact on the income derived from future license agreements.

As regards interest rate risk, external financing as of December 31, 2017 is broken down as follows: 78% consists of financing from bank borrowings, and 22% consists of other financial liabilities, mainly governmental financing in the form of reimbursable aid at an effective interest rate of 0% or 1%. As of December 31, 2017, the Company has not entered into interest rate

derivatives contracts that materially cover such risk; the interest rate risk is moderate, as 22% of the loans were subject to a fixed interest rate within the range of 0% to 1%, and the remaining 78% was subject to an average variable interest rate of 2.6%.

The average interest rate on all outstanding loans as of December 31, 2017 was 2.11% (2.11% as of December 31, 2016).

A sensitivity analysis on interest rates on outstanding balances for the twelve-month periods ended December 31, 2017 and December 31, 2016 shows an incremental change of EUR140 thousand and 210 thousand, respectively, thousand for every 100 percentage points of increase in interest rates, applicable to variable rates and subject to possible negative impacts.

II. INFORMATION ABOUT THE ISSUER

1. PERSONS RESPONSIBLE

1.1 Identification of the persons responsible for the Registration Document

Mr. Carlos Manuel Buesa Arjol, on behalf of ORYZON and in its name, by virtue of the powers expressly vested therein by the Board of Directors of the Company on February 19, 2018, which was executed as a public deed before the Notary Ms. Eloisa López-Monis Gallego on June 4, 2018 and recorded in her notarial book of records under number 1,069.

1.2 Declaration by those responsible for the Registration Document

Mr. Carlos Manuel Buesa Arjol, in use of the representative capacity vested therein, declares that, having taken reasonable care to ensure that such is the case, the information contained in the Registration Document is, to the best of his knowledge, in accordance with the facts and contains no omission likely to affect its import.

2. STATUTORY AUDITORS

2.1. Names and addresses of the issuer's auditors for the period covered by the historical financial information (together with their membership in a professional body)

GRANT THORNTON, S.L.P. ("Grant Thornton"), with a registered office at Avenida Diagonal 615, 08028 Barcelona and Tax Identification Code B-08914830 and registered with the Official Registry of Auditors (*Registro Oficial de Auditores de Cuentas*) (ROAC) under number SO231, has audited the annual financial statements of the Company for the annual periods ended December 31, 2015, 2016 and 2017.

On April 4, 2018, the shareholders acting at the Ordinary General Meeting appointed the company DELOITTE, S.L., with a registered office in Madrid, at Plaza Pablo Ruiz Picasso 1, 28020, Torre Picasso, with Tax Identification Code B-79104469 and registered with the Official Register of Statutory Auditors (ROAC) under number SO692, as statutory auditor of the Company to perform the audit for fiscal years 2018, 2019 and 2020.

2.2. If auditors have resigned, been removed or not been re-appointed during the period covered by the historical financial information, provide details if material

At the Company's General Shareholders' Meeting held on November 3, 2015, the shareholders resolved to appoint GRANT THORNTON, S.L.P. as the external auditors of the Company for the fiscal years 2015, 2016 and 2017. GRANT THORNTON, S.L.P. has not resigned or been removed from its duties during the period covered by the historical financial information referred to in this Registration Document.

3. SELECTED FINANCIAL INFORMATION

3.1. Selected historical financial information regarding the issuer, presented, for each financial year for the period covered by the historical financial information, and any subsequent interim financial period, in the same currency as the financial information

The key figures summarizing the Company's financial situation and its performance during the period covered by the historical financial information are included below. These figures have been obtained from the Company's financial statements for the fiscal years ended December 31, 2017, 2016 and 2015 audited by Grant Thornton.

The information contained in this section should be read together with the financial information included in section 20 of Section II of this document.

Balance Sheet

The table below shows the key figures from the Issuer's balance sheet:

Balance Sheet					
€	**12.31.2017**	**12.31.2016**	**12.31.2015**	***Chg.16/17***	***Chg.15/16***
Intangible assets	22,457,756	18,810,398	15,188,231	*19.4%*	*23.8%*
Other non-current assets	2,455,889	2,458,372	2,862,099	*(0.1)%*	*(14.1)%*
Non-current assets	24,913,645	21,268,770	18,050,330	*17.1%*	*17.8%*
Current assets	36,130,093	28,475,457	22,680,560	*26.9%*	*25.6%*
Total assets	**61,043,737**	**49,744,228**	**40,730,890**	***22.7%***	***22.1%***
Equity	34,432,020	22,728,779	27,592,947	*51.5%*	*(17.6)%*
Non-current liabilities	17,915,474	19,418,941	7,841,016	*(7.7)%*	*147.7%*
Current liabilities	8,696,243	7,596,508	5,296,927	*14.5%*	*43.4%*
Total equity and liabilities	**61,043,737**	**49,744,228**	**40,730,890**	***22.7%***	***22.1%***

Income statement

The table below shows the key figures from the Issuer's income statement:

Income statement					
€	**2017**	**2016**	**2015**	**Chg.FY16/17**	**Chg.FY15/16**
Net revenues	16,764	735,312	4,253,586	*(97.7)%*	*(82.7)%*
(*) Operating income before depreciation, amortization and impairment losses	(3,497,502)	(3,721,243)	687,971	*(6.0)%*	*(640.9)%*
Operating income	(4,324,240)	(4,577,673)	(232,933)	*(5.5)%*	*1.865.2%*
Financial income	(927,961)	(902,159)	(722,018)	*2.9%*	*24.9%*
Profit/(loss) before tax	(5,252,201)	(5,479,832)	(954,951)	*(4.2)%*	*473.8%*
Profit/(loss) for the year	(5,197,159)	(5,448,257)	(991,903)	*(4.6)%*	*449.3%*

(*) The Company presents APMs as indicated in section 26 of Section II of this document.

3.2. Comparative data from the selected financial information for interim periods

Set forth below are the key figures providing a summary view of the financial position of the Company for the interim period ended March 31, 2018, and with respect to which an audit report has not been issued. The information contained in this section should be read together with the financial information included in section 20.6 of Section II of this document.

Balance Sheet

Balance Sheet			
€	**03.31.2018**	**12.31.2017**	***Chg. %***
Intangible assets	24,234,680	22,457,756	*7.9%*
Other non-current assets	2,433,459	2,455,889	*(0.9)%*
Non-current assets	26,668,139	24,913,645	*7.0%*
Current assets	32,352,699	36,130,093	*(10.5)%*
Total assets	**59,020,838**	**61,043,737**	***(3.3)%***
Equity	33,283,560	34,432,020	*(3.3)%*
Non-current liabilities	15,731,550	17,915,474	*(12.2)%*
Current liabilities	10,005,728	8,696,243	*15.1%*
Total equity and liabilities	**59,020,838**	**61,043,737**	***(3.3)%***

Income statement

Income statement			
€	**2018 (3 m)**	**2017 (3 m)**	***Chg. %***
Net revenues	-	16,764	(100.0)%
(*) Operating income before depreciation, amortization and impairment losses	(584,530)	(731,142)	(20.1)%
Operating income	(618,993)	(938,848)	(34.1)%
Financial income	(363,843)	(373,586)	(2.6)%
Profit/(loss) before tax	(982,836)	(1,312,434)	(25.1)%
Profit/(loss) for the year	(1,024,242)	(1,288,490)	(20.5)%

(*) The Company presents APMs as indicated in section 26 of Section II of this document.

4. RISK FACTORS

The information regarding the risks affecting the Issuer is provided in the preceding Section I of this document, relating to Risk Factors.

5. INFORMATION ABOUT THE ISSUER

5.1. History and Development of the Issuer

5.1.1. The legal and commercial name of the issuer

The full corporate name of the Company is ORYZON GENOMICS, S.A.

5.1.2. The place of registration of the issuer and its registration number

The Company is registered in the Commercial Registry of Madrid, in volume 36,553, sheet 133, page M-656,493. Its tax registration number (*número de identificación fiscal*) is A-62291919 and its LEI code is 95980063R15RDF29DK13.

5.1.3. The date of incorporation and the length of life of the issuer, except where indefinite

The Company was incorporated for an indefinite period by Mr. Carlos Manuel Buesa Arjol and Ms. Tamara Maes, by means of an instrument executed in Barcelona on 2 June 2000, before the Notary Mr. Miguel Tarragona Coromina, with the name ORYZON GENOMICS, S.L., and recorded in his notarial record book under number 2,516.

The Company was converted into a corporation by means of an instrument executed on November 20, 2002 before the Notary of Barcelona Mr. José María Costa Torres, and recorded in his notarial record book under number 2,713.

5.1.4. The domicile and legal form of the issuer, the legislation under which the issuer operates, its country of incorporation, and the address and telephone number of its registered office (or principal place of business if different from its registered office)

5.1.4.1. Domicile and legal form

ORYZON is domiciled in the province of Madrid, at Carrera de San Jerónimo, nº 15, 28014. However, it is stated for the record that ORYZON's previous registered office was located at Calle Sant Ferran, nº 74, 08940, Cornellà de Llobregat, Barcelona. The registered office was changed pursuant to a resolution adopted by ORYZON's Board of Directors at its meeting on October 2, 2017, which was registered as a public deed by means of an instrument executed before the Notary of Madrid Mr. Carlos de Prada Guaita on October 4, 2017, and recorded in his notarial record book under number 1,492.

The Company is of Spanish nationality, is of a commercial nature, and has the legal form of a corporation (*sociedad anónima*). Consequently, it is subject to the provisions of the Companies Act (*Ley de Sociedades de Capital*) and other similar legislation, as well as to the regulation specific to its sector of activity.

The telephone contact number for shareholders and investors is: (+34) 93 70 74 100.

E-mail: accionistas@oryzon.com

Website: http://www.oryzon.com

5.1.4.2. Regulatory framework

In accordance with the provisions of article 2 of its Bylaws, the Company may dedicate itself, very broadly, to the following activities:

- The discovery, development and application of genomic, molecular and genetic biomarkers and tools to obtain personalized medical products or acquire modified organisms of pharmaceutical, industrial or agricultural interest.

- The performance of clinical tests in the fields of diagnosis and prognosis in humans or in other organisms of health-related or industrial interest.
- The provision of various scientific research services, such as pharmacological, chemical, biological, industrial, nutritional and other services of interest in human beings, animals and organisms or model systems.
- The development of chemical molecules, peptides, proteins or antibodies with therapeutic applications in humans and other organisms and clinical research into new human therapies.
- Research, investigation, development and discovery of new pharmaceutical products, provision of scientific, technical or business consulting and advice in the area of biotechnology, pharmaceutics and medicine.
- Manufacturing in general of software tools for diagnostic use, of health-related in vitro diagnostic products, and of human health therapeutic products.

Notwithstanding the foregoing, the corporate purpose and aims of the Issuer have focused in recent years, as contemplated in its business plan, on the study, research, development and discovery of new drugs through the development of chemical molecules with therapeutic applications in humans and clinical research in humans for new therapies using these molecules. The Company's scope of activity primarily covers the area of epigenetics in various indications, with special on oncology and neurodegenerative disorders. The Company may selectively rely on alliances with academic institutions and other companies in order to explore the potential of epigenetic drugs for other indications (such as viral or inflammatory disorders).

All these activities are subject to legal regimes that shape and condition the functioning of the Company. The regulatory framework to which the aforementioned activities are subject is listed below.

5.1.4.2.1. Spanish law

- Legislative framework for medicinal products for human use:
    - Law 28/2009 of December 30 amending Law 29/2006 of July 26 on guarantees and rational use of medicinal and healthcare products.
    - Royal Legislative Decree 1/2015 of July 24 approving the revised text of Law 29/2006 of July 26 on guarantees and rational use of medicinal and healthcare products.
    - Correction of errors in Royal Legislative Decree 1/2015 of July 24 approving the revised text of the law on guarantees and rational use of medicinal and healthcare products.
    - Law 10/2013 of July 24 incorporating into the Spanish legal order Directives 2010/84/EU of the European Parliament and of the Council of 15 December 2010 as regards pharmacovigilance, and 2011/62/EU of the European Parliament and of the Council of 8 June 2011 as regards the prevention of the entry into the legal supply chain of falsified medicinal products, and amending Law 29/2006 of 26 July on guarantees and rational use of medicinal and healthcare products.
    - Royal Decree 1345/2007 of October 11 regulating the procedure for authorization, registration and exemption conditions of industrially manufactured medicinal products for human use.

- Royal Decree 686/2013 of September 16 amending Royal Decree 1345/2007 of October 11 regulating the procedure for authorization, registration and exemption conditions of industrially manufactured medicinal products for human use.
- Royal Decree 1091/2010 of September 3 amending Royal Decree 1345/2007 of October 11 regulating the procedure for authorization, registration and exemption conditions of industrially manufactured medicinal products for human use, and Royal Decree 1246/2008 of July 18 regulating the procedure for authorization, registration and pharmacovigilance of industrially manufactured medicinal products for veterinary use.
- Royal Decree 577/2013 of July 26 regulating the pharmacovigilance of medicinal products for human use.
- Royal Decree 782/2013 of October 11 regarding the distribution of medicinal products for human use.

- Legislative framework for clinical studies with medicinal products for human use:
  - Instructions from the Spanish Medicines and Medical Products Agency (*Agencia Española de Medicamentos y Productos Sanitarios*) for performing clinical trials in Spain, version 9, dated February 22, 2018, published on March 19, 2018.
  - Royal Decree 1090/2015 of February 4 regulating clinical studies with medicinal products, Ethical Medicinal Product Research Committees (*Comités de Ética de la Investigación con medicamentos*), and the Spanish Clinical Studies Registry (*Registro Español de Estudios Clínicos*).
  - Royal Decree 824/2010 of June 25 regulating pharmaceutical laboratories, manufacturers of active pharmaceutical ingredients and foreign trade in medicinal products and investigational medicinal products, amended by the First Final Provision of Royal Decree 782/2013 of October 11 regarding the distribution of medicinal products for human use.
  - Order SCO/362/2008 of February 4, 2008 amending Order SCO/256/2007 establishing principles and detailed guidelines for GCP and the requirements to authorize the manufacture or importation of investigational medicinal products for human use.
  - Resolution of October 16, 2009 of the Undersecretary authorizing the submission by means of electronic registration by the department of specified documents, notifications and requests relating to clinical studies with medicinal products addressed to Ethical Clinical Research Committees (*Comités Éticos de Investigación Clínica*) or to the Spanish Medicines and Medical Products Agency (*Agencia Española de Medicamentos y Productos Sanitarios*).
  - Annex VIIIC: Instructions for updating the Personal Data Protection section of the subject information sheet *(SIS/IC)* pursuant to General Data Protection Regulation (EU) No. 2016/679, version of May 16, 2018 (published on May 21, 2018).
- Other applicable legal provisions:
  - Basic Law 41/2002 of November 14 on the autonomy of the patient.

- Law 14/2007 of July 3 on biomedical research.
- Law 9/2003 of April 25 establishing the legal regime for the restricted use, voluntary release and commercialization of genetically modified organisms.

5.1.4.2.2. European law

- Directive 2005/28/EC laying down principles and detailed guidelines for good clinical practice as regards investigational medicinal products for human use, as well as the requirements for authorisation of the manufacturing or importation of such products (transposed into Spanish law by Order SCO 256/2007 of February 5, amended by Order SCO/362/2008 of February 4).
- Declaration of Helsinki-Fortaleza, Brazil, October 2013; Oviedo Convention of April 4, 1997 on human rights and biomedicine, ratified in the Official State Gazette (*BOE*) on October 20, 1999; Belmont Report of April 18, 1979 on ethical principles and guidelines for the protection of human subjects of research; and the Nuremberg Code (1946).
- Directive 2004/27/EC, transposed into Spanish law by Royal Decree 1345/2007 of October 11 regulating the authorization, registration and dispensing of medicinal products for human use.
- Directive 2010/84/EU of the European Parliament and of the Council of 15 December 2010 amending, as regards pharmacovigilance, Directive 2001/83/EC on the Community code relating to medicinal products for human use.
- Directive 2012/26/EU of the European Parliament and of the Council of 25 October 2012 amending Directive 2001/83/EC as regards pharmacovigilance.
- Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency.
- Regulation (EU) No 1027/2012 of the European Parliament and of the Council of 25 October 2012 amending Regulation (EC) No 726/2004 as regards pharmacovigilance.
- Regulation (EU) No 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC (General Data Protection Regulation).

- Legal provisions relating to orphan medicinal products or clinical studies with children:
  - Regulation (EC) No 141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products.
  - Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for pediatric use and amending Regulation (EEC) No 1768/92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) No. 726/2004.
  - Regulation (EC) No 1902/2006 of the European Parliament and of the Council of 20 December 2006 amending Regulation (EC) No 1901/2006 on medicinal products for paediatric use.

- Regulation (EC) No 1394/2007 of the European Parliament and of the Council of 13 November 2007 on advanced therapy medicinal products and amending Directive 2001/83/EC and Regulation (EC) No 726/2004.

- Regulations on clinical studies in Europe:

  - Regulation (EU) No. 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC (Text with EEA relevance).
  - Correction of errors in Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC.
  - Commission Implementing Regulation (EU) 2015/292 of 24 February 2015 approving carbon dioxide as an active substance for use in biocidal products for product-type 15 (Text with EEA relevance).

- The directives and regulations for issues such as pharmacovigilance that affect both pre-commercialization (clinical studies) and post-commercialization are:

  - Regulation (EU) No 1235/2010 of the European Parliament and of the Council of 15 December 2010 amending, as regards pharmacovigilance of medicinal products for human use, Regulation (EC) No 726/2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency, and Regulation (EC) No 1394/2007 on advanced therapy medicinal products.
  - Commission Implementing Regulation No 520/2012 of 19 June 2012 on the performance of pharmacovigilance activities provided for in Regulation (EC) No. 726/2004 of the European Parliament and of the Council and Directive 2001/83/EC of the European Parliament and of the Council.

5.1.4.2.3. US law

- The Federal Food, Drug, and Cosmetic Act (Chapter V and others) and subsequent amending statutes, codified into Title 21, Chapter 9 of the United States Code and Chapter 1 (Food and Drug Administration, Department of Health and Human Services), Subchapter A (General).
- Food and Drug Administration Amendments Act of 2007.
- The Food and Drug Administration Safety and Innovation Act (FDASIA).

5.1.5. **The important events in the development of the issuer's business**

5.1.5.1. ORYZON from 2000 to 2008

The Company was initially created as a company based on a genomics platform, with the mission of identifying genetic biomarkers and proteins with agricultural, industrial or medical uses. This identification of biomarkers was (and is currently) carried out through a technological platform based on genomics, proteomics and bioinformatics. The horizontal nature of this platform allows the Company to carry out selective service programs in other fields and to advance in its own programs. For this reason, there were basically two (2) keys to the Company's revenue generation during the 2000–2008 period:

- Revenues from external R&D and diagnostic services for the pharmaceutical and agricultural industries or from activities directly commercializing the portfolio of diagnostic products; and
- Development and commercialization (direct or indirect via license) of proprietary diagnostic and prognostic products and solutions for oncological and neurodegenerative disorders.

At the financial level, ORYZON obtained its first financial resources through rounds of financing covered by private investors in 2001 and 2002. At the beginning of 2003, a venture capital company (NAJETI CAPITAL, S.C.R., S.A., now NAJETI CAPITAL, S.A.) invested in the Company, which investment permitted the financing of the first qualitative leap forward by ORYZON. Along these lines, by means of a capital increase, NAJETI CAPITAL, S.C.R., S.A. acquired shares representing 28% of the share capital of ORYZON for the amount of EUR 800,043.90. At the date of registration of this document, NAJETI CAPITAL, S.A. holds no interest in the share capital of ORYZON. Furthermore, in 2006, pursuant to the capital increase approved by the shareholders at a General Shareholders' Meeting of ORYZON held on June 15, 2006, GRUPO FERRER INTERNACIONAL, S.A. acquired a 3.93% minority shareholding in ORYZON for the amount of EUR 600,052.92. At present, GRUPO FERRER INTERNACIONAL, S.A. holds no interest in the share capital of ORYZON.

From the outset, the Company had solid growth in collaborations at the national and international level, participating in various consortia and even leading projects at the European level.

During that period, ORYZON participated in various CENITs, which involved, depending on the focus of the consortium, the strengthening of the Company's technological capacities while obtaining resources and covering a part of the internal R&D activities carried out by the Company through grants. Of particular note in the first area are the Oncnosis Project (with a budget of EUR 6 million during the 2006–2009 period) and the I+DEA project (which generated EUR 2.1 million in grants during the 2007–2010 period).

5.1.5.2. ORYZON from 2008 to 2014

At the end of 2008, the objective was established of transforming the Company into a biotechnology company aimed at developing proprietary products, with a significant reduction in the provision of services to third parties.

The Company obtained new financial resources for this purpose. Thus, a round of equity financing was closed in 2008, in three (3) tranches, with a share premium, in the total amount of EUR 8,612,736, which, together with additional financial indebtedness, gave it the resources needed to Implement the 2008–2013 strategic plan.

Pursuant to the capital increase approved by the shareholders at a General Shareholders' Meeting of ORYZON held on November 5, 2007, the principal investors acquiring a shareholding in such round of financing were:

- CORPORACIÓN SANT BERNAT, S.L. acquired a 5% minority shareholding in ORYZON for the amount of EUR 2,410,637. CORPORACIÓN SANT BERNAT, S.L. currently holds no interest in the share capital of ORYZON.
- INVERSIONES COSTEX, S.L. acquired a 5% minority shareholding in ORYZON for the amount of EUR 2,410,637. The stake in ORYZON's share capital that was held by INVERSIONES COSTEX, S.L. is now held by ARRIENDOS VENFERCA, S.L. due to the total split-off of the former company, pursuant to which it transferred various assets

to ARRIENDOS VENFERCA, S.L. by universal succession, including ownership of the shares of ORYZON. ARRIENDOS VENFERCA, S.L. currently holds 5.87% of ORYZON's share capital.

- NAJETI CAPITAL, S.A. acquired an additional shareholding of 3.78% in ORYZON for the amount of EUR 1,824,522. At the date of registration of this document, NAJETI CAPITAL, S.A. holds no interest in the share capital of ORYZON.

Twenty-four (24) minority investors, representing a total of 4.08% of the Company's share capital on the date of said increase, acquired the remaining shares for the amount of EUR 1,966,940.

Along the same lines, the financial needs involved in implementing the Company's strategic plan were supplemented through public programs for financing innovation, which contributed to advancing the development of the Company's own products without diluting the shareholders.

Of note in this regard are the MIND project, which generated EUR 2.5 million of direct grants (2008–2011) for the Company's epigenetic program, the DENDRIA project, which generated EUR 2.5 million of direct grants (2010–2014) focused on disorders affecting the nervous system, as well as the ONCOLOGICA project. On completing the CENIT programs, the Company used various calls within the INNPACTO program to strengthen its internal R&D, including the HumanFarma and PolyFarma projects, with a budget of EUR 750,000 for each one distributed between 2012 and 2014.

The business plan approved in 2008 extended the utilities of the biomarker search program from diagnostic to therapeutic applications, a field with enormous economic potential as is shown by the appetite of the pharmaceutical market for novel small chemical compounds. To do so, ORYZON created a Medicinal Chemistry department to develop small-drug therapeutic programs in 2008. Since then, the Company has developed more than one thousand seven hundred (1,700) new drugs, protected by numerous patents.

Additionally, in 2009 ORYZON acquired CRYSTAX, a biotechnology company with nine (9) scientists dedicated to developing anti-cancer drugs. CRYSTAX also had a platform for structural genomics, crystallography and NMR-fragment screening, which strategically complemented that of ORYZON.

With respect to facilities, in 2009 the Company moved to the Parc Cientific in Barcelona, to a new corporate building in Cornellà de Llobregat, where it can perform all of its R&D, commercial and corporate activities in an integrated manner. The building was obtained by way of a long-term lease.

The implementation of the 2008–2013 business plan, on which basis the value proposal for that period was prepared, included the following events:

- Commercialization of one (1) or two (2) molecular diagnostic products within four (4) years. In this respect, it is important to note that the Company successfully developed its first proprietary product in the diagnostic field: GynEC-Dx.
- Development of at least one (1) proprietary drug prior to Phase I of clinical development, and another one during the pre-clinical regulatory phase (development candidate phase). The Company sought to license at least one drug from its pipeline.
- The Company committed to a model of collaborations with pharmaceutical companies that would establish the value of the programs and reduce their financial risk.

5.1.5.3. ORYZON today

In 2013, ORYZON met its proposed objectives, bringing to market its first diagnostic product GynEC-Dx, which it had co-developed with Laboratorios Reig Jofré. This product, the technical portion of which was developed by ORYZON, has a negative predictive value of 99.6% when applied in conjunction with biopsy, and represents a technological milestone due to its robustness, as was shown in its multicenter clinical study covering eleven (11) hospitals and almost five hundred (500) patients. The need to position the Company as an international leader in the field of therapy in epigenetic targets, and the weak purchasing power of Spanish hospitals during the toughest period of the crisis (2010–2013), led the Company to divest its diagnostics activity, selling 75.01% of its interest in OGDSL for EUR 1,187,500 to a group of investors led by INVEREADY CAPITAL COMPANY, S.L. (which held a 43.98% interest in the consortium) and REIG JOFRÉ INVESTMENTS, S.L. (which held a 24.99% interest in the consortium), with the Company retaining an interest corresponding to the remaining 24.99%, until the final divestment of what at that time was a non-strategic investment classified as a simple available-for-sale financial interest, through the transfer of its interest to LABORATORIO REIG JOFRÉ, S.A. on May 30, 2016 for the amount of EUR 150,000. ORYZON generated capital gains in the amount of EUR 792,842.81.

In the same way in which the Company decided to abandon its diagnostics activities and become a business focused on drug development, as a result of interaction with the investment community and dialogue with other pharmaceutical companies and the need to optimize its financial and human resources, ORYZON also decided to abandon its activities in the development of monoclonal antibodies, so as to focus all of its efforts on becoming a recognized international leader in the development of small epigenetic drugs, which is the core of ORYZON's current activity. The Company rejects any projects that do not form part of its core business of epigenetics in cancer and neurodegenerative disorders, discontinuing investments in such projects as a strategic decision, with the resulting disappearance of the possibility of obtaining a cash flow return that justifies the book value of the intangibles.

In 2013, the Company successfully developed its first antitumor drug (ORY-1001) for the treatment of acute leukemia. In August 2013 the EMA granted ORYZON the "orphan drug" designation (issued to products for life-threatening or chronically debilitating conditions affecting no more than five (5) people in ten thousand (10,000) in the EU or which usually receive incentives to justify the necessary investment, and for which there is no satisfactory alternative method; or, if there is, the proposed treatment would be of significant benefit) for ORY-1001 for the treatment of AML. In December 2013 the Company received approval from the Spanish Medicines and Medical Products Agency *(AEMPS)* for a clinical study of ORY-1001, and in January 2014 the Company obtained approval from the MHRA for a clinical trial of ORY-1001 in the United Kingdom.

In January 2014, the Phase I multicenter trial was initiated, and in March the Company entered into a license agreement with Roche, effective April 1, 2014, for two (2) patent families that provided initial income of USD 21 million (EUR 15,983,863.64), received in two (2) tranches: the first as an initial payment of USD 17 million (EUR 12,347,500) when the Agreement was signed (received in the first half of 2014) and the second dependent on reaching the clinical milestone consisting of determining the recommended dose in Phase I, which was achieved in June 2015 and resulted in receipt of the remaining USD 4 million (EUR 3,636,363.64) in July 2015. The License Agreement signed in April 2014 also included an agreement under which joint development funded by Roche was to be conducted over a period of at least two (2) years, pursuant to which ORYZON received financial compensation for assigning researchers from the Company, or third parties subcontracted by the Company, to the development project. On July 19, 2017 Roche notified the Company that due to a strategic reprioritization of its portfolio it

had decided to discontinue the clinical development of the experimental drug ORY-1001 that it had begun under the terms of the License Agreement entered into by the two Companies on April 1, 2014. As a result of this decision, the development and commercialization rights licensed to Roche were recovered by ORYZON in January 2018 under the terms of the Agreement, at no cost to the Company and without creating current obligations arising from past events that would have entailed liabilities or contingencies for the Company. The payments received by the Company while the Agreement was in effect are not refundable and will remain in the Company's possession.

Additionally, in order to confront the period of crisis in the Spanish economy and the reduction in state and regional aid, ORYZON has increased its capacity to develop experimental drugs by obtaining international funds. In this regard, the Company has participated or is participating in various international projects: (i) ORYZON led the European FP6 INDABIP project focused on Parkinson's disease; and (ii) participated in the DDPDGENES Project, also focused on Parkinson's disease, with Cambridge University, the Karolinska Institute in Stockholm, the Inbiomed institute in San Sebastian and the Swiss Federal Institute of Technology in Lausanne. Moreover, ORYZON led two (2) European EUROSTARS programs, one in cancer (the EPILETH Project, focused on leukemias) and another in epigenetic applications for cancer and the CNS (the EMTherapy Project). In 2010, the Company received reimbursable support in the amount of USD 300,000 in two (2) tranches from the ADDF, and additional reimbursable support from this foundation in 2015 in the amount of USD 270,000, also in two (2) tranches, to accelerate the pre-clinical development of the experimental drug ORY-2001. The right to reimbursement of the support entailed by these two loans was fulfilled by means of the exercise of a right to acquire the Company's own shares.

In 2015, the Ministry of Economy and Competitiveness, with the participation of the EU (FEDER Funds), gave the Company two (2) multi-year subsidies within the framework of the RETOS Collaboration 2015 program in the amount of approximately EUR 1.2 million, in the form of reduced-rate loans. These loans were given to promote the development of the Company's epigenetic inhibitors against neurodegenerative and oncological disorders. The two (2) loans covered the funding of two (2) projects that were being led by ORYZON in collaboration with various public and private institutions. Both projects had a term of thirty-four (34) months from March 1, 2015, and ended on December 31, 2017. The loans had a fixed interest rate of 0.329% and the period for repayment of the loans is ten (10) years, with a grace period of three (3) years. Additionally, the public institutions collaborating on these projects received funds to cover all the costs of their experimental research in the form of a non-refundable grant. The first loan was for the project called "*Evaluation of the efficacy of epigenetic inhibitors in experimental models of human pathologies,*" which was performed in collaboration with the Autonomous University of Barcelona and the Bosch i Gimpera Foundation. The overall budget was EUR 990,000 and was focused on further investigation of the role of ORY-2001 and other compounds in various neurological disorders, such as Huntington's disease.

The second loan was utilized to fund the project entitled "*Discovery and combination of new therapies for the treatment of cancer based on the modulation of epigenetic targets and adenosine receptors*." The participants for this project included ORYZON, PALO BIOPHARMA, the University of Santiago de Compostela, and Leitat Technological Center, all located in Spain. This program had a budget of nearly EUR 1.5 million. The project was dedicated to exploring the role of new inhibitors aimed at epigenetic targets other than LSD1 in oncological indications.

The Company was also granted funding in 2016 for an additional project of the Ministry of Economy (Secretariat of State for Research, Development and Innovation) of the Government of Spain within the "RETOS INFLAM" program in the total amount of EUR 742,861.90 at 0.06%

interest for 10 years, with a grace period of three (3) years, to be received during the period between 2016 and 2018.

In 2017, the ADDF granted and disbursed repayable aid to the Company in the amount of USD 300,000, awarded in one (1) tranche, for the development of biomarkers useful in clinical studies of ORY-2001. The right to reimbursement of the aid was fulfilled through the exercise of a right to acquire the Company's own shares.

In 2018, the Center for the Development of Industrial Technology (*Centro para el Desarrollo Tecnológico Industrial*) awarded the Company, through its R&D project development program, partially repayable aid with a total value of EUR 1,465,536 for the development of ORY-2001 for the treatment of multiple sclerosis. This aid consists of: (i) one non-repayable tranche of 30%, provided that all obligations arising from this or any other contract are fulfilled beforehand and that this fulfillment is confirmed by the Center for the Development of Industrial Technology (*Centro para el Desarrollo Tecnológico Industrial*); and (ii) another tranche, which is repayable at an interest rate of 0.00% over ten (10) years, with a grace period of four (4) years.

The Company is currently centering its efforts around the clinical development of experimental drugs in epigenetics, focused on:

(i) The field of oncological diseases and, in particular, the drug ORY-1001, especially in the area of solid tumors such as SCLC and myeloid leukemia. In 2018 ORYZON recovered the development and commercialization rights to this drug. These rights had been licensed to Roche in April 2014, but Roche decided to discontinue the license for internal reasons associated with the reprioritization of its pipeline. Regarding these rights, ORYZON plans to continue clinical development of the drug. The Phase IIa clinical study on AML (ALICE) and the Phase IIa clinical trial on SCLC (CLEPSIDRA) are expected to begin with respect to this drug within the next few months:

- ALICE (An AML trial with LSD1i in Combination with azacitidine in the Elderly): a Phase IIa pilot study for dose-finding and to evaluate the safety, tolerability and efficacy of ORY-1001 in combination with azacitidine in first-line therapy in elderly patients with AML who are not eligible for intensive chemotherapy.
- For SCLC the Company plans soon to begin CLEPSIDRA (A Combination trial of LSD1 and Etop-Platinum in relapsed Small Cell Lung Cancer Patients), a Phase IIa pilot study for dose-finding and to evaluate the safety, tolerability and efficacy of ORY-1001 in combination with cisplatin-etoposide, in which the Company intends to introduce the use of biomarkers that it has identified

In March 2018, scientists from the Company published an article on the role of ORY-1001 in AML in the prestigious journal *Cancer Cell* (T. Maes et al., *Cancer Cell*, 2018, 33(3):495-511). The article was the subject of an editorial comment, a practice which is reserved for articles deemed to be of special importance in each monthly issue of *Cancer Cell* (https://www.cell.com/cancer-cell/fulltext/S1535-6108(18)30023-0 and https://doi.org/10.1016/j.ccell.2018.02.002)

(ii) Development of ORY-2001, a dual LSD1 and MAO-B inhibitor for the treatment of multiple sclerosis and AD.

In a recent Phase I study conducted on one hundred and six (106) healthy volunteers, the drug proved to be safe and well tolerated under the conditions of the study. There were no adverse events related to the drug, nor were there significant side effects or any detectable clinical changes. It should be noted that no hematopoietic effects were observed for the doses in the multiple-dose phase. Brain penetrance was measured

in eighteen (18) volunteers and inhibition of the brain enzyme LSD1 was determined separately.

The Company is currently conducting a Phase IIa clinical trial of ORY-2001 in patients with multiple sclerosis. The study, named SATEEN, is being conducted in nine (9) different Spanish hospitals and is designed as a thirty-six (36) week randomized, double-blind, placebo-controlled, three-arm (3) parallel-group study to evaluate the safety and tolerability of ORY-2001 in patients with RRMS and SPMS. The first patient was recruited in January of this year.

In addition to the Phase IIa trial in multiple sclerosis, the Company has begun a Phase IIa trial of ORY-2001 in patients with AD, after receiving approval from Spanish, French and British regulatory authorities.

ORY-2001 is a small oral drug that acts as a highly selective dual inhibitor of LSD1-MAO-B. The Company recently gave presentations at various scientific conferences describing how ORY-2001 has a holistic effect on the various types of pathological changes that are also observed in patients with AD and other neurodegenerative diseases. In patients with AD and other neurodegenerative diseases, cognitive decline is often accompanied by episodes of agitation, psychosis, apathy and depression. Various experiments suggest that ORY-2001 acts as a disease-modifying drug. In pre-clinical studies, ORY-2001 not only restores memory but also reduces the exacerbated aggressiveness of SAMP8 mice to normal levels, in addition to reducing social avoidance in models of rats kept in isolation, and increasing sociability in three (3)-compartment studies conducted on mice. ORY-2001 also exhibits a very fast, powerful and lasting anti-inflammatory and neuroprotective effect in various preclinical multiple sclerosis models.

The study, called ETHERAL (Epigenetic THERapy in ALzheimer's Disease), will be conducted in various Spanish, British and French hospitals and is designed as a twenty-six (26) week randomized, double-blind, controlled study with three (3) parallel arms, one (1) with a placebo and two (2) with active doses, to evaluate the safety and tolerability of ORY-2001 in patients with mild-to-moderate-stage AD. The study will recruit ninety (90) patients and will also include, as secondary objectives, the various dimensions manifested by patients with this disease, not only in terms of memory evolution but also changes in behavior, such as aggression and social disconnection. The study will also measure the levels of various biomarkers in the cerebrospinal fluid. The Company expects to launch a twin study in the USA in the coming months.

(iii) Development of the preclinical candidate ORY-3001 for diseases that have not yet been disclosed, for which ORYZON presented pre-clinical data in December 2017 on its effectiveness in sickle-cell anemia at the American Society of Hematology Meeting held in Atlanta (Georgia, USA). Dr. Donald Lavelle, of the School of Medicine of the University of Illinois (Chicago, USA), who leads the collaboration with ORYZON, gave an oral presentation entitled "*Oral Administration of the LSD1 Inhibitor OG-S1335 Increases Fetal Hemoglobin in Humanized Transgenic Sickle Cell Disease Mice and in Baboons*."

Sickle-cell anemia is a genetic disease in which the adult hemoglobin gene is defective and abnormally shaped red blood cells are produced. The cells are sickle-shaped and do not function as well as normal ones, leading to anemia and obstructing blood vessels, thereby causing mini-strokes. This leads to tissue oxygen deprivation, causing inflammatory crises, acute pain and organic lesions. Professor Lavelle presented data

confirming that inhibition of LSD1 leads to the disinhibition of unmutated fetal hemoglobin genes which can replace the function of defective adult genes, improving clinical features. Administration of ORY-3001 increases fetal hemoglobin by a factor of up to ten (10) in humanized transgenic sickle-cell mice and increases levels of fetal reticulocytes (-F) by up to 300%, compensating for the anemia. In baboons, increased levels of F-reticulocytes are up to eight (8) times higher than baseline levels. These findings and other data confirm that the inhibition of LSD1 with ORYZON's drugs is a promising alternative for the treatment of sickle-cell anemia.

In 2014 sickle-cell anemia affected roughly one hundred and fifty thousand (150,000) people in the USA and there is no cure for it – only palliative treatments. In 1994, estimated median survival in the USA in 1994 was forty-two (42) years for men and forty-eight (48) years for women. The average cost per pediatric patient is USD 15,000 annually. From 1989 to 1993, an average of 75,000 hospital admissions associated with the disease were recorded in the USA, with an approximate total cost of USD 475 million.

(iv) Development of its earliest programs for other epigenetic targets.

(v) Internationalization in the USA, with the aim of making the Company a global leader for epigenetic drugs.

5.2. Investments

5.2.1. A description (including the amount) of the issuer's principal investments for each financial year for the period covered by the historical financial information up to the date of the registration document

ORYZON has high-level and technologically advanced equipment that was integrated during 2009 and 2010, for which reason significant additional investments have not been required for this item, nor have significant new short- or medium-term investments been deemed necessary.

The Company has principally focused its investments on the area of intangible assets, mainly in development.

Investments in development from January 1, 2015 through December 31, 2017 and through March 31, 2018 totaled EUR 11,505,554 and 13,284,173, respectively.

The distribution of capitalized investments in development, broken down for the period between January 1, 2015 and March 31, 2018, is shown for the following lines of development:

Capitalized investments in development				
€	**03.31. 2018**	**03.31.2017**	**03.31.2016**	**03.31.2015**
Neurodegenerative Epigenetics	827,339	2,486,689	2,855,761	2,077,694
New Epigenetic Therapies	694,868	1,644,435	1,418,301	853,323
New oncological Epigenetic Therapies	256,412	169,351	-	-
Total	**1,778,619**	**4,300,475**	**4,274,062**	**2,931,017**

In turn, the Company divested its molecular diagnostics activities in 2013 and decided not to continue research into monoclonal antibodies so as to optimize its resources in the area of epigenetics. There were no impairments or decreases December 31, 2017, at December 31, 2016 or at December 31, 2015.

Furthermore, the audited change in development costs capitalized in 2017 is shown in the following table:

Lines of development	Net balance 12.31.2016	Increases	Transfers / Decreases	Impairment	Depreciation	Net balance 12.31.2017
€						
Neurodegenerative Epigenetics	13,869,429	2,486,689	-	-	-	16,356,118
Oncological Epigenetics	657,400	-	-	-	(657,400)	-
New Epigenetic Therapies	4,259,300	1,644,435	-	-	-	5,903,735
Monoclonal antibodies	-	169,351	-	-	-	169,351
Total	**18,786,129**	**4,300,475**	**-**	**-**	**(657,400)**	**22,429,203**

These investments are financed through loans provided by credit institutions, grants from public agencies and the capital increases described in section 10.1.1.1 of Section II of this document.

5.2.2. A description of the issuer's principal investments that are currently in progress, including the distribution of these investments geographically (home and abroad) and the method of financing (internal or external)

The Company's principal investments in progress are focused on capitalizing its development costs. These investments are located in Spain. Total capitalized development costs between January 1 and March 31, 2018 amounted to EUR 1,778,619, of which EUR 827,339 was invested in the Neurodegenerative Epigenetics line of research, EUR 694,868 in New Epigenetic Therapies and EUR 256,412 in New Oncological Epigenetic Therapies.

5.2.3. Information concerning the issuer's principal future investments on which its management bodies have already made firm commitments

The Issuer's Board of Directors has not made firm commitments as to future investment in tangible or intangible assets (rights to license third-party patents). The Issuer's only future investments are the capitalization of the costs incurred in development programs in oncology, neurodegenerative disorders and other undisclosed therapies, which represent its main activity, and with respect to which there may be service agreements may be signed with subcontracted third parties such as hospitals, CROs and other providers, amounting to approximately EUR 2,700,000, for which the conditions for accrual and recognition in the Company's financial statements had not yet been fulfilled as of March 31, 2018, and approximately 97% of which correspond to commitments entered into in relation to Phase II of ORY-2001 and 3% to other R&D programs.

6. BUSINESS OVERVIEW

6.1. Principal activities

6.1.1. A description of, and key factors relating to, the nature of the issuer's operations and its principal activities, stating the main categories of products sold and/or services performed for each financial year for the period covered by the historical financial information

6.1.1.1. The biopharmaceutical sector and its value chain

ORYZON develops experimental pharmaceuticals for indications where there is a great need for medical research, such as cancer and neurodegenerative disorders.

The development of pharmaceuticals is a process heavily regulated by national and international agencies. It is a time-consuming research process and requires increasing investments. After performing the pertinent pre-clinical studies, a CTA in Europe or an IND in the USA must be made in order to begin clinical studies. The waiting period for the IND, once submitted and after its approval by the FDA, is approximately thirty (30) days, while in Europe this period rises to approximately sixty (60) days. In turn, the CTA may be requested from the EMA, which is the route for a subsequent centralized registration, or from the corresponding national regulatory agencies (the AEMPS in Spain). After approval by the relevant agency or agencies, the pharmaceutical company may begin to test the drug on humans, commencing the clinical research phase consisting of the following clinical trial phases:

- Phase I clinical trial: During this phase, the new medicinal product is usually administered to twenty to eighty (20–80) healthy subjects (volunteers) in carefully increasing doses so as to study its safety and tolerability, determine its pharmacokinetics and, if possible and on a preliminary basis, measure its activity. This process takes around one (1) and a half or even two (2) years and, if successful, will lead to Phase II clinical trials. In the case of cancer or other life-threatening diseases without effective treatments, Phase I may be performed directly on patients.

- Phase II clinical trial: During Phase II trials, the drug is usually administered to one hundred to three hundred (100–300) subjects who are suffering from the disease under study. The fundamental goal of this phase is to determine the appropriate doses and guidelines for patient treatment and to make an initial evaluation of efficacy. This phase normally takes around two to three (2-3) years depending on the studies and the lack of alternative therapies.

- Phase III clinical trial: In this phase, in which the safety and efficacy of the drug are evaluated, the patient population for inclusion in the trial will usually consist of one thousand to three thousand (1,000-3,000) patients who are suffering from the specific disease. Normally it is performed at different healthcare centers and in different countries to ensure different populations. In rare diseases, the number of patients to be included in the trial can be substantially lower. The physician-researchers carry out intensive monitoring of their patients in order to identify possible adverse effects and to determine whether there are other side effects not previously described. This phase will statistically and scientifically confirm whether the medicinal product is effective and safe and is normally performed over two (2) to three (3) years. For a new drug, it will be sufficient to demonstrate its efficacy and safety, while a drug that is aimed at diseases for which patients are already being treated with other pre-existing drugs must be proven to be more effective and equally safe or safer.

Following the successful completion of the three (3) clinical trial phases described above, the drug dossier will be ready for approval to be requested from the relevant agency or agencies, for which purpose the company must submit a New Drug Application to the FDA or a Marketing Authorisation Application (MAA) in Europe, and must clearly demonstrate the efficacy and safety of the drug in such dossier, providing all of the scientific information relating to the product starting from the synthesis thereof. Although the harmonization process has recently been accelerated, both within the EU and between the EU and the USA, authorization from the regulatory agencies may take between six (6) months and one (1) year. In the EU, the process for establishing prices then begins at the national level.

Once the regulatory procedures have been completed and with the approval of the responsible agencies (FDA, EMA or national agencies), the medicinal product is made available to doctors for prescription to patients. However, the Company remains responsible for making periodic safety or pharmacovigilance reports to the FDA/EMA or other corresponding agencies. These reports will communicate the possible unknown side effects that may arise after approval and that only become apparent as the number of treatments increases significantly.

For some medicinal products, the FDA/EMA requires additional post-approval studies. These are known as Phase IV clinical trials and are used to obtain more data on long-term safety and efficacy.

International estimates state that the cost of developing a drug can vary from USD 150 million to USD 250–300 million. Adding to the successfully developed drugs the cost of the failed projects would considerably increase the required levels of investment. For this reason, the pharmaceutical and biotechnology sector has been organized in a complementary manner. Only a few companies with significant technological and financial strength are capable of covering the whole value chain and are fully vertically integrated; they are often very large multinational companies.

Despite the enormous investments that the sector makes in R&D, both internally and externally (purchasing programs and products or even companies), the sector is one of the most profitable in the world economy and is the best-performing sector in times of crisis, as it is considered to be acyclical to a certain degree.

A significant part of the sector positions itself in a specific segment of the value chain, ultimately operating on a business-to-business basis, where experimental medicinal products are developed to a certain level and are made available commercially, through license agreements, to very large multinational companies that are capable of completing the development and bringing the product to market. These agreements allow the exercise of the rights of exploitation of the drug and the patents that protect it in different medical indications and territories.

License agreements and their commercial terms vary very widely, and they may contain joint sales clauses where the licensor reserves a share of the market for itself or else transfers all of the commercial rights to the licensee.

Typically, the agreements call for certain payments upon the signing of the agreement (up-front payments), payments as the drug passes certain types of development and sales-based milestones, and royalties for net sales of the drug once it has been commercialized. The agreements become progressively larger in financial size and in terms of the rights for the licensor as the project develops further and therefore poses a lower technical risk.

Biotechnology and biopharmaceutical companies such as ORYZON typically develop their experimental drugs to Phase I or even to Phase II, in which the safety of the drug is demonstrated

in patient populations and the first signs of efficacy are established. This stage of development is the suitable one for licensing due to the relationship between value capture and the necessary investment.

Phase II or "proof of concept" trials are conducted in a sufficiently large group of patients (between one hundred (100) and three hundred (300)) with a particular disease in order to confirm the optimal dose, explore the therapeutic effect, and continue obtaining information on the safety of the drug explored in Phase I. These trials can be divided into Phase IIa, when their main objective is to determine the dose and the therapeutic guidelines, and Phase IIb trials, when their main objective is to assess the preliminary efficacy of the investigational drug. However, there is really no formal or regulatory definition for these two subcategories.

6.1.1.2. Epigenetics

ORYZON is focused on epigenetic targets. These targets are proteins, enzymes and chromatin modulators, which involve the way in which chromosomes are spatially organized.

Epigenetic enzymes add (write), erase (delete) or interpret (read) the presence or absence of small chemical signals in the histones, which are the proteins that function as the structure of the chromosome and around which DNA fibers are coiled. As a consequence of these changes, specific regions of the chromosome move from an active to an inactive state and vice versa, and permit the expression of all the genes located in that chromosome region. The aberrant functioning of this regulation in the activation of the chromatin is the basis of many diseases.

Among the aforementioned chemical signals is the addition or elimination of acetyl groups, of methyl groups, of phosphate groups, and so forth. Each one of these modifications may involve one or more of the different histones that constitute the chromatin and do so by affecting a variety of the different amino acids, such as lysines, arginines and serines, among others. These responses may be carried out by different enzymes, which in turn are differentiated therapeutic targets.

The potential of drugs that interfere with the processes of acetylation and deacetylation has been under exploration for a number of years. The inhibitors of HDAC enzymes are, therefore, an expression of “first-generation” epigenetics. The difficulty of developing sufficiently selective drugs has been an obstacle to the progress of these drugs. This is not the case for “second-generation” epigenetics, where it has been possible to develop highly selective drugs directed against KDMs, histone methyltransferases or various “reader” drugs, such as bromodomain and extra-terminal inhibitors.

ORYZON began its epigenetic drug development activities in 2009, and today stands out in this field because of its number of patents and also because it was the first company to enter clinical phases with a drug directed against a KDM (eraser drugs), which are pharmacological targets that have aroused great interest in the industry due to their potential for engaging in the selective treatment of certain types of cancers.

The Company currently has a program of LSD1 inhibitors.

In the field of oncological diseases and, in particular, regarding the drug ORY-1001, for the treatment of solid tumors such as SCLC and myeloid leukemia, in January 2018 ORYZON recovered the rights to the development and commercial sale of this drug, which rights had been licensed to Roche in April 2014 and which that company decided to discontinue for internal reasons involving the reprioritization of its pipeline. ORYZON is continuing the clinical development of this drug.

In the development of ORY-2001, for the treatment of neurodegenerative diseases, the Company is currently conducting separate Phase IIa clinical trials on patients with multiple sclerosis and on patients with AD.

The first study, called SATEEN, is currently being conducted in nine (9) different Spanish hospitals, and is designed as a randomized double-blind placebo-controlled study with three (3) arms and over thirty-six (36) weeks on parallel groups in order to evaluate the safety and tolerability of ORY-2001 in patients with RRMS and SPMS. The first patient was recruited in January 2018, and as of the date of registration of this document several patients had been recruited.

The second study (ETHERAL), which is also a Phase IIa trial within the context of the clinical development of ORY-2001, is aimed at the treatment of patients with AD in the mild or moderate stage. In April 2018 ETHERAL received approval from the AEMPS and in May 2018 approval from the ANSM and the MHRA. The Company also announced the enrollment of the first patients in the study in May 2018.

ETHERAL is designed as a randomized double-blind controlled study with three (3) parallel arms, one (1) with placebo and two (2) with active doses, and a duration of twenty-six (26) weeks, to evaluate the safety and tolerability of ORY-2001 in patients with EA in the mild and moderate stage. The study will initially recruit ninety (90) patients, and will also incorporate, as secondary goals, the various dimensions of this disease as manifested in the patients, including not only changes in memory but also behavioral changes such as aggressiveness and social disconnection. The trial will also measure the levels of various biomarkers in cerebrospinal fluid. The Company expects to launch a twin study in the USA within the next few months. This study will be conducted in seventeen (17) Spanish, British and French hospitals.

The Company is also preparing an additional clinical trial with ORY-2001, REIMAGINE, an open exploratory “basket” trial to evaluate the effect of ORY-2001 on the reduction of aggression in patients with various neurodegenerative and psychiatric indications, such as:

– AD

– LBD

– ADHD

– Autistic Syndrome Spectrum

– Borderline personality disorders

ORYZON also has a third LSD1 inhibitor, the pre-clinical candidate ORY-3001, for diseases not yet disclosed, and for which ORYZON presented pre-clinical data on efficacy against sickle cell anemia to the American Society of Hematology in December 2017.

The Company also has other programs addressing other epigenetic targets, principally other histone demethylases, in the early stage of development.

6.1.1.3. ORYZON’s pipeline or business opportunities

The Company focuses its activity on the development of experimental drugs to inhibit a sub-group of therapeutic targets called KDMs.

ORYZON has developed a platform to create inhibitor drugs for a class of enzymes known as KDMs, with around thirty (30) members that belong to two (2) “superfamilies.” This platform benefits from the historical background of the Company in identifying genomic biomarkers. This fact, together with ORYZON’s compound library and its biological knowledge in the sphere of

epigenetics, has led the Company to possess one of the most extensive patent portfolios in this area. To date, the Company has prioritized a small group of KDM targets, including LSD1, as primary objectives for innovative customized therapies, according to their involvement in the disease and the potential for druggability.

The pipeline of products being developed by the Company is shown below:

(1) Approved. Recruitment ongoing
(2) CTA submitted
(3) CTA in preparation

6.1.1.4. *ORY 1001 and AML*

Leukemia is a blood cancer caused by the uncontrolled proliferation of precursors to white blood cells. There are many different types of leukemia with various genetic and epigenetic origins.

AML is a type of cancer arising from the myeloid line of hematopoietic stem cells. It is a clonal hematopoietic disorder that may arise from any hematopoietic stem cell or from a progenitor cell from a specific line, the most frequent cause being genetic alteration or damage in stem cells. Apart from the causes due to genetic damage, there is a group of diseases with a congenital predisposition such as Fanconi anemia, Bloom syndrome, ataxia telangiectasia and Down syndrome. There have also been links to external factors involved in the pathogenesis of leukemias, with exposure to ionizing radiation and some organic solvents being of particular note. It has not been possible to demonstrate a specifically viral origin in acute leukemias, although this has been shown in some proliferative disorders such as leukemia / adult T-cell lymphoma, related to the HTLV-1 virus, and Burkitt lymphoma, related to the Epstein-Barr virus.

The differentiating characteristic of ORYZON's anti-tumor program against LSD1 (also called KDM1A) in leukemia is that LSD1 is an absolutely necessary enzyme for leukemic stem cells to

survive and spread the tumor, at least in certain types of leukemia such as AML-MLL, for which there are very few therapeutic options. Moreover, the normal hematopoietic cells that the remaining blood cells produce are not affected by the temporary inhibition of LSD1, which contributes toward improving the safety profile of the compound.

If these findings obtained in animal experiments were to be confirmed in human patients, the inhibition of LSD1 would impede the function of the leukemic stem cells, and therefore would extinguish the tumor itself (or cancer cells) by differentiating the tumor cells, and would also prevent its possible recurrence, because the cancerous stem cells would disappear.

During the 2009–2013 period ORYZON developed an advanced program in LSD1 inhibitors, as evidenced by the fact that some of the leading international scientific articles, such as the one published in 2012 in *Cancer Cell* (2012;21:473–478), used ORYZON drugs. Then, in 2013, ORYZON completed the pre-clinical safety profile of its inhibitor ORY-1001, which is a highly potent and selective LSD1 inhibitor. This pharmaceutical development was recently published by the Company's scientists (see T. Maes et al., in *Cancer Cell*, Volume 33, Issue 3, pp. 495–511.e12, 12 March 2018).

In August 2013, the EMA granted to ORYZON the status of orphan drug for ORY-1001 in the treatment of AML.

A first Phase I human clinical trial, with an extension in which patients with certain genetic subvarieties of leukemia were selected in order to measure a first efficacy sample (which in the sector is usually known as a Ib or IIa arm), was submitted to the AEMPS for consideration, and permission to start Clinical Phase I in humans in Spain was obtained in December 2013. It was also submitted to the MHRA for consideration, and permission was obtained to start Clinical Phase I in humans in the United Kingdom in January 2014. Permission to start this phase in France was subsequently obtained.

This clinical trial has been completed, and its results are in the manuscript preparation phase for publication in a specialized scientific journal. The preliminary results were presented at the 58th Annual Scientific Conference of the American Society of Hematology (ASH-2016) on December 5, 2016. In this trial, the drug was administered to forty-one (41) patients for various types of acute leukemia, with patients recruited at ten (10) hospitals located in three (3) European countries (Spain, the United Kingdom and France).

The Phase I results showed that ORY-1001 is a drug that is safe and well tolerated by patients, with a good pharmacokinetic profile. Pharmacodynamic biomarkers were also identified that permit the response to the drug to be predicted in certain subtypes of acute leukemia, and the recommended maximum dose was determined. It is especially noteworthy that in this first dose-escalation phase, complete remission (CRi) was achieved, and five (5) additional patients showed signs of anti-leukemic activity, defined as a reduction in the percentage of blast cells in peripheral blood. In an expansion arm of the same trial, an attempt was made to identify indications of effectiveness in patients with type MLL and M6 acute leukemia. Such additional arms, known colloquially within the industry as Phase Ib or Phase IIa, permit the observation of indications of clinical effectiveness, although they lack the statistical strength to make determinations with certainty. In this arm of the trial fourteen (14) patients were treated, ten (10) of whom had MLL leukemia subtypes and four (4) of whom had M6 erythroleukemias. A high percentage of differentiation was also observed through evaluation at the molecular level by the expression of genes involved in the differentiation and through evaluation by morphological differentiation of the cancer cells. Three (3) partial bone-marrow responses (reduction in blast cells) and two (2) cases of stabilization of the disease were also observed.

Overall, twelve (12) patients out of the forty-one (41) study participants showed signs of anti-leukemic activity, including one response that satisfied the criteria of the international working group regarding diagnosis, standardization of the response criteria, results of the treatment, and disclosure standards for therapeutic trials involving AML in terms of complete remission with incomplete blood maturation (CRi).

The Company, supported by the opinion of its clinical researchers, believes that the drug should continue to be investigated under various clinical conditions.

The Company also worked intensely during 2018 to complete preparations for individual Phase IIa clinical trials with ORY-1001, one of them on myeloid leukemia, after recovering all of the rights to the drug from Roche, at no cost, toward the end of January 2018. Thus, with the assistance of internationally renowned expert oncologists, a Phase IIa study of AML was designed whose subjects were elderly patients who were not eligible for conventional chemotherapy in combination with another biomethylating agent. The Company recently requested approval from the relevant regulatory agencies to conduct this new clinical trial, and will provide further information thereon in due course.

The potential of the LSD1 inhibitors developed by the Company was demonstrated in one of the first studies to establish a link between epigenetics and, specifically, LSD1 in immune-oncology, conducted by Harvard Medical School, the Dana Farber Cancer Institute and Boston Children's Hospital, among other prestigious institutions, using drugs developed by the Company ("LSD1 ablation stimulates anti-tumor immunity and enables checkpoint blockade," Sheng et al., 2018, https://doi.org/10.1016/j.cell.2018.05.052). Immuno-oncology is a paradigm shift away from the scientific approximations that have been made to date in the cancer field, "teaching and training" the immune system to combat the cancer cells. This link between immuno-oncology and LSD1 is relevant because the study shows that LSD1 is one of the agents responsible for the defensive blocking that the tumor cells employ against the attack by the immune system, suggesting that inhibition of LSD1, combined with treatment with the PD-(L)1 antibody – a star drug in immuno-oncology that is yielding very promising results in various types of tumors – is a very promising combination for use in different types of cancers. These research findings are extremely important for companies like ORYZON, which is one of the few companies that have a clinical drug, ORY-1001, that is an advanced LSD1-inhibitor and is indicated and therefore ready for combined clinical studies with immuno-oncology.

6.1.1.5. ORY-1001 and other cancers

Beyond AML, findings published in the scientific literature indicate that LSD1 inhibition may be a valid therapeutic alternative in other blood cancers such as acute lymphoblastic leukemia and certain types of solid cancers such as SCLC and certain subtypes of breast cancer and others. Although these findings are leading to suggestions regarding the possible clinical development of ORY-1001 in different solid tumors, investors should be aware that these findings were produced in a significant number of university laboratories and clinics in different countries and that they are totally external to ORYZON, which cannot therefore be held accountable for the correctness of the data published or for the interpretations made by their authors.

CELGENE recently launched a clinical trial with its LSD1 inhibitor CC-90011 in relapsed or refractory patients with various solid tumors and non-Hodgkin lymphoma (basket trial). SALARIUS is also developing its LSD1 inhibitor (Seclidemstat) in Ewing's sarcoma and in other tumors.

6.1.1.5.1. Lung cancer

Regarding lung cancer, scientists from GSK demonstrated the potential of LSD1 inhibition as a therapeutic approach to the treatment of a type of lung cancer known as SCLC. GSK started the development of its LSD1 inhibitor in a Phase I/II clinical trial for this indication, although at the end of 2017 it stated that it would not continue with this trial, concentrating instead on indications consisting of AML and myelodysplastic syndrome (MDS). Incyte Corporation is also developing an LSD1 inhibitor in SCLC (INCB59872). Therefore, the possible expansion to SCLC within the future developments of ORY-1001 in solid tumors appears to be a reasonable step in the overall development of the drug. Along these lines, Roche requested and obtained permission from the various regulatory authorities involved to start a clinical trial to evaluate the safety, tolerability, and indications of clinical efficacy of ORY-1001 in cancer patients with SCLC.

The details of the study of the clinical efficacy of ORY-1001 in patients with SCLC are available at the website (https://clinicaltrials.gov/) of the US National Institute of Health, under Identifier No. NCT02913443, and is entitled *A Dose Finding and Expansion Study of RO7051790 Administered Orally in Participants With Relapsed, Extensive-Stage Disease Small Cell Lung Cancer (ED SCLC).* This was a dose-finding and expansion study seeking indications of the efficacy of RO7051790 (Roche's internal code for ORY-1001, also known under Roche's other internal code, RG6016), with oral administration in patients with advanced SCLC in various European countries and Canada. From a regulatory perspective, it was a Phase I, open-label, multicenter study designed to assess the safety and tolerability of RO7051790 (ORY-1001) in patients with relapsed SCLC. This dose-expansion study was initially intended to determine the maximum tolerated dose and/or the optimal biological dose as a recommended Phase II dose for RO7051790 (ORY-1001), based on the safety, tolerability, pharmacokinetic and pharmacodynamic profiles observed after oral administration of the drug. Along these lines, seventy (70) patients were expected to be recruited for the study. The cited study began toward the end of 2016 and was expected to be completed in 2019. However, the decision by Roche to halt its LSD1 program for strategic reasons precluded the completion of the program as initially planned.

The Company worked intensely during 2018 to complete the preparations for individual Phase IIa clinical trials with ORY-1001, one of them on myeloid leukemia and the other one on SCLC, after recovering all of the rights to the drug from Roche, at no cost, toward the end of January 2018. Thus, with the assistance of internationally renowned expert oncologists, a Phase IIa study was designed whose subjects were patients with SCLC in a first-line relapse who were sensitive to chemotherapy in combination with the standard agent. The Company has requested approval from the AEMPS to conduct this new clinical trial, and will provide further information thereon in due course.

6.1.1.5.2. Breast cancer

LSD1 may be a useful therapeutic target in various types of breast cancer. In particular, LSD1 inhibitors may be useful in the treatment of ER-α -negative cancers, for which there are minimal therapeutic options based on data published by third parties in the scientific literature. For these reasons, various groups have studied the relationship between LDS1 and ER-α and have shown in scientific publications that the inhibition of demethylation produced by LSD1 reduces or eliminates the capacity of ER-α to bind to the control regions of estrogen receptor genes and gives rise to a strong anti-proliferative effect in breast cancer cells. In fact, combined therapy consisting of anti-estrogens and LSD1 inhibitors showed a significantly better therapeutic effect compared to endocrine therapy alone in inhibiting cell growth. It was ultimately suggested that LSD1 inhibitors might restore the sensitivity of breast cancer cells that are resistant to therapy

with hormonal treatment. SALARIUS is developing its LSD1 inhibitor (Seclidemstat) in TNBC breast cancer and ovarian cancer.

6.1.1.6. LSD1 inhibitors in other diseases: use in neurodegenerative diseases

Inhibitors of LSD1 and of other epigenetic enzymes may also play a role in non-malignant diseases such as certain hematological conditions, inflammatory diseases and in viral infections. In addition to these conditions, epigenetic inhibitors may play a very important role in neurodegenerative diseases.

Scientific findings over recent decades have shown conclusively that the inhibition of certain epigenetic enzymes such as HDAC-1 and HDAC-2 via inhibitor drugs produces highly significant improvements in various animal models of different human neurodegenerative diseases. These HDAC inhibitors have not been able to advance in human clinical studies due to their insufficient selectivity and extensive side effects. In the brain, however, HDAC1 and HDAC2 are frequently members of the same molecular regulatory complexes, which could potentially be destabilized by LSD1 and anti-LSD1 drugs without causing significant side effects.

ORYZON has been a pioneer in this field in identifying the therapeutic potential of the new epigenetic inhibitors and more specifically of the inhibitors of KDMs such as LSD1 in neurodegenerative diseases such as AD, Parkinson's disease or Huntington's chorea.

The LSD1 inhibitors developed by ORYZON have shown in different animal models of Huntington's disease (vinegar flies and transgenic mice) that they are capable of producing certain improvements in some of the parameters (motor and/or cognitive) that were measured. As described in greater detail below, the ORY-2001 drug has clearly demonstrated that it radically slows cognitive deterioration in SAMP8 model mice for AD. Chronic treatment in these animals is well tolerated and does not produce appreciable side effects.

6.1.1.7. ORYZON'S ORY-2001 Program for the treatment of Alzheimer's

The LSD1 inhibitor program had already shown activity in animal models for other diseases such as Huntington's chorea and Parkinson's disease with prototype drugs.

In recent years, the Company has developed a much more advanced and refined drug (ORY-2001) that has been able to demonstrate very striking results in SAMP8 mouse models with accelerated aging. These mice, originally developed at Kyoto University (Japan), age at a much faster rate than their normal peers and show highly accelerated memory loss from the fourth month. SAMP8 mice treated orally with ORY-2001 for one (1) week, one (1) month, two (2) months, or four (4) months showed full recovery of their memory capacity to the levels of their normal peers. In cross-arm experiments it was shown that the beneficial effect is durable, even one (1) month after the last administration of the drug. When the start was delayed by one (1) or three (3) months, the mice continued to be capable of fully regaining their memory in the tests that were performed in comparison with the other groups of animals treated with the drug. These results suggest a capacity for modification of the disease. Positive results in terms of memory recovery were also observed with ORY-2001 in 6/1 model mice for Huntington's chorea.

The cost of these experiments was partially covered (with a first reimbursable grant of USD 300,000 provided in 2010 and a second reimbursable grant of USD 270,000 provided in 2015) by the ADDF, one of the most powerful charitable patient organizations fighting this disease in the USA. These first two (2) grants covered the experiments pertaining to the pre-clinical development model of ORY-2001 in SAMP8 mice. Subsequently, in 2017, the ADDF provided a third grant, in the amount of USD 300,000, for the development of biomarkers that would be clinically useful for the monitoring and follow-up of treatment with the ORY-2001 drug.

It should be pointed out that ORYZON is the only Spanish company that has received funding from the ADDF to date.

As of the date of registration of this document, the ADDF had exercised all of the stock options that it had been awarded by virtue of the reimbursable grants. The ADDF has thus become a shareholder of the Company, and holds a 0.63% interest in its share capital.

Progress has also been made in new pre-clinical experiments with ORY-2001 and in the characterization of the mechanism of action for other indications in diseases of the central nervous system that the Company believes may be a relevant option in the clinical development of the drug. These include pre-clinical experiments that produce improvements in the management of and response to stress, reduced aggression and social disconnection, and increased sociability of the animals. It is important to point out that these results may be transferable to the treatment of behavioral changes that are present in patients with various diseases such as Parkinson's, autistic syndrome, depression, and others. Thus, these data might significantly expand the potential clinical development of ORY-2001 beyond the current indications of AD and multiple sclerosis, for which the Company is currently making clinical progress. With this goal in mind, ORYZON is preparing a first "basket" trial on aggression in patients with various indications.

6.1.1.8. ORYZON'S ORY-2001 Program for the treatment of multiple sclerosis

Experiments performed on model mice for Alzheimer's disease revealed that in the hippocampus of those animals (the region of the brain in which memories are created), there is a decrease in the gene expression of a number of genes involved in the inflammatory response, including S100A9, a proinflammatory protein involved in various pathological processes. The neuroinflammation process has been linked in several ways to the genesis and progression of Alzheimer's. In fact, S100A9 is one of the ten (10) proteins most overexpressed in the cerebral cortex in the development of AD, but has also been widely described in other diseases.

The complexes of proinflammatory proteins with S100A9 are expressed and released at inflammatory sites. A correlation has also been observed between serum levels of S100A9 and the level of activity of inflammatory disorders. The pharmaceutical industry has been exploring drugs that are directed against S100A9 as a treatment for autoimmune/inflammatory diseases in humans. One of these, Laquinimod, is of particular interest and is currently being investigated for the treatment of multiple sclerosis with two (2) Phase III trials (ALLEGRO, Assessment of Oral Laquinimod in Preventing Progression in Multiple Sclerosis, and BRAVO, Benefit–Risk Assessment of Avonex and LaquinimOd), and also for Huntington's disease in a Phase II trial (LEGATO-HD: A Clinical Study in Subjects With Huntington's Disease to Assess the Efficacy and Safety of Three Oral Doses of Laquinimod).

The Company decided to research the effect of the ORY-2001 drug in additional models of diseases in which it has been found that S100A9 is overexpressed. One of these models is of experimental autoimmune encephalomyelitis in mice, which is considered to be a significant model, with a high prediction for transferability for multiple sclerosis.

The results obtained with this model clearly showed that ORY-2001 had a strong protective effect on treated animals, which did not die or develop significant motor paralyses. Nor did spinal-cord lesions appear as areas of infiltration of cells in the immune system or as areas of demyelination. Comparative parallel experiments with Fingolimod (Gilenya,® sold by Novartis and viewed as one of the standard drugs in the treatment of multiple sclerosis) showed that in the initial phases (effector phase) of the autoimmune attack, outbreak or flare-up, the animals were better protected when they were treated with ORY-2001 than when they were treated

with Fingolimod. The response to ORY-2001 was faster and more intense in this phase. This was the first occasion on which the benefit of inhibiting histone demethylation – a field in which ORYZON is a leader – had been reported in autoimmune diseases, and suggested a potential for ORY-2001 as a therapeutic alternative in multiple sclerosis. The cited results were presented at the ECTRIMS-ACTRIMS 2017 International Congress held in Paris in October 2017, among others.

Experiments with other animal models of multiple sclerosis, such as the Theiler viral encephalomyelitis model, also show that ORY-2001 provides strong clinical protection, reduces microglial activation and improves axonal protection. These results were presented by the Company in February 2018, at the 3rd annual ACTRIMS Forum international conference in San Diego, in a poster entitled "ORY-2001 reduces the infiltration of inflammatory cells in the Theiler murine model of the encephalomyelitis virus, showing the epigenetic component in MS".

Analyses of the significance of the results, which were also verified by renowned independent experts on this disease, led the Company to broaden the range of clinical indications toward which ORY-2001 is directed to include multiple sclerosis, thereby helping to expand the commercial potential of the program.

In this regard, ORYZON has strengthened its analytical capacity in the assessment of this disease with the appointment of Dr. Xavier Montalbán to the Company's Scientific Advisory Committee. Dr. Montalbán is a leading international expert in the field of multiple sclerosis and is the director of the leading international center CEMCAT.

6.1.1.9. The ORY-2001 program in clinical Phase I

At the end of 2015, the Company submitted the regulatory dossier to the AEMPS to obtain authorization for the Phase I clinical trial. The goal of this study was to evaluate the safety, tolerability and pharmacokinetics of ORY-2001 in healthy men and women as well as in the elderly population. The trial was conducted at the Hospital Sant Pau de Barcelona, in Spain. This Phase I clinical trial was a double-blind, parallel and single and multiple ascending-dose study.

In April 2016, the Company announced the start of the Phase I clinical trial with ORY-2001. The inclusion of the first subject thus launched the clinical development of the drug. In July 2016, the Company announced the success of the first part of Phase I, which demonstrated, under the design conditions of the trial, the safety and tolerability of the drug, with the characterization for the first time of the pharmacokinetics and pharmacodynamics of ORY-2001 in humans. It was also demonstrated that ORY-2001 is an oral drug that crosses the blood-brain barrier, reaching the brain, where it selectively inhibits the LSD1 and MAO-B enzymes.

This positive outcome of the study took ORY-2001 to Phase II of the clinical development program in 2017 for patients with multiple sclerosis and AD.

On October 31, 2017, the Society received approval from the AEMPS to conduct a Phase IIa clinical trial with ORY-2001 in multiple sclerosis (MS) patients. The study, called SATEEN (SAfety, Tolerability and Efficacy of an EpigeNetic approach to the treatment of multiple sclerosis) is being conducted in nine (9) Spanish hospitals and is designed as a randomized double-blind placebo-controlled study with three (3) parallel arms over thirty-six (36) weeks, to evaluate the safety and tolerability of ORY-2001 in patients with RRMS and secondary progressive multiple sclerosis. In January 2018, the Company announced the recruitment of the first patient in this trial. As of the date of registration of this document, the recruitment of this clinical study is ongoing, and several patients have been treated for several months with no detection to date of any safety problems.

In April 2018, the Company announced approval by the AEMPS for a Phase IIa trial with ORY-2001 in patients with AD. The study, called ETHERAL, will be conducted at various Spanish,

British and French hospitals. Approval by the ANSM and the MHRA was announced in May 2018, and the inclusion of the three (3) first patients in the study was announced on May 14. ETHERAL is designed as a randomized double-blind controlled study with three (3) parallel arms, one (1) with placebo and two (2) with active doses, and a duration of twenty-six (26) weeks, to evaluate the safety and tolerability of ORY-2001 in patients with AD at the mild and moderate stage. The study will initially recruit ninety (90) patients, and will also incorporate, as secondary goals, the various dimensions of this disease as manifested in the patients, including not only changes in memory but also behavioral changes such as aggressiveness and social disconnection. The trial will also measure the levels of various biomarkers in cerebrospinal fluid, including S100A9. The Company expects to launch a twin study in the USA within the next few months.

ORYZON has shown that it has the capacity at the regulatory level to obtain the approval of experimental drug files from the various Drug Agencies and to design and manage human clinical trials; and, no less importantly, that it can also reach agreements having a high financial value with leading global pharmaceutical companies, aiming for new targets and pioneering ("first in class") drugs in the international industry.

6.1.2. An indication of any significant new products and/or services that have been introduced and, to the extent the development of new products or services has been publicly disclosed, give the status of development

As indicated in the preceding sections, the ORY-2001 drug for the treatment of AD and other neurodegenerative diseases has been under intensive development. Its pharmacological characterization and the pre-clinical data have been the subject of multiple presentations at international conferences that have been collected in the press releases, which can be viewed on the Company's corporate website (www.oryzon.com). ORY-2001 is in Phase IIa in its clinical development. These Phase IIa clinical trials are multicenter trials conducted with randomized assignment under double-blind conditions, controlled against placebo, in order to investigate the safety, pharmacokinetics (PK) and pharmacodynamics (PD) of the drug in patients and to identify the first signs of clinical activity.

Similarly, since the recovery of the rights to ORY-1001, the Company has worked intensively during 2018 to complete the preparations for individual Phase IIa clinical trials with ORY-1001 in AML and in SCLC. The Company has requested or plans to soon request approval from the regulatory agencies to conduct these new clinical trials, and will provide further information thereon in due course.

ORYZON also has ORY-3001, a drug that was identified in the middle of 2016 as a pre-clinical candidate for other diseases that were not disclosed for competitive and patent protection reasons. ORY-3001, which is in the pre-clinical phase for non-oncological indications, successfully completed the regulatory toxicology procedures that are necessary in order to obtain permission to start the clinical trials.

The other pipeline products are in an earlier phase, and it is difficult to predict the conclusion of the pre-clinical trials. Moreover, the decision to start the pre-clinical regulatory phase and clinical trials will depend on both the success of the internal program and the assessment of the status of competitors' development programs. The Company is engaged in a scouting or exploration process with a view toward the possible inclusion of more epigenetic projects to supplement those in the pipeline.

6.2. Principal Markets. A description of the principal markets in which the issuer competes, including a breakdown of total revenues by category of activity and

geographic market for each financial year for the period covered by the historical financial information

All of the Company's revenues are obtained in the European market and are described in sections 20.1.2.1, 20.1.2.2 and 20.1.2.4 of Section II of this document. Because the Company's products are aimed at a global market, the corresponding license agreement will include the provisions required to ensure future sales in all of the relevant markets.

6.3. Where the information given pursuant to items 6.1. and 6.2. has been influenced by exceptional factors, mention that fact

In April 2014, the Company signed a License Agreement with Roche (described in Subsection 6.4.2. of Section II of this document), which was terminated in July 2017, with the Company recovering the rights to the development and commercialization of ORY-1001 in January 2018.

6.4. If material to the issuer's business or profitability, disclose summary information regarding the extent to which the issuer is dependent on patents or licences, industrial, commercial or financial contracts or new manufacturing processes

6.4.1. Significant agreements with CROs

ORYZON's diversification with respect to its suppliers is considered satisfactory and does not present a concentration that endangers the supply of key material for the conduct of its activity and progress in its R&D activities. Pre-clinical development is carried out with various CROs, which maintain appropriate quality standards (whether good laboratory practices (GLP) or good manufacturing practices (GMP)) and which for critical processes (such as regulatory toxicity studies) are being audited by the competent regulatory authorities.

The clinical trials are being supported by clinical research organizations, which handle the implementation, follow-up, and operational and quality control of the clinical trials, and which are unique to each clinical trial, thereby posing a risk of concentration. To mitigate this risk of concentration, the Company subcontracts directly for activities such as analytics and imaging studies.

6.4.2. License agreement for the drug ORY-1001

On March 28, 2014, ORYZON signed an exclusive License Agreement with the multinational pharmaceutical company Roche, effective April 1, 2014, for two (2) of the nineteen (19) families of patents that the Company held at that time regarding the LSD1 target product.

Pursuant to the terms of the Agreement, ORYZON received USD 21 million (EUR 15,983,863.64) (which amount was accrued and collected), broken down as follows: (i) USD 17 million (EUR 12,347,500) as an upfront payment, and (ii) USD 4 million (EUR 3,636,363.64) for the achievement of a clinical milestone relating to the determination of the recommended dose.

Regarding the Roche Agreement, the Company capitalized an intangible asset on its balance sheet at December 31, 2013 in the gross amount of EUR 3,287 thousand, which amount was fully amortized. The net book value of the project associated with the Agreement at December 31, 2017 was EUR 0, with its accumulated amortization at that date amounting to EUR 3,287 thousand.

The Agreement also included a Program for the period between the months of April 2014 and March 2016, with a possible extension if required. The goal of this Program was to obtain a better understanding of the potential of LSD1 inhibitors in oncology and hematology. The corresponding service contract, which was included in the Agreement, was renewed for a period of one (1) year, under new conditions and with resources conforming to the requirements for

reaching its goals. The extension of the said contract covered the period between the months of April 2016 and March 2017.

In addition to the USD 21 million, the following amounts were invoiced under the Agreement, as described in this section, under the heading of income from services, as compensation for its collaboration in the Program: (i) during the period between April 1, 2014 and December 31, 2014, the Company invoiced the amount of EUR 610,484 for this item; (ii) during the period between January 1, 2015 and December 31, 2015, the Company invoiced EUR 1,036,721; (iii) during the period between January 1, 2016 and December 31, 2016, the Company invoiced EUR 372,130; and (iv) during the period between January 1, 2017 and December 31, 2017, the Company invoiced EUR 19,906.

On July 19, 2017, Roche informed the Company that, due to a change in the strategic priorities of its portfolio, it had decided to discontinue the clinical development of the experimental drug ORY-1001 (RG6016). As a result of this decision, the development and commercialization rights were recovered by ORYZON, at no cost to the Company and with no refund of the amounts that had been received under the associated contract.

Pursuant to the terms of the Agreement, ORYZON recovered ORY-1001 with an effective date of January 19, 2018. This drug is in a more advanced state than it was when the license was issued in 2014, when Phase I commenced, and it is currently ready to start Phase IIa trials. The Company has begun work in order to continue with the clinical development of ORY-1001 with the goal of entering into new license agreements.

6.4.3. Dependence on patents

Patent ownership constitutes a fundamental and strategic element of ORYZON's business.

In this regard, section 11 of Section II of this document includes a general description of ORYZON's patent portfolio, as well as a brief description of the patent status of the most important products that ORYZON exploits.

6.5. The basis for any statements made by the issuer regarding its competitive position

6.5.1. Competitive position in epigenetics and in the field of oncology

ORYZON is positioned as a biopharmaceutical company specializing in the field of epigenetics.

The first characterized epigenetic targets were the HDACs that were described in the late 1990s, and the first pharmaceutical compounds (HDAC inhibitors), referenced in the foregoing illustration as first-generation epigenetics, were developed soon after. However, HDACs are made up of eighteen (18) families with some members that are very similar to each other, which complicates their use in the development of sufficiently selective drugs. Second-generation epigenetics explore a new group of targets that cause other histone modifications and that to date can be grouped in three (3) "superfamilies": (i) demethylase inhibitors (KDMs, histone demethylases); (ii) methyltransferase inhibitors (HMTs, histone methyltransferases); and (iii) Bromodomain and Extra-Terminal inhibitors. All of these new targets are much more differentiated and have enabled the development of more selective pharmaceutical compounds.

The therapeutic potential of first-generation epigenetic inhibitors was initially explored in the neurology field, with research soon expanded to cancer and other diseases. Likewise, second-generation inhibitors are being explored in cancer and gradually in other therapeutic areas.

Among the small companies, a limited number of them (EPIZYME, CONSTELLATION and ORYZON) have various drugs in their pipelines. The following table summarizes the current situation (in a non-exhaustive manner). Other companies are developing their LSD1 inhibitors or their inhibitors of other epigenetic pharmacological targets for more than one indication (IMAGO for AML and myelodysplastic syndrome (MDS), and SALARIUS for breast, ovarian and prostate cancer, and for Ewing's sarcoma):

Company	Drug	Description	Indication	Stage
Image Biosciences	IMG7289	LSD1 inhibitor	AML / MDS	Phase I
RESERVLOGIX	RVX-208 apabetalone	BET bromodomain inhibitor	Atherosclerosis (MACE)	Phase III
ORYZON GENOMICS	ORY-1001	Lysine-specific demethylase 1 inhibitor (LSD1)	Acute myelogenic leukemia (AML)	Phase IIa
	0RY-2001	Lysine-specific demethylase 1 inhibitor (LSD1)	SCLC	Phase IIa
	0RY-2001	Dual LSD1-MAOB inhibitor	Mild and moderate Alzheimer's disease	Phase IIa
	0RY-2001	Dual LSD1-MAOB inhibitor	Multiple sclerosis (RR and SP)	Phase IIa
	ORY-2001	Dual LSD1-MAOB inhibitor	"Basket" study of aggression	Phase IIa (in preparation)
	ORY-3001	LSD1-specific inhibitor	Undeclared orphan indication	Ready for Phase I
CONSTELLATION PHARMACEUTICALS	CPI-1205	EZH2 inhibitor	Metastatic castration-resistant prostate cancer	Phase I/II
	CPI-205	EZH2 inhibitor	other cancers	Phase I/II
	CPI-0610	BET bromodomain inhibitor	Myelofibrosis	Phase I/II
EPIZYME	EZP 6438 Tazemetostat	EZH2 inhibitor	Mesothelioma	Phase II
	EZP 6438 Tazemetostat	EZH2 inhibitor	Non-Hodgkin B-cell lymphoma	Phase II
	EZP 6438 Tazemetostat	EZH2 inhibitor	Molecularly defined solid tumors	Phase II
	EZP 6438 Tazemetostat	EZH2 inhibitor	Ovarian cancer	Phase II
	EZP 6438 Tazemetostat	EZH2 inhibitor	Non-small-cell lung cancer (NSCLC)	Phase I
SALARIUS PHARMACEUTICALS	Seclidemstat	LSD1 inhibitor	Ewing's sarcoma	Phase I
	Seclidemstat	LSD1 inhibitor	Prostate cancer	Phase I
	Seclidemstat	LSD1 inhibitor	Breast and ovarian cancer	Phase I

Among the large companies, several of them have various drugs in their pipelines. The following table summarizes (non-exhaustively) the current status of the pipelines of the most pertinent ones:

Company	Drug	Description	Indication	Stage
GSK	GSK2879552	LSD1 inhibitor	Acute myelogenic leukemia (AML) and MDS	Phase II
	GSK525762	Bromodomain Extra Terminal (BET) inhibitor	Cancers, including NUT midline carcinoma (nuclear protein in testis; C15 or f55)	Phase I
	GSK2816126	EZH2 inhibitor	Lymphomas, including those with EZH2 mutations	Phase I
MERCK (acquired ONCOETHIX)	OTX015	Bromodomain Extra Terminal (BET) inhibitor	Hematological neoplasias	Phase I

ROCHE (acquired Tensha)	TEN-010	Bromodomain Extra Terminal (BET) inhibitor	Cancers, including NUT midline carcinomas	Phase I
BAYER	BAY1239097	Bromodomain Extra Terminal (BET) inhibitor	Patients with solid tumors (all comers) and lymphoma	Phase I
CELGENE	CC-90011	LSD1 inhibitor	Relapsed and/or Refractory Solid Tumors and Non-Hodgkin's Lymphomas	Phase I
	CC90010	Bromodomain Extra Terminal (BET) inhibitor	Advanced solid tumors and refractory or relapsed Non-Hodgkin's lymphoma	Phase I
	Roclinostat (ACY-1215) (Acquired ACETYLON)	Oral selective histone deacetylase 6 inhibitor (HDAC6)	Multiple myeloma (MM)	Phase I/II
INCYTE CORPORATION	INCB054329	Bromodomain Inhibitor BET	Relapsed and/or refractory lymphoproliferative neoplasias or AML	Phase I
	INCB059872	Lysine-specific demethylase 1 inhibitor (LSD1)	Advanced cancers	Phase I
	INCB063896	Lysine-specific demethylase 1 inhibitor (LSD1)	SCD Sickle Cell disease/Anemia Falciforme	Pre-clinical

Regarding the first-generation epigenetics that explored the potential of HDAC inhibitors on a nearly exclusive basis, the first approved drugs in the area of cancer have already been created and, despite the difficulties caused by their lack of selectivity, certain clinical trials are seeking to broaden their therapeutic applications.

The following tables summarize, non-exhaustively, the current status of the Company's competitors in the field of first-generation epigenetics (a field in which the Company has no drugs):

FDA – Authorized epigenetic therapies					
Agent	**Class**	**Company**	**Authorization date**	**Authorized indication**	**Basis for authorization**
Azacitidine (Vidaza)	DNMT inhibitor	CELGENE CORPORATION	2004	Subtypes of FAB myelodysplastic syndrome	Phase III studies reflect a 15.7% ORR (primary analysis) and a 165.5-day average duration of partial or improved response
Decitabine (Dacogen)	DNMT inhibitor	EISAI	2006	Myelodysplastic syndrome	Phase III studies reflect a 17% ORR (in ITT population) and a 165.5-day average duration of response
Vorinostat (Zolinza)	Pan-HDAC inhibitor	MERCK	2006	Cutaneous T-cell lymphoma	Phase IIb studies reflect a 29.7% ORR; average duration of response not obtained but estimated at >6 months
Romidepsin	HDAC class inhibitor	CELGENE CORPORATION	2009	Cutaneous T-cell lymphoma	2 studies show 34%–35% ORRs

(Istodax)					and 11–15 months for average duration of response
Ruxolitinib (Jakafi)	JAK 1/2 inhibitor	INCYTE PHARMACEUTICALS	2011	Intermediate or high-risk myelofibrosis	COMFORT-I (vs. placebo) and COMFORT-II (vs. best available therapy) Phase III studies reflect a reduction in the volume of surrounding spleen of 35% of base in 41.9% of patients within 24 weeks and 28.5% of patients within 48 weeks, respectively

** DNMT refers to DNA methyltransferase; HDAC, histone deacetylase; ITT, intention to treat; JAK, Janus kinase; ORR, overall response rate. Source: Prescription information for individual agents.*

More information at: http://www.onclive.com/publications/Oncology-live/2013/october-2013/Targeting-Epigenetics-for-Cancer-Therapy-Scores-of-Agents-Capture-Interest-of-Researchers#sthash.zUmMuyyT.dpuf

Selected epigenetic therapies in clinical development			
Agent	**Class**	**Sponsor**	**Development status**
Panobinostat (LBH589)	Pan-HDAC inhibitor	NOVARTIS	Phase III studies in Hodgkin's lymphoma and multiple melanoma; phase II/III studies in cutaneous cell lymphoma (NCT01034163, NCT01023308, NCT00425555)
Entinostat (MS-275, SNDX-275)	HDAC class inhibitor	SYNDAX PHARMACEUTICALS, NATIONAL CANCER INSTITUTE	Phase I and II studies across a range of indications including Hodgkin's lymphoma and kidney cancer. Phase II studies in breast cancer led to FDA designation as a "Breakthrough Therapy" in 2013. Phase III studies in breast cancer are currently in the selection process. (NCT00866333, NCT01038778, NCT01349959)
Belinostat (PXD101)	Pan-HDAC inhibitor	TOPOTARGET/ SPECTRUM PHARMACEUTICALS, NATIONAL CANCER INSTITUTE	Phase II studies in T-cell lymphoma, non-small cell lung cancer, ovarian cancer and hematological tumors (NCT00357032, NCT01310244, NCT00274651, NCT00301756)
Pracinostat (SB939)	HDAC inhibitor	MEI PHARMA/ SYNTERACT HCR, NCIC CLINICAL TRIALS GROUP	Phase II studies in myelodysplastic syndrome, AML, metastatic/recurrent sarcoma (NCT01873703, NCT01912274, NCT01112384)
Givinostat	HDAC inhibitor	INCYTE PHARMACEUTICALS	Phase II study in myeloproliferative neoplasms (NCT01761968)
Phenelzine sulfate	HDM inhibitor	ITALFARMACO	Phase II study in prostate cancer (NCT01253642)
EGCG (green tea extract)	DNMT inhibitor	OHSU KNIGHT CANCER INSTITUTE/ NATIONAL CANCER INSTITUTE	Phase II study in multiple myeloma (NCT01589887)

Valproic acid	HDAC inhibitor	BARBARA ANN KARMANOS CANCER INSTITUTE/ NATIONAL CANCER INSTITUTE	Phase II study in breast cancer (NCT01900730)

** DNMT refers to DNA methyltransferase; HDAC, histone deacetylase; HDM, histone demethylase. Source: NIH Registry of Clinical Trials, www.ClinicalTrials.gov.*

More information at: http://www.onclive.com/publications/Oncology-live/2013/october-2013/Targeting-Epigenetics-for-Cancer-Therapy-Scores-of-Agents-Capture-Interest-of-Researchers#sthash.zUmMuyyT.dpuf

Type of cancer	Epigenetic therapy	Drug combination	Patient selection	Response	Target validation	References
Gastrointestinal stromal tumors	Panobinostat (pan-deacetylase inhibitor)	Panobinostat and imatinib	Patients with metastatic gastrointestinal stromal tumor refractory to imatinib and sunitinib therapies	1 of 11 partial responses; 7 of 11 stable diseases; 3 of 11 progressive diseases	Yes	87
KRAS-type metastatic collateral cancer	Decitabine (demethylating agent)	Decitabine and panitumumab (a monoclonal antibody targeting EGFR)	Patients with progressive diseases in standard therapy and previously treated with cetuximab	2 of 20 partial responses; 11 of 20 stable diseases; 1 of 20 progressive diseases	No	88
Advanced solid tumors	Azacitidine (demethylating agent); Valproic acid (pan-deacetylase inhibitor)	Azacitidine, valproic acid and carboplatin	Advanced cancer and progression after standard therapy (based on platin) or unavailability of effective standard therapy	6 of 32 stable diseases; 26 of 32 progressive diseases 3 of 15 CA125 partial responses; 1 of 15 RECIST partial responses 1 of 17 complete responses 5 of 17 partial responses	Yes	89
Epithelial ovarian cancer	Decitabine (demethylating agent) Azacitadine (demethylating agent)	Decitabine and carboplatin Azacitadine and carboplatin	Initial RECIST and/or CA125 and then progressing 6–12 months after previous platinum therapy	1 of 29 complete responses; 3 of 29 partial responses 19 of 34 PSADT >3 months	Yes	90

			Progression or recurrence within 6 months after a platinum-based compound	11 of 34 PSADT >6 months 9 of 34 PSADT >9 months 8 of 34 partial responses		
Epithelial ovarian cancer	Belinostat (pan-deacetylase inhibitor)	Belinostat and carboplatin	Reappearance of the disease at or before 6 months after the last platinum and taxol treatment	2 of 27 objective responses 15 of 35 objective responses	No	93
Epithelial ovarian cancer	Azacitidine (demethylating agent)	Azacitidine analogue of luteinizing hormone-releasing hormone (LHRH) and anti-androgens	Progression or reappearance within 6 months after a platinum-based compound	1 of 29 complete responses; 3 of 29 partial responses	Yes	90
Prostate cancer	Azacitidine (demethylating agent)	Azacitidine and carboplatin	Progression in combined androgen blockades	19 of 34 PSADT >3 months 11 of 34 PSADT >6 months 9 of 34 PSADT >9 months	Yes	91
ER- and PR-positive breast cancer	Vorinostat (pan-deacetylase inhibitor)	Vorinostat and tamoxifen	Progression or repetition in any of the aromatase inhibitors, or completion of tamoxifen for one year	8 of 34 partial responses	Yes	92
Epithelial ovarian cancer	Belinostat (pan-deacetylase inhibitor)	Belinostat and carboplatin	Reappearance of the disease at or before 6 months after the last platinum and taxol treatment	2 of 27 objective responses	No	93
Epithelial ovarian cancer	Belinostat (pan-deacetylase inhibitor)	Belinostat, carboplatin and paclitaxel	Disease resistant or refractory to platinum	15 of 35 objective responses	No	94

*EGFR, epidermal growth factor receptor; ER, estrogen receptor; LHRH, luteinizing hormone-releasing hormone; PR, progesterone receptor; PSADT, prostate-specific antigen doubling time; RECIST, response evaluation criteria in solid tumors. *Pharmacodynamic validation refers to the existence of evidence regarding surrogate epigenetic responses or patient tumor tissue. The publications have been identified using the PubMed Search terms: HDAC inhibitor, decitabine or 5 azadeoxycytidine or azacitidine or 5 azacitidine or demethylating agent, and cancer. The only clinical trials on solid tumors that were included were those in which a chemotherapeutic agent was used to which patients were resistant.*

6.5.2. Competitive position in neurodegeneration and in diseases of the nervous system

There have been no significant developments of new therapeutic options for neurodegenerative diseases or the development of drugs to fight AD and other neurodegenerative diseases in recent years, although sixty-four (64) clinical trials were recorded in 2013. The following tables summarize the drugs that have been approved and the major programs in various stages of development that are being conducted by other companies that are competitors of ORYZON, and the status of those trials.

In this context, as indicated in the following table, the only drugs that have been approved are those intended for the treatment of cognitive symptoms:

Drugs approved and sold for the treatment of AD symptoms			
Molecule	**Commercial name**	**Mechanism of action**	**Indication**
Rivastigmine	Exelon® (Novartis), now generic	AChe inhibitor	Mild and moderate AD
Galantamine	Razadyne® / Reminyl® (Shire), now generic	AChe inhibitor	Mild and moderate AD
Donepezil	Aricept® (Eisai/Pfizer), now generic	AChe inhibitor	Moderate and advanced AD
Memantine	Namenda® (Merz GmbH & Co. KGaA), now generic	NMDA receptor antagonist	Mild, moderate and advanced AD
Donepezil / memantine	Namzaric® (Merz GmbH & Co. KGaA)	AChE inhibitor/NMDA receptor antagonist	Mild, moderate and advanced AD

Phase III includes drugs under development for which their sponsors claim that they may act as "modifiers of the course of the disease."

It should be noted that there is a sizable concentration of drugs aimed at the Abeta/BACE target in both Phase III and Phase II, which illustrates the scarcity of new therapeutic approaches.

Pipeline of therapies potentially modifying Alzheimer's disease in Clinical Phase III					
Molecule	**Sponsor**	**Indication**	**Target**	**Type**	**Notes**
Aducanumab	Biogen / Neurimmune	Prodromal AD/MCI	Aβ	MAb	CTAD-2018 Torino some positive interim results
Crenezumab	Roche / AC Immune	Prodromal AD/MCI	Aβ	MAb	After 2 Phase II previous failures, Genentech to Start Second Phase 3 Trial of Crenezumab as AD Treatment
Gantenerumab	MorphoSys / Roche	Prodromal AD/MCI; mild AD; preclinical AD	Aβ	MAb	New Phase IIIs announced by Roche
CAD106	Novartis / Amgen	Preclinical AD	Aβ	Vaccine	In combination with CNP520 only
CNP520	Novartis / Amgen	Preclinical AD	BACE (Aβ)	SMI	The "Generation Program" consists of two pivotal Phase 2/3 studies
Elenbecestat (E2609)	Eisai / Biogen	Early AD	BACE (Aβ)	SMI	A 24-Month Study Phase III in patients w. Early Alzheimer's Disease (MissionAD2) Started Jan 2017
JNJ54861911	Johnson & Johnson	Preclinical AD	BACE (Aβ)	SMI	Janssen is conducting a Phase 2b/3 trial comparing JNJ54861911 and a placebo's ability to slow cognitive decline in people who are at risk of developing Alzheimer's but have yet to develop
Albutein® + Flebogama® DIF	Grifols Biologicals	Mild to moderate AD	Aβ	Protein	Treatment procedure with plasma exchange. En 2018 la compañía prevé presentar los resultados de la fase III de su ensayo clínico AMBAR (Alzheimer Management By Albumin
ALZT-OP1	AZTherapies	Prodromal AD/MCI	Mast cells, Aβ	SMI	ALZT-OP1 is a combination regimen of two FDA-approved drugs, cromolyn (designated ALZT OP1a) and ibuprofen (designated ALZT OP1b). In the ALZT-OP1 regimen, cromolyn is delivered via
AD-4833 / TOMM40 (pioglitazone)	Takeda / Zinfandel Pharmaceuticals	Preclinical AD	PPAR-γ	SMI	Approved for diabetes, generics available
LMTX® (TRx0237)	TauRx Pharmaceuticals	Mild to moderate AD	Tau	SMI	Two Phase III failures but further analysis of the results of TRx-015 suggested that a subset of patients who were taking LMTX as a monotherapy showed a significant decrease in the rate of

Phase III also includes drugs under development for which their sponsors claim that they may improve certain symptoms that appear during the course of the disease.

Pipeline of therapies directed towards symptoms of Alzheimer's disease in in Clinical Phase III					
Molecule	**Sponsor**	**Indication**	**Target**	**Type**	**Notes**
AVP-786	Avanir Pharmaceuticals / Concert Pharmaceuticals	Agitation/aggression in AD	NMDA and sigma-1 receptors	SMI	Deuterated Nudexta® (FDC of dextromethorphan and quinidine sulfate), results due H2 2018
AXS-05	Axsome Therapeutics	Agitation/aggression in AD	NMDA and sigma-1 receptors	SMI	
Lumateperone	Intra-Cellular Therapeutics	Agitation/aggression in AD	Serotonin 5-HT2A and dopamine D2 receptors	SMI	
Rexulti® (brexpiprazole)	Otsuka/Lundbeck	Agitation/aggression in AD	Dopamine D2 receptor	SMI	Mixed Phase III results, FDA discussion planned
Belsomra® (suvorexant)	Merck & Co.	Sleep disorders in AD	Orexin receptors	SMI	Approved for insomnia in 2014

Phase II includes drugs under development for which their sponsors claim that they may act as "modifiers of the course of the disease."

Pipeline of therapies potentially modifying Alzheimer's disease in in Clinical Phase II					
Molecule	**Sponsor**	**Indication**	**Target**	**Type**	**Notes**
ACI-24	AC Immune SA	Mild to moderate AD	Aβ	Vaccine	
UBITh Amyloid-beta (UB-311)	United Biomedical Inc.	Mild AD	Aβ	Vaccine	
BAN2401	Eisai / Biogen / BioArctic Neuroscience AB	Prodromal AD/MCI	Aβ	MAb	Adaptive trial design, results due Q3 2018
CT1812	Cognition Therapeutics	Mild to moderate AD	Aβ	SMI	
PQ912	Probiodrug AG	Prodromal AD/MCI; mild AD	Glutaminyl cyclase (pGlu-Aβ)	SMI	Positive Phase IIa results
LY3202626	Eli Lilly	Mild AD	BACE (Aβ)	SMI	
Bryostatin-1	Neurotrope Inc.	Moderate to severe AD	Protein kinase C ε (Aβ)	SMI	Phase II failure. Subgroup being analyzed
Posiphen	Horizon Pharma / QR Pharma	Prodromal AD/MCI; mild AD	Iron regulatory protein-1 (Aβ); α-synuclein; tau	SMI	Targets common sequence on mRNAs encoding neurotoxic aggregating proteins
AADvac1	Axon Neuroscience	Prodromal AD/MCI	Tau	Vaccine	
ABvac40	Araclon Biotech (Grifols)	Prodromal AD/MCI; mild AD	Tau	Vaccine	
ABBV-8E12	C2N Diagnostics	Prodromal AD/MCI	Tau	MAb	
IONIS-MAPTRX	Ionis Pharmaceuticals / Biogen	Mild AD	Tau	Antisense oligonucleotide	
ORY-2001	**ORYZON**	**Mild to moderate AD**	**LSD1-MAOB**	**SMI Epigenetics**	
AstroStem	Nature Cell Co.	Mild to moderate AD	N/A	Stem cell therapy	Adipose-derived mesenchymal stem cells
CB-AC-02	CHA Biotech	Mild to moderate AD	N/A	Stem cell therapy	Placenta-derived mesenchymal stem cells
itMSCs	Stemedica Cell Technologies	Mild to moderate AD	N/A	Stem cell therapy	Ischaemic tolerant mesenchymal stem cells
NEUROSTEM®-AD	Medipost	Mild to moderate AD	N/A	Stem cell therapy	Umbilical cord blood-derived mesenchymal stem cells
BI409306	Boehringer Ingelheim	Prodromal AD/MCI	PDE-9	SMI	
DB959	Bayer AG / T3D Therapeutics	Mild to moderate AD	PPAR-Δ, PPAR-γ	SMI	
CERE 110	Sangamo Therapeutics	Mild to moderate AD	NGF-mediated neuronal regeneration	Viral gene therapy	
			P75 neurotrophin receptor		

Phase II also includes drugs under development for which their sponsors claim that they may improve certain symptoms that appear during the course of the disease.

Pipeline of therapies directed towards symptoms of Alzheimer's disease in in Clinical Phase II					
Molecule	**Sponsor**	**Indication**	**Target**	**Type**	**Notes**
ASP-3662	Astellas	Agitation/aggression in AD	HSD1	SMI	
CPC-201	Allergan	Moderate to severe AD	AChE	SMI	FDC of old drugs donepezil (approved for AD) and solifenacin
DH1401	Daehwa Pharmaceutical Co.	Mild to moderate AD	AMPA receptor	SMI	
Leborexant	Eisai	Sleep disorders in AD	Orexin receptors	SMI	
Namisol® (dronabinol)	Echo Pharmaceuticals BV	Agitation/aggression in AD	Cannabinoid receptors	SMI	Old cannabis-derived compound, Phase II completed but results not reported, no recent progress updates
Nuplazid® (pimavanserin)	ACADIA Pharmaceuticals	Agitation/Aggression in AD; psychosis in AD	Serotonin 5-HT2A receptor	SMI	Positive Phase II results, Phase III initiation expected in H2 2017
ORM-12741	Johnson & Johnson / Orion Corp.	Agitation/aggression in AD		SMI	Adrenergic receptor alpha 2c
ORY-2001	**ORYZON**	**Agression /Social withdrawal in Mild to moderate AD**	**LSD1-MAOB**	**SMI Epigenetics**	
Piromelatine	Neurim Pharmaceuticals	Mild AD	Serotonin receptors, melatonin receptors	SMI	
PXT-864	Pharnext SAS	Mild AD	GABA A receptor	SMI	FDC of old drugs baclofen and acamprostate. Positive Phase IIa results, Phase IIb initiation expected in H2 2017
S47445	Servier / RespireRx Pharmaceuticals Inc.	Depression in AD	AMPA glutamate receptor	SMI	
SUVN-502	Suven Life Sciences Ltd.	Moderate AD	Serotonin 5-HT$_6$ receptor	SMI	Results expected Q3 2018
T-817MA	Toyama Chemical Co. Ltd.	Mild to moderate AD	Not disclosed	SMI	

7. ORGANISATIONAL STRUCTURE

7.1. If the issuer is part of a group, a brief description of the group and the issuer's position within the group

The only company forming part of the Issuer's group was ORYZON Corp., 100% of the share capital of which was held by ORYZON and with respect to which ORYZON was excused from the obligation to consolidate financial statements by application of Sections 7.1.a and 7.1.c of Royal Decree 1159/2010 of September 17 approving the standards for the preparation of consolidated financial statements and amending the National Chart of Accounts and the Chart of Accounts for Small and Medium-sized Enterprises approved by Royal Decree 1515/2007 of November 16. Notwithstanding the foregoing, on December 20, 2016, ORYZON CORP. resolved to dissolve and liquidate, which was duly recorded with the Secretary of State of the State of Delaware on December 29, 2016. Therefore, the Company does not form part of any group as of the date of registration of this document.

7.2. A list of the issuer's significant subsidiaries, including name, country of incorporation or residence, proportion of ownership interest and, if different, proportion of voting power held

The Company does not have subsidiaries on the registration date of this document.

8. PROPERTY, PLANT AND EQUIPMENT

8.1. Information regarding any existing or planned material tangible fixed assets, including leased properties, and any major encumbrances thereon

Fixed assets (property, plant and equipment) essentially consist of machinery, facilities, furniture and laboratory equipment suitable for carrying out the development work which gives rise to the intangible assets. The Company has high-level technologically advanced equipment, mainly acquired in 2009 and 2010, for which reason significant investment has not been required under this heading. The breakdown of fixed assets is as follows:

Fixed assets			
€	**12.31.2017**	**12.31.2016**	**12.31.2015**
Cost			
Technical facilities and machinery	1,877,737	1,853,898	1,851,476
Other fixed assets	1,094,962	1,013,787	1,007,570
Total cost fixed assets	**2,972,700**	**2,867,685**	**2,859,046**
Accumulated depreciation			
Technical facilities and machinery	(1,618,729)	(1,524,191)	(1,418,333)
Other fixed assets	(715,691)	(647,624)	(587,152)
Total accumulated depreciation	**(2,334,421)**	**(2,171,815)**	**(2,005,485)**
Net book value			
Technical facilities and machinery	259,008	329,707	433,143
Other fixed assets	379,271	366,163	420,418
Total net book value	**638,279**	**695,870**	**853,561**

The value of the items of fixed assets that are fully depreciated and in use at December 31, 2017, December 31, 2016 and December 31, 2015 was EUR 1,264,920, EUR 1,022,320 and EUR 668,343, respectively.

The Company's registered office is in a building located at Carrera de San Jerónimo, nº 15, 28014, Madrid. The Company moved to this building, which houses the corporate headquarters, in 2017, with the laboratories located within the old registered office at Calle Sant Ferran, nº 74, 08940, Cornellà de Llobregat (Barcelona). However, the Company is not the owner of either of these buildings, but rather leases them. On May 15, 2015, the Company signed a new lease agreement to lease the building at Cornellà de Llobregat for ten (10) years, which included a minimum stay period of two (2) years from the date of signing. The minimum stay obligations expired on May 15, 2017 at the end of the expiration period of such clause. The Company previously relinquished its option to purchase the building. The annual cost actually incurred by the Company for the lease of the building is EUR 137,918.

8.2. A description of any environmental issues that may affect the issuer's utilization of tangible fixed assets

In accordance with Section 4 of Decree 93/1999 of April 6 on waste management procedures, the Company is registered in the registry of Waste Producers with Producer code P-58357.1.

The law applicable to waste management is Law 20/2009 of December 4 of the Generalitat de Catalunya (Autonomous Community of Catalonia) on environmental prevention and control of activities.

The Company currently generates biological, cytotoxic and common waste, toners, contaminated glass, basic chemical solutions, laboratory reagents and computer materials. This waste is duly stored in specific areas and containers for this purpose, in accordance with each type of waste. To manage the waste, the Company has hired SITA SPE IBÉRICA, S.L.U. (Waste Manager code E-21/89), which collects waste for treatment and disposal in accordance with the applicable legal provisions.

Pursuant to Law 22/2011 of July 28 on waste and contaminated soil, and Royal Decree 833/1988 of July 20 approving the Regulations for the implementation of Law 20/1986, the basic law on toxic and dangerous waste, the Company is exempted from submitting an annual waste declaration, as it generates less than ten (10) tons of hazardous waste annually.

9. OPERATIONAL AND FINANCIAL REVIEW

9.1. Financial condition

See sections 10.1 and 20.1 of Section II of this document.

9.2. Operating results

See section 20.1 of Section II of this document.

9.2.1. **I**nformation regarding significant factors, including unusual or infrequent events or new developments, materially affecting the issuer's income from operations, indicating the extent to which income was so affected

The Issuer's income may be affected by licensing agreements regarding the development of its own products. See section 9.2.2 of Section II of this document.

9.2.2. Where the financial statements disclose material changes in net sales or revenues, provide a narrative discussion of the reasons for such change

The business model for the biotechnology sector is characterized by non-recurring income. This means that there are major fluctuations in income each year. The largest change in net sales figures occurred during fiscal year 2014. The main reason for the increase in the sales figure for fiscal year 2014 was the signing of the Roche Agreement.

During the year, the Issuer's revenues increased by EUR 13,077,103, rising from EUR 43,786 in 2013 to EUR 13,120,889 in 2014. Later, net sales for fiscal year 2015 decreased by EUR 8,867,303 from the prior fiscal year, dropping from EUR 13,120,889 to EUR 4,253,586 in 2015. This decrease mainly corresponded to the difference between the income from the Roche Agreement in 2014 and the deferred income in 2015 regarding compliance in June 2015 with a milestone described in this Agreement.

Net sales for fiscal year 2017 were EUR 16,764, compared to EUR 735,312 for fiscal year 2016 and 4,253,586 for fiscal year 2015. There was a recognition of deferred income in 2017 and 2016 from the achievement of a milestone in June 2015, with 2016 including income from the services agreement signed and then extended with Roche, without reaching any new milestone established in such Agreement during the period in question.

As noted in section 5.1.5.3 of Section II of this document, the Roche Agreement provided an initial income of USD 21 million to be paid in two (2) parts, the first as an initial payment of USD 17 million (EUR 12,347,500) on signing the Agreement (received in the first half of 2014) and the second depending on a near-term milestone, the determination of the recommended dose in Phase I, which was achieved in June 2015, meaning that the remaining USD 4 million (EUR 3,636,363.64) was received in July 2015; the income corresponding to this near-term milestone is not fully recognized in the income statement, but will be accrued in the balance sheet in proportion to the obligations to complete Phase I development, with the corresponding portion of the income being transferred as progress is made. In addition, in April 2014 the two companies signed an agreement to carry out joint development financed by Roche for a period of two (2) years, for which ORYZON received financial compensation for devoting either its own or subcontracted researchers to the development project.

On July 19, 2017, Roche notified the Company that, due to a change in strategic priorities for its portfolio, it decided to discontinue clinical development of the experimental drug ORY-1001 (GR6016), and as a result of this decision, the development and sale rights were recovered by ORYZON on January 19, 2018 at no cost to ORYZON and no return of the amounts received under such Agreement.

ORYZON has recovered ORY-1001 in a more advanced state, and has commenced work to continue the development thereof, in order to reach new license agreement, which could once again entail major changes in net sales or revenues.

9.2.3. Information regarding any governmental, economic, fiscal, monetary or political policies or factors that have materially affected, or could materially affect, directly or indirectly, the issuer's operations

The main factors that might affect the Issuer's operations are the Risk Factors described in subsections 1.1.1, 1.1.2, 1.1.4, 1.2.1, 1.2.2, 1.2.3, 1.2.4, 1.2.5, 1.2.6, 1.2.7 and 1.3 of Section I of this document regarding Risk Factors.

10. CAPITAL RESOURCES

10.1. Information concerning the issuer's financial resources (both short and long term)

This section contains a summary of the Issuer's status with regard to shareholders' equity and indebtedness at March 31, 2018 and December 31, 2017, 2016 and 2015.

The composition of net equity and liabilities on the balance sheet is as follows:

Equity and liabilities				
€	**3.31.2018**	**12.31.2017**	**12.31.2016**	**12.31.2015**
Equity	33,283,560	34,432,020	22,728,779	27,592,947
% of total	*56.4%*	*56.4%*	*45.7%*	*67.7%*
Non-current liabilities	15,731,550	17,915,474	19,418,941	7,841,016
% of total	*26.7%*	*29.3%*	*39.0%*	*19.3%*
Current liabilities	10,005,728	8,696,243	7,596,508	5,296,927
% of total	*16.9%*	*14.2%*	*15.3%*	*13.0%*
Total	**59,020,838**	**61,043,737**	**49,744,228**	**40,730,890**

External financing as of December 31, 2017 is broken down as follows: 78% consists of financing from bank borrowings, and 23% consists of other financial liabilities, mainly governmental financing in the form of reimbursable aid at an effective interest rate of 0% to 1%. As of December 31, 2017, the Company has not entered into interest rate derivatives contracts; the interest rate risk is moderate, as 78% of the loans were subject to a fixed interest rate within the range of 0% to 1%, and the remaining 22% was subject to an average variable interest rate of 2.6%.

Bank borrowings includes a loan provided on June 23, 2016 in the amount of EUR 750,000, with a grace period of one (1) year and EUR 566,277 outstanding on March 31, 2018, with a final maturity in 2020 and a fixed interest rate of 1.8%, and an implicit derivative that would only be paid in the event of early termination or change in the terms or amounts of the loan installments, given that the entity providing the loan at that time hedged the fixed rate to replace the variable interest rate (EURIBOR) typically used in the market. However, the Company does not intend to exercise early termination, for which reason the financial statements do not include any amount with respect to this derivative.

The average interest rate for all outstanding loans at December 31, 2017 and December 31, 2016 was 2.11% and 2.11%, respectively.

10.1.1. Equity

The breakdown of equity is as follows:

Equity				
€	**03.31.2018**	**12.31.2017**	**12.31.2016**	**12.31.2015**
Capital	1,708,070	1,708,070	1,423,391	1,138,713
Share premium	47,760,319	47,760,319	29,825,590	30,110,268
Reserves	(4,009,184)	(4,009,184)	(2,288,463)	(2,765,905)
(Treasury shares and interests)	(1,539,745)	(1,539,745)	(1,791,234)	(1,711,290)
Profit/(loss) from previous years	(14,740,025)	(9,542,866)	(4,094,609)	(3,102,706)
Profit/(loss) for the year	(1,024,241)	(5,197,159)	(5,448,257)	(991,903)
Other equity instruments	-	-	-	(76,964)
Total Shareholders' equity	28,155,194	29,179,435	17,626,418	22,600,213
Valuation adjustments	-	-	-	-

Grants, gifts and bequests received	5,128,366	5,252,585	5,102,360	4,992,734
Total equity	**33,283,560**	**34,432,020**	**22,728,779**	**27,592,947**

10.1.1.1. Shareholders' equity

At December 31, 2017, the Company's capital stood at EUR 1,708,069.55, consisting of 34,161,391 shares with a par value of EUR 0.05 each, all of the same class and series, fully subscribed and paid up, giving the same rights to the holders thereof.

The share premium forms the leading component of shareholders' equity, standing at EUR 47,760,319 on December 31, 2017, as a consequence of the various capital increases implemented by the Company.

On July 24, 2015, the Issuer completed a capital increase of 14.21% over the resulting capital, in the total nominal amount of EUR 156,342.20 and a total share premium of EUR 13,093,659.25, i.e., EUR 3.35 per share, through the issuance and placement into circulation of 3,908,555 shares of a single class with a par value of EUR 0.04 each, represented in book-entry form and with the same rights as the shares previously issued. As a consequence of the foregoing, the Company's capital stands at EUR 1,099,972.04, consisting of 27,499,301 shares with a par value of EUR 0.04 each, numbered sequentially from 1 to 27,499,301 inclusive, fully subscribed and paid up.

On October 13, 2015, there was a capital increase of 3.40% over the resulting capital, in the total nominal amount of EUR 38,741 and a total share premium of EUR 3,244,558.75, i.e., EUR 3.35 per share, through the issuance and placement into circulation of 968,525 shares of a single class with a par value of EUR 0.04 each, represented in book-entry form and with the same rights as the shares previously issued.

Furthermore, on June 29, 2016, the Company approved another capital increase by means of an increase in the par value of the outstanding shares, from EUR 0.04 to EUR 0.05, charged to the share premium account, in the amount of EUR 284,678.26, increasing the share capital to EUR 1,423,391.30. Equity is not changed provided that such capital increase is implemented by increasing the par value of the outstanding shares of the Company.

Finally, on April 4, 2017, in exercise of the delegation granted by the shareholders at the General Shareholders' Meeting held on June 29, 2016, the Board of Directors resolved to increase share capital with the exclusion of preemptive rights in the maximum nominal amount of EUR 284,678.25 through the issuance and placement into circulation of a maximum of 5,693,565 ordinary shares with a par value of EUR 0.05 and a minimum share price of EUR 3.06 each, with the subscription via private placement of 5,693,565 shares at a price of EUR 3.20 per share, which represented a 16.67% increase in capital compared to the resulting share capital of EUR 1,708,069.55. Therefore, the capital was increased by EUR 18,217,408, of which EUR 284,678.25 correspond to share capital and EUR 17,934,729.75 correspond to the share premium, through the issuance of 5,693 ordinary shares having a par value of EUR .05 each, represented by book entries and with the same rights as the shares previously issued. As a result of all of the foregoing, the share capital of the Company is EUR 1,708,069.55, represented by 34,161,391 shares with a par value of EUR 0.05 each, numbered consecutively from 1 to 34,161,391, both inclusive, and which are fully subscribed and paid up.

The remaining shareholders' equity basically consists of other reserves, treasury shares, results from prior years, and the results from the current year.

At December 31, 2015, the Company had shareholders' equity of EUR 22,600,213, an increase of EUR 13,810,709 (157%) over the amount at December 31, 2014, as a result of the various capital increases during 2015.

At December 31, 2016, the Company had shareholders' equity of EUR 17,626,418, a decrease of EUR 4,973,795 (22%) compared to the amount at December 31, 2015, mainly as a result of the negative results for the year obtained to date.

At December 31, 2017, the Company had shareholders' equity of EUR 29,179,435, an increase of EUR 11,553,017 (66%) over the amount at December 31, 2016, mainly as a result of the increase in capital implemented during fiscal year 2017.

10.1.1.2. Valuation adjustments

In 2015, the value of ORYZON's interest in OGDSL was impaired due to the deterioration in OGDSL's economic/financial condition, with EUR 169,991 being charged against valuation adjustments to shareholders' equity, leaving this heading at zero (in addition to charging EUR 56,664 against deferred tax liabilities and EUR 168,967 against results for the current year.

On May 30, 2016, there was a sale of the investment classified as available-for-sale financial interest by means of the transfer to LABORATORIO REIG JOFRÉ, S.A. of OGDSL's 24.99% interest for EUR 150,000.

10.1.1.3. Grants, gifts and bequests received

The amounts booked under the heading of grants, gifts and bequests received correspond to capital grants provided by public bodies from which the tax rate is subtracted (this amount is included under the heading "deferred tax liabilities." It also includes the subsidized part of the interest rates of the repayable aid (loans) reduced by the tax rate, which have been recognized at fair value according to the market interest rate.

The balances and changes in the items making up grants, gifts and bequests received are as follows:

Grants, gifts and bequests				
Contributing body	**Balance 03.31.2018**	**Balance 12.31.2017**	**Balance 12.31.2016**	**Balance 12.31.2015**
Capital grants				
CIDEM	598,133	598,133	598,133	598,133
CIDEM	116,299	116,299	116,299	116,299
Ministry of Science and Innovation	1,602,457	1,602,457	1,602,457	1,602,457
Ministry of Science and Innovation	472,892	472,892	472,892	472,892
European Commission	278,616	278,616	278,616	278,590
European Commission	-	-	25,981	51,961
European Commission	205,026	205,026	205,026	207,838
European Commission	87,429	87,429	87,429	87,429
European Commission	321,583	321,583	321,583	-
European Commission	222,113	222,113	-	-
European Commission (b)	39,357	-	-	-
Ministry of Economy and Competitiveness	17,945	17,945	17,945	17,945
Ministry of Economy and Competitiveness	10,200	10,200	10,200	10,469
Ministry of Economy and Competitiveness	82,384	82,384	82,384	82,384
Ministry of Economy and Competitiveness	54,186	54,186	54,186	54,186

Grants, gifts and bequests				
Ministry of Economy and Competitiveness	315,416	315,416	319,141	300,037
Total capital grants	**4,424,035**	**4,384,678**	**4,192,271**	**3,880,619**
Interest-free loan grants				
Ministry of Science and Innovation – Novapsa 2007	24,767	24,767	34,005	44,473
Ministry of Science and Innovation – Novapsa 2008	49,508	49,508	64,749	81,674
Ministry of Industry – Project Scint 2008	14,703	14,703	19,229	24,255
Ministry of Industry – Project Scint 2009	1,948	1,948	3,818	6,238
Ministry of Science and Innovation – Polyfarma 2011	13,244	19,479	26,865	35,135
Ministry of Industry – Project humafarma	12,444	18,301	25,127	32,863
Ministry of Industry – Project Terapark 2008	12,161	12,161	15,905	20,062
Ministry of Economy and Competitiveness – Terapark 2009	5,807	5,807	11,382	18,596
Ministry of Economy and Competitiveness – Polyfarma	18,846	25,981	34,096	44,322
Ministry of Science and Innovation – Polyfarma	5,763	7,538	9,508	20,322
Ministry of Economy and Competitiveness – Humanfarma	19,135	26,271	34,359	43,340
Ministry of Economy and Competitiveness – Humanfarma	27,612	36,112	45,551	54,421
Ministry of Economy and Competitiveness – Nanoscale	4,067	8,309	13,667	20,153
Ministry of Economy and Competitiveness – Nanoscale	2,312	6,653	11,850	18,127
Ministry of Economy and Competitiveness – Hemafarma	4,515	8,954	20,644	21,358
Ministry of Economy and Competitiveness – Hemafarma	21,633	50,542	71,942	74,476
Ministry of Education and Science – MIT	5,866	5,866	14,095	14,826
Ministry of Finance and Public Administrations	8,124	8,124	13,274	19,523
Ministry of Economy and Competitiveness – Hemafarma	12,214	17,902	24,494	30,611
Ministry of Economy and Competitiveness – Retos Onco 2015	30,722	37,463	43,769	-
Ministry of Economy and Competitiveness – Retos Onco 2016	44,557	52,057	59,070	-
Ministry of Economy and Competitiveness – Retos Onco 2017	27,748	31,487	-	-
Ministry of Economy and Competitiveness – Retos Explora 2015	42,066	51,295	59,929	-
Ministry of Economy and Competitiveness – Retos Explora 2016	41,213	48,149	54,636	-

Grants, gifts and bequests				
Ministry of Economy and Competitiveness – Retos Explora 2017 [(a)]	34,108	38,704	-	-
Ministry of Economy and Competitiveness – Retos Inflam 2016[(a)]	50,124	58,636	-	-
Ministry of Economy and Competitiveness – Retos Inflam 2017[(a)]	71,612	81,371	-	-
Total Interest-free loans	**606,819**	**748,090**	**711,962**	**624,776**
Soft loan grants				
ENISA	-	-	10,557	28,770
ADDF	-	-	-	16,448
ADDF -2	-	-	-	24,796
Deutsche bank	-	-	-	46,112
Unnim	-	-	-	11,172
Banco de Sabadell	-	-	-	2,309
ICF	32,697	40,090	79,660	123,810
LA CAIXA – CDTI	64,815	79,727	107,909	139,607
Banco Popular	-	-	-	2,618
Caja Sol	-	-	-	26,345
Banco Popular	-	-	-	2,920
Caixa Catalunya	-		-	62,433
Total soft loan grants	**97,512**	**119,817**	**198,126**	**487,340**
Total grants, gifts and bequests	**5,128,366**	**5,252,585**	**5,102,360**	**4,992,734**

[(a)] *Amount of subsidies provided in 2017 or multi-year subsidies regarding annual payments from 2017.*

[(b)] *Amount of subsidies provided during the period between January 1 and March 31, 2018 or on a multi-year basis regarding the annual payment for the first quarter of 2018.*

10.1.2. Indebtedness

The following table shows the position regarding the Company's net financial debt:

Net financial indebtedness				
€	**03.31.2018**	**12.31.2017**	**12.31.2016**	**12.31.2015**
Non-current payables				
Bank borrowings	11,232,036	13,107,596	14,933,811	3,069,763
Other financial liabilities	2,647,505	2,933,984	2,789,310	3,107,008
Total non-current payables	13,879,542	16,041,579	17,723,121	6,176,771
Current payables				
Bank borrowings	6,859,936	6,385,271	4,250,423	1,403,060
Other financial liabilities	1,016,915	968,348	1,226,971	1,492,330
Total current payables	7,876,851	7,353,619	5,477,394	2,895,390
Total financial debt	**21,756,393**	**23,395,198**	**23,200,515**	**9,072,161**
Cash and cash equivalents	(30,718,596)	(34,950,334)	(22,028,192)	(19,467,099)
Current financial assets	(182,046)	(213,183)	(5,241,556)	(2,241,556)
Total net financial debt	**(9,144,249)**	**(11,768,319)**	**(4,069,233)**	**(12,636,494)**

In December 2015, the Company had EUR 9 million in debt and EUR 21.5 million in cash and current financial assets. The EUR 14.3 million increase in debt in 2017 is intended to fund the development of R&D activities in the field of epigenetics and to meet debt structuring and servicing costs during this fiscal year in order to provide the Company with a stable financial position.

The Company entered into two (2) loans with the ADDF that gave the right to acquire shares of the Company under certain conditions. As for the conditions for the exercise of the right to acquire the shares by ADDF, the latter was entitled to request the acquisition of shares upon expiration of a period of five (5) years from the drawdown date of each of the tranches of the First ADDF Loan and from the drawdown date of the Second ADDF Loan, at an exercise price of EUR 2.43 per share for the first loan, and of EUR 2.54 per share in the event that it exercised the right to acquire shares under the second loan, with respect to the amounts actually drawn.

The ADDF exercised all of its rights to acquire shares on April 26, 2016 and September 26, 2016, acquiring 4,423 shares and 175,071 shares, respectively, representing in the aggregate 0.63% of the share capital of the Company, with no rights remaining to exercise with respect to such loans.

In 2017, the ADDF approved a grant of USD 300,000 to support ORYZON's "*clinical development of a supplemental biomarker for use with the dual inhibitor LSD1/MAOB ORY-2001*" project, and pursuant to the terms of the agreement received 82,029 ordinary shares of ORYXON at a Price of EUR 3.41 per share, obtaining a 0.86% interest in the capital of the Company.

During the period between January 1 and March 31, 2018, there were no significant disbursements for financial transactions such as loans, refundable grants or subsidies other than those listed in section 10.1.3 of Section II of this document. Along these lines, the Company has regularly complied with the Schedule for repayments of principal and has reclassified it from non-current to current in accordance with the quarterly maturities.

10.1.2.1. Bank borrowings

The Issuer has signed various financing agreements with different financial institutions at market interest rates. The maturities of the bank borrowings are described in section 10.1.2.3 below. During 2016, the Issuer engaged in a first round of bank financing in order to obtain additional funds allowing it to finance its R&D programs and its structuring costs. This round of financing, together with the debt repayment schedule and the reclassification of the payment periods from long term to short term, were reflected by the EUR 11,864,048 increase in the long-term bank borrowings heading for the period December 31, 2015 to December 31, 2016, as well as a EUR 2,847,363 increase in the short-term bank borrowings heading for the same period.

During 2017, the Issuer obtained new bank financing in order to obtain additional funds to finance its R&D programs and structuring costs. This round of financing, together with the debt repayment schedule and the reclassification of two payment periods from non-current to current, are reflected in a EUR 1,826,215 reduction in the heading non-current bank borrowings for the period between December 31, 2016 and December 31, 2017.

10.1.2.2. Other financial liabilities

The Other financial liabilities heading corresponds mainly to subsidized loans provided by public bodies for the development of various R&D projects and are interest-free or have rates of up to 1%. These financial liabilities are valued and included in the balance sheet in accordance with their amortized cost, using the effective interest rate for this purpose. The breakdown of the subsidized loans at December 31, 2017, differentiating between the principal of the debt and the debt valued at amortized cost is as follows:

Other financial liabilities – 12.31.2017

€	Debt principal		Debt at amortized cost		Type
	Short-term	Long-term	Short-term	Long-term	
Subsidized loans					
Ministry of Industry - Profit 2005	31,137	62,275	31,137	51,441	Zero
Ministry of Industry - MIT 2005/2006	22,479	44,958	22,479	37,138	Zero
Ministry of Science and Innovation - Novopsa 07	39,501	158,003	39,501	124,980	Zero
Ministry of Science and Innovation - Novopsa 08	57,510	287,548	57,510	221,538	Zero
Ministry of Industry - IAP Scint 2008	17,080	85,401	17,080	65,797	Zero
Ministry of Industry - IAP Scint 2009	14,633	14,633	14,633	12,036	Zero
Ministry of Industry - IAP Terapark 2008	14,126	70,631	14,126	54,417	Zero
Ministry of Industry - IAP Terapark 2009	43,619	43,619	43,619	35,877	Zero
Impacto Polyfarma 2011	51,441	51,441	51,441	51,441	Zero
Impacto Humafarma 2011	37,138	37,138	37,138	37,138	Zero
Impacto Humafarma 2012	124,980	124,980	124,980	124,980	Zero
Impacto Polyfarma 2012	221,538	221,538	221,538	221,538	Zero
Impacto Hemafarma 2012	65,797	65,797	65,797	65,797	Soft
Impacto Nanoscale 2012	12,036	12,036	12,036	12,036	Soft
Impacto Hemafarma 2013	54,417	54,417	54,417	54,417	Soft
Impacto Nanoscale 2013	35,877	35,877	35,877	35,877	Soft
Impacto Minoryx 2013	51,441	51,441	51,441	51,441	Soft
Impacto Polyfarma 2013	37,138	37,138	37,138	37,138	Zero
Impacto Humanfarma 2013	124,980	124,980	124,980	124,980	Zero
Impacto Minoryx 2014	221,538	221,538	221,538	221,538	Soft
Impacto Hemafarma 2014	65,797	65,797	65,797	65,797	Soft
Retos Onco 2015	54,417	54,417	54,417	54,417	Soft
Retos Explora 2015	35,877	35,877	35,877	35,877	Soft
Retos Onco 2016	-	237,164	-	167,755	Soft
Retos Explora 2016	-	219,362	-	155,163	Soft
Retos Inflam 2016	-	257,221	-	179,039	Soft
Retos Onco 2017	-	126,003		84,021	Soft
Retos Explora 2017	-	154,882		103,278	Soft
Retos Inflam 2017	-	313,948	-	205,452	Soft
Total subsidized loans	**741,132**	**3,931,439**	**741,132**	**2,933,984**	
Guarantees received	227,215	-	227,215	-	
Total other financial liabilities	**968,348**	**3,931,439**	**968,348**	**2,933,984**	

Other financial liabilities also include amounts withheld by way of security from other companies which participate together with ORYZON in consortia seeking grants in which the Company acts as coordinator. At December 31, 2017 and December 31, 2016, the balance stood at EUR 227,215.

10.1.2.3. Maturity and average interest rate

The maturity schedule of financial debt on December 31, 2017 (valued at amortized cost) was as follows:

Financial liabilities by maturity

€	Current	December 2019	December 2020	December 2021	December 2022	December 2023 and later	Total
Bank borrowings	6,385,271	7,019,171	4,356,001	1,188,582	435,092	108,750	19,492,867
Other financial liabilities	968,348	506,714	539,492	508,724	430,617	948,437	3,902,332
Total	**7,353,619**	**7,525,885**	**4,895,492**	**1,697,306**	**865,709**	**1,057,187**	**23,395,199**

The average interest rate of all outstanding loans at December 31, 2017 was 2.1%.

10.2. An explanation of the sources and amounts of and a narrative description of the issuer's cash flows

Section 20.1.4 of Section II of this document includes a table of the Issuer's statements of cash flows for the years ended December 31, 2017, 2016 and 2015, with an explanation of the main variations. They are nevertheless summarized below:

Statement of Cash Flows			
€	**2017**	**2016**	**2015**
Total cash flows from operating activities	(4,707,895)	(5,007,301)	523,141
Total cash flows from investment activities	642,941	(7,101,184)	111,474
Total cash flows from financing activities	16,987,096	14,669,578	15,199,967
Net increase/decrease in cash and equivalents	**12,922,142**	**2,561,093**	**15,834,582**

10.3. Information on the borrowing requirements and funding structure of the issuer

See section 10.1 of Section II of this document.

10.4. Information regarding any restrictions on the use of capital resources that have materially affected, or could materially affect, directly or indirectly, the issuer's operations

The loan provided by INSTITUT CATALÀ DE FINANCES in 2008, in the amount of EUR 3,300,000, stipulated that dividends could only be distributed without the prior consent of the INSTITUT CATALÀ DE FINANCES if the principal pending repayment was less than EUR 2,120,000. At December 31, 2017, the amount outstanding on this loan was EUR 811,000. Hence, the conditions established by the INSTITUT CATALÀ DE FINANCES no longer constitute a restriction on the distribution of dividends.

In addition, on June 30, 2010, a participating loan of EUR 750,000 (repaid in full as of December 31, 2017) was formalized with EMPRESA NACIONAL DE INNOVACIÓN, S.A. (ENISA). Pursuant to the loan, the Company had to create a fund or reserve from its profits, after meeting legal and bylaw obligations, for the purpose of repaying the principal of the loan. Give that such loan has been repaid as of the date hereof, there is no obligation to maintain such fund or reserve.

10.5. Information regarding the anticipated sources of funds needed to fulfill commitments referred to in items 5.2.3 and 8.1

As indicated in section 5.2.3 of Section II of this document, there is no plan for future investments approved by any of the Company's bodies in an amount that could be deemed significant.

11. RESEARCH AND DEVELOPMENT, PATENTS AND LICENCES

11.1. Patents

Set forth below is a breakdown of ORYZON's current portfolio of patents, grouped by families:

Each block is a patent family and for each family the data of the basic application made under the PCT are shown (title, application number and application date), together with the countries in which the PCT is validated and current (international extensions), indicating the status of the patent and its expiration date in each country. A patent family may contain more than one patent application in the same country, in which case the applications are distinguished by a number.

Title	Application no.	Filing date	International coverage[1]	Situación2	Expiration date[3]
Oxidase inhibitors and their use	PCT/EP2009/063685	10/19/2009	EP	Approved	10/19/2029
			US	Granted (09/03/2013)	10/19/2029
Phenylcyclopropyl amine derivatives and their medical use	PCT/EP2010/050697	01/21/2010	EP	Pending	01/21/2030
			US	Granted (03/31/2015)	01/21/2030
Substituted heteroaryl- and aryl-cyclopropylamine acetamides and their use	PCT/EP2010/055103	04/19/2010	EP	Approved	04/19/2030
			US	Granted (02/03/2015)	04/19/2030
Lysine Specific Demethylase-1 inhibitors and their use	PCT/EP2010/055131	04/19/2010	EP	Approved	04/19/2030
			KR	Granted (05/10/2017)	04/19/2030
			MX	Granted (03/30/2016)	04/19/2030
			US	Granted (10/14/2014)	10/19/2029
Lysine demethylase inhibitors for diseases and disorders associated with hepadnaviridae	PCT/US2011/026140	02/24/2011	US	Granted (11/17/2015)	02/24/2031
Inhibitors for antiviral use	PCT/US2011/026141	02/24/2011	US	Granted (04/11/2017)	02/24/2031
Lysine specific demethylase-1 inhibitors and their use	PCT/EP2011/056279	04/19/2011	AU	Granted (03/31/2016)	04/19/2031
			BR	Pending	04/19/2031
			CN	Granted (07/29/2015)	04/19/2031
			EP1	Granted (10/19/2016)	04/19/2031
			EP2	Pending	04/19/2031
			IL	Granted (12/01/2015)	04/19/2031
			IN	Pending	04/19/2031

			JP	Granted (01/15/2016)	04/19/2031
			KR	Granted (10/31/2017)	04/19/2031
			MX	Granted (01/21/2015)	04/19/2031
			RU	Granted (09/14/2016)	04/19/2031
			US1	Granted (05/31/2014)	04/19/2031
			US2	Granted (10/06/2015)	04/19/2031
			US3	Pending	04/19/2031
Cyclopropylamine derivatives as LSD1 inhibitors	PCT/EP2011/062947	07/27/2011	EP	Approved	07/27/2031
			US1	Granted (04/14/2015)	07/27/2031
			US2	Granted (06/13/2017)	07/27/2031
Arylcyclopropylamine based demethylase inhibitors of lsd1 and their medical use	PCT/EP2011/062949	07/27/2011	AU	Granted (10/29/2015)	07/27/2031
			BR	Pending	07/27/2031
			CA	Pending	07/27/2031
			CN	Granted (05/20/2015)	07/27/2031
			EP1	Granted (04/04/2018)	07/27/2031
			EP2	Pending	07/27/2031
			HK	Pending	07/27/2031
			IL	Granted (05/29/2017)	07/27/2031
			IN	Pending	07/27/2031
			JP	Granted (12/09/2016)	07/27/2031
			KR	Granted (05/06/2018)	07/27/2031
			MX	Granted (08/30/2016)	07/27/2031
			RU	Granted (02/22/2017)	07/27/2031
			US1	Granted (11/10/2015)	07/27/2031

			US2	Granted (07/18/2017)	07/27/2031
			US3	Pending	07/27/2031
Cyclopropylamine inhibitors of oxidases	PCT/EP2011/067608	10/07/2011	US	Granted (06/23/2015)	10/07/2031
Lysine demethylase inhibitors for diseases and disorders associated with flaviviridae	PCT/EP2011/071444	11/30/2011	US	Granted (10/17/2017)	11/30/2031
Lysine demethylase inhibitors for myeloproliferative disorders	PCT/EP2012/052144	02/08/2012	EP	Pending	02/08/2032
			US	Granted (03/06/2018)	10/19/2029
Lysine demethylase inhibitors for inflammatory diseases or conditions	PCT/EP2012/059377	05/21/2012	EP	Pending	05/21/2032
			US	Pending	05/21/2032
(hetero)aryl cyclopropylamine compounds as lsd1 inhibitors	PCT/EP2012/070898	10/22/2012	AU1	Granted (11/16/2017)	10/22/2032
			AU2	Pending	10/22/2032
			BR	Pending	10/22/2032
			CA	Pending	10/22/2032
			CN1	Granted (07/11/2017)	10/22/2032
			CN2	Pending	10/22/2032
			EP	Approved	10/22/2032
			HK	Pending	10/22/2032
			IL	Granted (04/01/2018)	10/22/2032
			IN	Pending	10/22/2032
			JP1	Granted (09/29/2017)	10/22/2032
			JP2	Pending	10/22/2032
			KR	Pending	10/22/2032
			MX	Approved	10/22/2032

			RU	Pending	10/22/2032
			US1	Granted (11/08/2016)	10/22/2032
			US2	Granted (04/17/2018)	10/22/2032
			US3	Pending	10/22/2032
(hetero)aryl cyclopropylamine compounds as lsd1 inhibitors	PCT/EP2012/070900	10/22/2012	AU	Granted (07/28/2017)	10/22/2032
			BR	Pending	10/22/2032
			CA	Pending	10/22/2032
			CL	Granted (08/09/2017)	10/22/2032
			CN	Granted (03/08/2017)	10/22/2032
			CO1	Granted (12/24/2015)	10/22/2032
			CO2	Granted (12/23/2016)	10/22/2032
			CR	Pending	10/22/2032
			DZ	Pending	10/22/2032
			EG	Pending	10/22/2032
			EP	Approved	10/22/2032
			HK1	Granted (04/13/2018)	10/22/2032
			HK2	Pending	10/22/2032
			ID	Pending	10/22/2032
			IL	Pending	10/22/2032
			IN	Pending	10/22/2032
			JP1	Granted (11/25/2016)	10/22/2032
			JP2	Pending	10/22/2032
			KR	Pending	10/22/2032
			MA	Granted (03/11/2014)	10/22/2032
			MX	Granted (11/01/2017)	10/22/2032
			MY	Pending	10/22/2032
			NZ	Granted (08/02/2016)	10/22/2032
			PE	Pending	10/22/2032

			PH	Granted (10/27/2017)	10/22/2032
			RU	Pending	10/22/2032
			SG	Granted (02/23/2016)	10/22/2032
			TH	Pending	10/22/2032
			UA	Approved	10/22/2032
			US1	Granted (10/18/2016)	10/22/2032
			US2	Granted (06/06/2017)	10/22/2032
			US3	Pending	10/22/2032
			VN	Pending	10/22/2032
			ZA	Pending	10/22/2032
Biomarkers associated with LSD1 inhibitors and use thereof	PCT/EP2016/063368	06/10/2016	AU	Pending	06/10/2036
			CA	Pending	06/10/2036
			CN	Pending	06/10/2036
			EP	Pending	06/10/2036
			IL	Pending	06/10/2036
			JP	Pending	06/10/2036
			KR	Pending	06/10/2036
			MX	Pending	06/10/2036
			MY	Pending	06/10/2036
			NZ	Pending	06/10/2036
			SG	Pending	06/10/2036
			US	Pending	06/10/2036
			ZA	Pending	06/10/2036
Methods for determining the binding of the KDM1A inhibitor and chemical probes useful for such purpose	PCT/EP2017/056330	16/03/2016	N.A. [4]	Pending	03/16/2037
Solid forms	PCT/EP2016/059726	02/05/2016	AR	Pending	05/03/2036

			AU	Pending	05/02/2036
			BR	Pending	05/02/2036
			CA	Pending	05/02/2036
			CN	Pending	05/02/2036
			EP	Pending	05/02/2036
			HK	Pending	05/02/2036
			IL	Pending	05/02/2036
			JP	Pending	05/02/2036
			KR	Pending	05/02/2036
			MX	Pending	05/02/2036
			US	Pending	05/02/2036
Gene expression biomarkers for the individualized treatment of cancer with epigenetic modifying agents	PCT/EP2016/073821	10/06/2016	AR	Pending	10/07/2036
			EP	Pending	10/06/2036
			US	Pending	10/06/2036
Combinations of LSD1 inhibitors for the treatment of hematological cancers	PCT/EP2017/055763	03/13/2017	AR	Pending	03/14/2037
			PCT4	Pending	03/13/2037
			US	Pending	03/14/2037
Combinations of LSD1 inhibitors for the treatment of solid tumors	PCT/EP2017/055784	03/13/2017	AR	Pending	03/14/2037
			PCT4	Pending	03/13/2037
			US	Pending	03/14/2037
	PCT/EP2017/063573	06/02/2017	N.A. [4]	Pending	06/02/2037
Heteroaryl-carboxylic acids as histone demethylases inhibitors	PCT/EP2017/063585	06/02/2017	N.A. [4]	Pending	06/02/2037
Methods for the treatment of multiple sclerosis	PCT/EP2017/064206	06/09/2017	AU	Granted (06/14/2018)	06/09/2037
			CA	Pending	06/09/2037
			CN	Pending	06/09/2037

			EP	Approved	06/09/2037
			IL	Pending	06/09/2037
			JP	Pending	06/09/2037
			KR	Pending	06/09/2037
			MX	Pending	06/09/2037
			MY	Pending	06/09/2037
			NZ	Pending	06/09/2037
			SG	Pending	06/09/2037
			US	Pending	06/09/2037
			ZA	Pending	06/09/2037
Pharmacodynamic biomarkers for the individualized treatment of cancer using epigenetic modifier agents	PCT/EP2017/077994	11/02/2017	N.A. [4]	Pending	11/02/2037
Biomarkers to determine response to LSD1 inhibitors	PCT/EP2017/078084	11/02/2017	N.A. [4]	Pending	11/02/2037
-	PCT/EP2018/053925	02/16/2018	N.A. [4]	Pending	02/16/2038
-	EP17382545.6	08/03/2017	N.A. [4]	Pending	08/03/2038[5]
-	EP17382835.1	12/05/2017	N.A. [4]	Pending	12/05/2038[5]
-	EP17382836.9	12/05/2017	N.A. [4]	Pending	12/05/2038[5]
-	EP18170938.7	05/04/2018	N.A.	Pending	05/04/2039[5]
-	EP18382500.9	07/05/2018	N.A.[4]	Pending	05/07/20395

1. Country codes:

AR	*Argentina*	*CN*	*China*	*EP*	*Europe*	*JP*	*Japan*	*NZ*	*New Zealand*	*TH*	*Thailand*
AU	*Australia*	*CO*	*Colombia*	*HK*	*Hong Kong*	*KR*	*Korea (South)*	*PE*	*Peru*	*UA*	*Ukraine*
BR	*Brazil*	*CR*	*Costa Rica*	*ID*	*Indonesia*	*MA*	*Morocco*	*PH*	*Philippines*	*US*	*USA*

CA	*Canada*	*DZ*	*Algeria*	*IL*	*Israel*	*MX*	*Mexico*	*RU*	*Russia*	*VN*	*Vietnam*
CL	*Chile*	*EG*	*Egypt*	*IN*	*India*	*MY*	*Malaysia*	*SG*	*Singapore*	*ZA*	*South Africa*

2. Status: indicates whether the patent application is pending, approved or granted; in the latter case, the date is shown in brackets. Approved means that the application has been accepted by the patent office but the patent has not yet been officially granted.

The time that elapses between the filing of a patent application and its granting can vary greatly between countries, depending on factors such as the examination procedures of each country, the backlog of applications and even the procedural strategy adopted by the applicant. The process can often take several years and even longer in countries with deferred examination such as Canada, Japan and South Korea, where applicants may delay requesting the examination of their application for as long as several years after presenting the application.

3. Expiration date: this column reflects the initial term, which is twenty (20) years from the date of the corresponding PCT application and is the minimum term of the patent. On an exceptional basis in the USA, there may be shorter terms in certain cases. It does not include possible extensions of the patent via extensions of pharmaceutical patents (which exist in the EU, USA, Japan and other countries, with a maximum extension of five (5) years, nor any other type of patent extensions (such as extensions arising from delays in processing by the patent office, available in the USA, and which have in fact been obtained for some of the patents in our portfolio in the USA).

4. N.A.: Not Applicable - no international extensions have yet been made as it is a recent application and is still within the priority year or in the PCT phase. Patent applications for which the title is listed as "-" are for applications that are not yet public, and for which the content thereof is therefore still confidential.

5. Shows the expiration date of the international patents arising from this priority application, to be presented at the end of this application's priority year.

11.2. Trademarks and domain names

The Company owns the ORYZON trademark and may use it in Spain and the EU. The international ORYZON trademark for use in the USA was requested on April 17, 2015 and the application was granted on March 15, 2016.

The Company is not aware of any litigation or opposition procedures with regard to the trademarks it owns. The Company has an active policy of defending its trademarks and in the past has launched opposition proceedings against trademark applications by other parties that it believed might conflict with its own trademarks, and may do so again in the future.

ORYZON is the owner of the following domain names:

- oryzon.com;
- oryzon.es;
- oryzon.cat;
- oryzon.eu;
- oryzon.net;
- oryzon.biz;
- oryzon.info;
- oryzon.mobi; and
- oryzon.barcelona.

11.3. Registers

Not applicable.

12. TREND INFORMATION

12.1. The most significant recent trends in production, sales and inventory, and costs and selling prices since the end of the last financial year to the date of the prospectus

Section 20.1 of Section II of this document mentions the most recent trends for the period ending December 31, 2017.

12.2. Information on any known trends, uncertainties, demands, commitments or events that are reasonably likely to have a material effect on the issuer's prospects for at least the current financial year

The main factors that might affect the Issuer's prospects are those detailed in sections 1.1.1, 1.1.2, 1.1.3, 1.1.4, 1.2.1, 1.2.2, 1.2.3, 1.2.4, 1.2.5, 1.2.6, 1.2.7, and 1.3 of Section I of this document regarding Risk Factors.

13. PROFIT FORECASTS OR ESTIMATES

13.1. A statement setting out the principal assumptions upon which the issuer has based its forecast, or estimate

The information on the Issuer in this document does not include forecasts or estimates of earnings.

13.2. A report prepared by independent accountants or auditors stating that in the opinion of the independent accountants or auditors the forecast or estimate has been properly compiled on the basis stated and that the basis of accounting used for the profit forecast or estimate is consistent with the accounting policies of the issuer

Not applicable.

13.3. The profit forecast or estimate must be prepared on a basis comparable with the historical financial information

Not applicable.

13.4. If the issuer has published a profit forecast in a prospectus which is still outstanding, provide a statement setting out whether or not that forecast is still correct as at the time of the registration document, and an explanation of why such forecast is no longer valid if that is the case

Not applicable.

14. ADMINISTRATIVE, MANAGEMENT, AND SUPERVISORY BODIES AND SENIOR MANAGEMENT

14.1. Names, business addresses and functions in the issuer of the following persons and an indication of the principal activities performed by them outside that issuer where these are significant with respect to that issuer

14.1.1. Members of the administrative, management or supervisory bodies

14.1.1.1. Members of the Board of Directors

Article 35 of ORYZON's Bylaws and Article 6 of the Regulations of the Board of Directors provide that the Company shall be administered by a Board of Directors that shall be made up of a minimum of five (5) and a maximum of twelve (12) members, with the shareholders acting at a General Shareholders' Meeting determining the exact number of directors between such limits. The Board of Directors held twelve (12) and sixteen (16) meetings, respectively, during fiscal year 2016 and fiscal year 2017.

Set forth below is the composition of the Board of Directors as of the date of this document, as well as the status of its members in accordance with the provisions of the Bylaws and the Regulations of the Board of Directors.

Name	Position	Status	Business address
Mr. Carlos Manuel Buesa Arjol	Chair	Executive	Carrera de San Jerónimo, nº 15, 28014, Madrid
Ms. Tamara Maes	First Vice Chair	Executive	Carrera de San Jerónimo, nº 15, 28014, Madrid
Mr. José María Echarri Torres	Member	Proprietary	Carrera de San Jerónimo, nº 15, 28014, Madrid
Mr. Antonio Fornieles Melero	Member and Lead Director	Independent	Carrera de San Jerónimo, nº 15, 28014, Madrid
Mr. Ramón Adell Ramón	Member and Chair of the Audit and Compliance Committee	Independent	Carrera de San Jerónimo, nº 15, 28014, Madrid
Ms. Isabel Aguilera Navarro	Member and Chair of the Appointments and Compensation Committee	Independent	Carrera de San Jerónimo, nº 15, 28014, Madrid
Mr. José Carlos Gutiérrez Ramos	Member	Independent	Carrera de San Jerónimo, nº 15, 28014, Madrid

It is hereby stated for the record that none of the members of the Board of Directors are involved in any instance of prohibition against or disqualification from holding the position of director, and particularly that none of those circumstances provided for in Section 213 of the Companies Act or in any other legal provision at the national or autonomous community level applies.

The non-director Secretary of the Board of Directors is Mr. Augusto Piñel Rubio and the non-director Assistant Secretary is Ms. Maitane de la Peña Perea, both of whom were appointed by the Board of Directors at its meeting held on December 4, 2014.

Set forth below is a brief summary of the professional profile of the members of the Company's Board of Directors:

Mr. Carlos Manuel Buesa Arjol

A founder of the Company in 2000, he has held the position of Chair of the Board of Directors since then. He earned his Ph.D. in Biochemistry from the University of Barcelona, and has completed various programs on finance and negotiation. He also completed the Senior Management Program (PADE) at IESE in 2005. In recent years, he has been a member of the board of various biotechnology companies: ONCNOSIS PHARMA AIE, NINFAS AIE, ORYCAMB-PROJECT AIE, GEADIGPHARMA AIE, NEUROTEC PHARMA, S.L., PALOBIOFARMA, S.L. He has been a member of the Advisory Board of NEUROSCIENCES TECHNOLOGIES and is a member of MENDELION LIFESCIENCES, S.L. He is ORYZON's representative on the Governing Board of the Asociación Española de Bioempresas (ASEBIO), of which ORYZON has been a member since 2005, except for the period between 2009 and 2011, during which ORYZON was appointed as Vice Chair of such Governing Board. The first vice chairmanship of ASEBIO is held by ORYZON since December 2015 and it was again re-elected at the last elections held at the end of 2017 for a term of two (2) years, ending in December 2019. Finally, he has been a member of the Board of Directors of INVEREADY SEED CAPITAL and of INVEREADY BIOTECH since September 7, 2008 and October 10, 2012, respectively.

Ms. Tamara Maes

A founder of the Company in 2000, she is the Scientific Director, a member of the Board of Directors since its foundation, and the First Vice Chair. She received her PhD in Biotechnology (genetics) from the University of Ghent (Belgium). She is also a director of MENDELION LIFESCIENCES, S.A., was a member of the Scientific Advisory Board of the Consejo Superior de Investigaciones Científicas (CSIC) from January 20, 2009 through January 22, 2013, has been a member of the Scientific Review Board of the ADDF since 2016 and has collaborated with CAIXA CAPITAL RISC in its mentoring program for new entrepreneurs since September 1, 2015.

Mr. José María Echarri Torres

B.Sc. in Economics, Actuarial Sciences and Financial Sciences from the University of Barcelona, and M.B.A. and M.Sc. in Financial Management from ESADE Business School, he acted as the Chief Financial Officer of ORYZON from 2003 through 2007, prior to which he was responsible for the first integral business technology company creation program developed by a Spanish government administration. He is currently the Chief Executive Officer of INVEREADY ASSET MANAGEMENT, S.G.E.C.R., S.A. and President of the Inveready Financial Group, companies of which he has been the founding member and of which he is currently the largest shareholder. He is a member of the Board of Directors of more than thirty (30) companies, mostly in the technology area, such as MASMÓVIL IBERCOM, S.A. (a company listed on the Continuous Market of which he is the Vice Chair), AGILE CONTENTS, S.L. (listed on the alternative market), ORYZON GENOMICS (listed on the continuous market), ATRYS HEALTH (listed on the alternative market), PALOBIOFARMA, S.L. and FERSA ENERGÍAS RENOVABLES, S.A. (listed on the continuous market); the last company of which he is an independent director and Chair of the Audit Committee.

Mr. Antonio Fornieles Melero (Independent Director and Lead Director)

He received a B.S in Economics and Business Studies from the Complutense University of Madrid (1981) and a Diploma in Senior Management in Business Management from the Instituto Internacional San Telmo (Seville) (2002).

He passed the examination to become an auditor in 1987, becoming a member of the ICJCE.

He has more than thirty (30) years of experience in the auditing profession, beginning in 1983, almost of all of which were at KPMG Auditores, S.L. (a partner since 1994), where he held the highest professional and management responsibilities, both domestic and international.

Since April 2017, he has been the President of the Register of Accounting Experts (*Registro de Expertos Contables*), an entity formed by the ICJCE and the Colegio de Economistas de España to give prestige to the accounting profession.

President of the 1st territorial grouping (Madrid and Castille-La Mancha) of the ICJCE for the period 2007-2013, during which he was a member of the Full Board and of the Permanent Commission of the national ICJCE.

He was a member of the Board of Directors of ABENGOA from January 2015 to November 2016, on which he first held the positions of Lead Independent Director and Second Vice-Chairman and Chairman of the Audit Committee. In March 2016, he was appointed executive Chairman of Abengoa, a position that he held until November 2016. During this period, he led the efforts to arrive at an agreement on restructuring the company with new investors and financial creditors permitting the viability of the company.

He has been a lecturer in the faculty of economics and business studies at the University of Cádiz. He is a regular speaker and lecturer at universities, professional corporations and businesses about issues related to financial reporting, business management and corporate governance and ethics. He has also published numerous articles in specialized media.

Mr. Ramón Adell Ramón (Independent Director and Chair of the Audit and Compliance Committee)

Bachelor's degree and PhD. in Economics and Business Administration from the University of Barcelona. B.A. in Law from the University of Barcelona. Certified Public Accountant by the Instituto de Censores de Cuentas de España and Financial Analyst. Full Professor of Financial Economics and Accounting with the Business Department of the University of Barcelona. He has held management positions at various companies throughout his professional career, forming part of the team that led the creation and development of the Futures and Options Markets in Spain. He has published various books and numerous articles relating to business economics and executive management.

He has been a member of the Board of Directors of NATURGY ENERGY GROUP, S.A. since June 2010 and Chair of that company's Audit Committee since November 2014. He is also a member of the Advisory Board of Planeta Formación y Universidades.

At the institutional level, he has been President of the "Societat d'Estudis Econòmics" since 2011, Honorary Chairman of the Spanish Association of Managers (*Asociación Española de Directivos*) (AED) since 2010, Vice Chairman of the board of trustees of "Foment del Treball Nacional" since 2014, of the CEDE since 1997, and of Fundación CEDE since 2005, as well as advisory member of the plenum of the Cambra de Comerç de Barcelona since 2009 and member of the Governing Board of the Institute for Economic Studies (*Instituto de Estudios Económicos*). He is also an Honorary Member of the European Council of Doctorate Degree Holders & Dr. H.C.

He has been a Fellow of the Spanish Royal Academy of Economic and Financial Sciences since 2016.

Ms. Isabel Aguilera Navarro (Independent Director and Chair of the Appointments and Compensation Committee)

She holds a degree in Architecture and Urban Planning from the Escuela Técnica Superior de Arquitectura de Sevilla. She has completed the Masters program in Commercial and Marketing Management from Instituto de Empresa and the General Management Program from IESE. She also completed the Programme for Senior Management of Leading Companies at Instituto San Telmo (Seville).

She is currently an independent director of LAR España Real Estate SOCIMI, S.A., of Banco Italiano Farmafactoring and of Egasa Siglo XXI. She is a member of the Advisory Board of Deusto Business School and of Human Age Institute (Manpower Group). She is an international speaker at the Thinking Heads Conference Agency and is an associate professor at ESADE.

She was previously an independent member of the Board of Directors of INDRA (from June 2005 to June 2017), BMN (Banco Marenostrum) from February 2013 to December 2017, of AEGÓN España (2014-2016), of the Board of Emergia Contact Center (2011-2016) and of Laureate, Inc. (2002-2006) and of the advisory boards of the industry association Farmaindustria (2009-2012), of Pelayo Mutua de Seguros (2008-2013), Oracle Iberia (2015-2017) and of the Advisory Board of Ikor (2009-2012), and has belonged to the Board of the Association for the Progress of Management (*Asociación para el Progreso de Dirección*) (APD) (2002-2010) as well as being a member of the International Advisory Board of IE Business School and Chair of the Social Board of the University of Seville (2011-2015).

She was a co-founder, shareholder and president of Twindocs Internacional (2009-2012), and founder of Isabel Aguilera Consultoría Empresarial en Estrategia, Operaciones e Innovación (2009-2017). She is the author of two books: "La Encrucijada de Carlota" ("*Carlota's Crossroads*", Espasa, 2011) and "Lo que estaba por llegar, ya está aquí" ("*What was to come has now arrived*", La Esfera de los Libros, 2016).

She was the President for Spain and Portugal of General Electric (2008-2009, Vice President for Spain and Portugal at Google, Inc. (2006-2008), Chief Operating Officer of the NH Hoteles Group (2002-2005) and CEO for Spain, Italy and Portugal of DELL Computer Corporation (1997-2002). She has also worked at Airtel Móvil (now Vodafone) and Hewlett-Packard-Compaq, holding various positions of responsibility in sales and marketing.

Mr. José Carlos Gutiérrez Ramos (Consejero Independiente)

José Carlos Gutiérrez Ramos obtained a Ph.D. in Biochemistry from the Molecular Biology Centre of the Autonomous University of Madrid, specializing in immunology, and then trained at the Max-Plank Institute for Immunobiology in Freiburg (Germany), and was subsequently a Research Member of the Hoffman-La Roche Basel Institute for Immunology Institute (Switzerland). He is a Research Professor (on leave) of the CSIC. He has been a Professor in the Genetics Department and Researcher at the Center for Blood Research at Harvard Medical School (Boston, USA) and a Professor at the MIT Sloan School of Management (Boston, USA).

He has more than twenty (20) years of experience in the biopharmaceutical industry, and from 2009-2015 held the position of Group Senior Vice President of the Pfizer Group and Global Head of BioTherapeutics Research at Pfizer, and head of its Research Center in Boston. Previously, from 2007 to 2010, he was Senior Vice President and Head of the Immuno-inflammation Center for Drug Discovery (iiCEDD) at GSK, where he founded the "Epinova" Epigenetic Unit. Prior to that he held leadership positions at Amgen, Peptimmune and Millenium Pharmaceuticals. During his time as Chairman and CEO of Synlogic from 2015 through May 2018, he brought in more than two hundred (200) million dollars with the participation of specialized high-level

investment funds such as Orbimed, Deerfield, Sofinova, NEA, Atlas, EcoR1, Millenium, Farallon, Perceptive and RockSprings, among others.

14.1.1.2. Members of the administrative, management or supervisory bodies

The Board of Directors of the Company has an Audit and Compliance Committee and an Appointments and Compensation Committee, the description, composition and powers of which are set forth in subsections 16.3.1 and 16.3.2 of Section II of this document.

The Company also has an Independent Scientific Advisory Board. This Board is not a governance or supervisory body, but is rather merely an advisory body supporting the Board of Directors. The Scientific Advisory Board is made up of independent scientists who are well-known in the areas of the Company's activity, and is intended to evaluate the scientific program of ORYZON, provide advice on specific parts thereof, compare it to other competitive programs, and detect and consider other possible scientific risks that occur in the Company's activities. Due to the nature of such Board, the composition thereof is dynamic, given that it must have scientists specializing in the areas in which ORYZON is developing its pipeline at any particular time. The expenses of the Scientific Advisory Board for fiscal years 2016 and 2017 were EUR 34,204 and EUR 18,512, respectively, and EUR 534 for the period between January 1 and March 31, 2018.

As it is merely an advisory body, the Bylaws do not provide for the creation or rules of composition or operation of the Scientific Advisory Body, but its creation was approved by the Board of Directors at its meeting held on July 19, 2015. It is currently made up of Mr. Isidro Ferrer Abizanda, Mr. Xavier Montalban, Mr. Harald Jürgen Hampel, Mr. Howard Fillit, Mr. José Luis Molinuevo, Mr. Leon Hooftman, Mr. Felipe Prósper Cardoso and Ms Lori A. Kunkel.

The work of the Scientific Advisory Body results in the issuance of recommendations addressed to the Board of Directors. These non-binding recommendations allow the Board of Directors to improve, compare and, if applicable, adjust and modulate the Company's scientific strategy.

Finally, it should be pointed out that the creation of a Financial Advisory Body was expected pursuant to the provisions of the shareholder agreement described in subsection 22.2.1 of Section II of this document. However, such Body is not currently operating and it is not expected to be created in the short term, as the shareholders entitled to appoint members to such Body have formally waived the exercise of such right as described in subsection 22.2.1 of Section II of this document.

14.1.2. Partners with unlimited liability, in the case of a limited partnership with a share capital;

Not applicable as it is a corporation (*sociedad anónima*).

14.1.3. Founders, if the issuer has been established for fewer than five years

Not applicable, as the Company was formed more than five (5) years ago.

14.1.4. Any senior manager who is relevant to establishing that the issuer has the appropriate expertise and experience for the management of the issuer's business

As of the date of this document, the management of the Company is made up of the persons identified below (in addition to the executive directors identified above):

Name	Position	Business address

Mr. Enric Rello Condomines	Chief Financial Officer and Chief Operating Officer	Calle Sant Ferran 74, 08940 Cornellà de Llobregat, (Barcelona)
Mr. Emili Torrell Cortada	Chief Business Development Officer	Calle Sant Ferran 74, 08940 Cornellà de Llobregat, (Barcelona)
Ms. Neus Virgili Bernadó	Chief Intellectual Property Officer	Calle Sant Ferran 74, 08940 Cornellà de Llobregat, (Barcelona)
Mr. Roger Bullock	Chief Medical Officer	Calle Sant Ferran 74, 08940 Cornellà de Llobregat, (Barcelona)
Ms. Sonia Gutiérrez Bezón	Chief of Clinical Operations	Calle Sant Ferran 74, 08940 Cornellà de Llobregat, (Barcelona)

Below is a brief description of the relevant expertise and professional experience of the current members of the Company's senior management. The expertise and professional experience of those members of senior management who are also directors of the Company is described in section 14.1.1.1 above.

Mr. Enric Rello Condomines (*Chief Financial Officer and Chief Operating Officer*)

Doctor (Ph.D.) in Economics & Business Administration, Master's degree in Administrative Management and a Degree in Business Administration and Management, in Law and in Economics from Universidad Abat Oliba – CEU (Barcelona). Degree in Business Administration from the University of Barcelona. Postgraduate degree in legal practice from ICAB. He has taken the Senior Management Program (PLB) and HBS Finance Excellence Program at Harvard Business School (Boston). Tax Specialist from Instituto de Economía Pública, Cooperativa y de Derecho Financiero of the University of Barcelona.

He began his professional career in the area of advisory services, auditing and consulting and later specialized in management control and in economic and financial management in the industrial machinery and environmental industries (2007-2011) and in the pharmaceutical industry (1993-2006). In this latter sector, he has served as Financial Controller, Controller Manager (BPA) and Chief Financial Officer (CFO) at SANDOZ INDUSTRIAL PRODUCTS, S.A. (NOVARTIS).

He joined ORYZON as Chief Financial Officer in May 2011 and later assumed the responsibilities of Chief Operating Officer. He is a university professor in the Economics and Business Department of Universitat Abat Oliba CEU.

Since May 2018 he has been a member of the Consultative Working Group (CWG) of the Corporate Finance Standing Committee (CFSC) of ESMA, a regulatory entity that contributes to protecting the stability of the EU financial system, improving investor protection and promoting stable and orderly financial markets. This working group advises and guides the EU on the development of Directives and Regulations on Prospectuses, Corporate Governance and disclosure relating to the Transparency Directive.

Mr. Emili Torrell Cortada (*Chief Business Development Officer*)

Degree in Veterinary Medicine from the Universidad Autónoma de Barcelona. MBA from ESADE, PDG from IESE and Master's in Documentation from Centro de Estudios de Documentación y Patentes.

He began his career in the development of the pharmaceutical business in 1990 at PRODESFARMA, S.A. as Business Development Manager. He later extended his experience in the international area as International Product Manager and International Marketing Manager at ALMIRALL PRODESFARMA, S.A. He was Senior Licensing Manager at LABORATORIOS ESTEVE, S.A. from 2004. In February 2007 he joined ORYZON as Chief Business Development Officer.

Ms. Neus Virgili Bernadó (*Chief Intellectual Property Officer*)

A qualified European Patent Agent, with more than twenty (20) years of experience in the industrial property area in the pharmaceutical industry. She began her career in the industrial property sector in 1991, at J. URIACH Y COMPAÑÍA, S.A. (Uriach Group), where she set up the Patents Department and was responsible for all patent activities of that company until 2006.

From 2006 to 2011 she worked at PALAU PHARMA, S.A., initially as Head of Patents and later as Chief Patent Officer & Legal Affairs Officer, responsible for coordinating all the legal affairs of the Company.

In September 2011, she joined ORYZON as Chief Intellectual Property Officer.

Mr. Roger Bullock (*Chief Medical Officer*)

Dr. Bullock completed his pre-clinical medical training at Keble College, Oxford University, gaining a BA (Hons) in Physiological Sciences in 1978 (converted to MA in 1985). This was followed by clinical medical training at St Bartholomew's Hospital in London where he gained the MB.BS in 1981.

In 1990, he specialized in psychiatry, gained membership of The Royal College of Psychiatry and undertook postgraduate psychiatric training including higher specialist training in geriatric psychiatry which concluded in 1993.

Dr. Bullock is considered a world KOL in the space of neurodegenerative diseases. He has extensive experience as clinical researcher, having participated in more than seventy (70) clinical trials in Alzheimer's disease and other CNS conditions. Over his research career of thirty (30) years, he has authored and co-authored more than one hundred (100) peer-reviewed publications and book chapters in this domain and presented at numerous conferences. Recently he has been working as a consultant for companies active in the CNS space, including Lilly and Merck.

Ms. Sonia Gutiérrez Bezón (*Chief of Clinical Operations*)

BA (Hons) Degree in Pharmacy from the University of Alcalá de Henares, Madrid, and Master in Sciences in Drug Research and Development from the University of Navarre, Pamplona. She completed her training with a postgraduate executive development program from Universitat Oberta de Cataluña, Barcelona.

Her professional career has covered clinical drug research at international pharmaceutical and biotechnology companies such as Synthelabo, Pharmacia-Upjohn, Sanofi, Lundbeck and Regeneron, both in local positions in Spain and in international allocations in Paris and Dublin. Throughout her professional career she has been appointed to different technical and management positions in the clinical research and operations field, contributing to the clinical development of new drugs in psychiatry, neurology, pain and oncology.

In October 2017, she joined Oryzon as Chief of Clinical Operations.

14.1.5. Nature of any family relationship between any of such persons

Except for Mr. Carlos Manuel Buesa Arjol, Chairman of the Board of Directors, and Ms. Tamara Maes, member of the Board of Directors of the Company, who are a de facto couple, there is no family relationship between the persons mentioned in this section 14.1 according to the definition of "close relatives" provided in applicable laws and regulations on related-party transactions (Order EHA/3050/2004 of September 15 on the information on related-party transactions to be provided by the issuers of securities admitted to trading on official secondary markets).

14.1.6. In the case of the members of the administrative, management or supervisory bodies of the issuer and of the persons described in sections 14.1.2 and 14.1.4, information on the relevant management expertise and experience of such persons, as well as the following information

14.1.6.1. Names of all companies and partnerships of which such person has been a member of the administrative, management or supervisory bodies or partner at any time in the previous five years, indicating whether or not the individual is still a member of the administrative, management or supervisory bodies, or partner. It is not necessary to list all the subsidiaries of an issuer of which the person is also a member of the administrative, management or supervisory bodies

The members of the Board of Directors, of the management or supervisory bodies and of the management of ORYZON have the duties and hold the positions described in their respective professional CVs. According to the information available to the Company, and except as stated in section 14.2 of Section II of this document, the members of the ORYZON's Board of Directors and management do not carry out, for their own account or for that of third parties, activities of the same, or a similar kind or activities that are supplemental to those that constitute the corporate purpose of ORYZON as defined in section 5.1.4.2 of Section II of this document.

14.1.6.2. Any convictions in relation to fraudulent offences for at least the previous five years

It is hereby stated for the record that none of the members of the Board of Directors, of the management or supervisory bodies or of the management of the Company has been convicted of fraudulent offences during the five (5) years prior to the date of this document.

14.1.6.3. Details of any bankruptcies, receiverships or liquidations with which a person described in sections 14.1.1. and 14.1.4., who was acting in the capacity of any of the positions set out in sections 14.1.1. and 14.1.4 was associated for at least the previous five years

It is hereby stated for the record that none of the members of the Board of Directors, or of the management or supervisory bodies, or of the management of the Company is associated, in his/her capacity as member of the Board of Directors or of the senior management of the Company, with any bankruptcy, receivership or liquidation of a commercial company during the five (5) years prior to the date of this document.

14.1.6.4. Details of any official public incrimination and/or sanctions of such person by the authorities established in the bylaws or regulatory authorities (including designated professional bodies) and whether such person has ever been disqualified by a court from acting as a member of the administrative, management or supervisory bodies of

an issuer or from acting in the management or conduct of the affairs of any issuer for at least the previous five years

It is hereby stated for the record that none of the members of the Board of Directors, of the management or supervisory bodies or of the management of the Company has been criminally convicted or governmentally sanctioned by the authorities established in the bylaws or by regulatory authorities, or disqualified by any court, from acting as a member of the administrative, management or supervisory bodies of an issuer, or from acting in the management and conduct of the affairs of an issuer during the five (5) years prior to the date of this document.

14.2. Administrative, Management and Supervisory bodies and Senior Management conflicts of interest

During the period covered by the historical financial information and through the date of registration of this document, according to the information provided to the Company, neither the members of the Board of Directors or of the management and supervisory bodies, nor the executive officers mentioned in section 14.1 of Section II of this document, have any conflict of interest between their duties to the Company and their private or other interests, nor do they carry out, for their own account or for the account of third parties, any activities that are of the same or a similar kind, or are supplemental to the type of activities that constitutes the corporate purpose of the Company pursuant to section 229 of the Companies Act, other than those described below, and none of the members of the Board of Directors have notified the Company of any conflict of interest:

Director	Company	Industry	% direct interest	% indirect interest	Position	Term
Mr. Carlos Manuel Buesa Arjol	PALOBIOFARMA, S.L.	Biotechnology	0.25	-	Member/shareholder	Yes
	MENDELION LIFESCIENCES, S.L.	Scientific and technical research	38.00	-	Member/shareholder	Yes
Ms. Tamara Maes	PALOBIOFARMA, S.L.	Biotechnology	0.25	-	Member/shareholder	Yes
	MENDELION LIFESCIENCES, S.L.	Scientific and technical research	38.00	-	Member	Indefinite
Mr. José María Echarri	PALOBIOFARMA, S.L.	Biotechnology	-	1.25	Member	Indefinite
	ATRYS HEALTH, S.L.	Biomedical	-	0.86	Member	05/24/2022
	ABILITY PHARMACEUTICALS, S.L.	Biopharmaceutical	-	0.91	Member	Indefinite
Mr. José Carlos Gutiérrez	MOMENTA PHARMACEUTICAL, INC.	Pharmaceutical	0.33%	-	Member	05/2020

Director	Company	Industry	% direct interest	% indirect interest	Position	Term
	SYNLOGIC THERAPEUTICS	Biomedical	0.7%	-	Member	05/2019

14.2.1. Any arrangement or understanding with major shareholders, customers, suppliers or others, pursuant to which any person referred to in section 14.1 was selected as a member of the administrative, management or supervisory bodies or member of senior management

Pursuant to the provisions of the shareholders' agreement of December 2, 2015, the termination of which was communicated on May 16, 2018 by means of a notice of significant event (*hecho relevante*), Mr. Carlos Manuel Buesa Arjol, Ms. Tamara Maes and Mr. José María Echarri Torres were appointed as members of the Board of Directors.

14.2.2. Details of any restrictions agreed by the persons referred to in section 14.1 on the disposal within a certain period of time of their holdings in the issuer's securities

The Company has no evidence of the existence of restrictions agreed to by the persons mentioned in section 14.1 of Section II of this document on the disposal of their interest in ORYZON within a certain period of time, or of any other time limitation on the transferability of the shares of the Company.

15. REMUNERATION AND BENEFITS

15.1. The amount of remuneration paid (including any contingent or deferred compensation), and benefits in kind granted to such persons by the issuer and its subsidiaries for services in all capacities to the issuer and its subsidiaries by any person

15.1.1. Compensation paid to members of the Board of Directors or of the management or supervisory bodies of the Company

Pursuant to the provisions of article 40 of the Bylaws and article 23 of the Regulations of the Board of Directors of the Company, the position of director shall be compensated. The compensatory nature of such position was approved by the resolution of the shareholders adopted at the General Shareholders' Meeting held on September 18, 2014. Prior to said date, such position was not compensated.

The Company's compensation policy is stated in the summary table below:

Board of Directors of ORYZON – Compensation Policy			
		Average expected frequency / year	**Compensation/ unit**
1	Signing bonus		€3,500.00
2	Compensation as Board Chairman or Vice Chairman or Chairman or Vice Chairman of a Committee (*) or Lead Director		€11,500.00
3	Compensation as member of a Committee		€7,000.00
4	Member of the Board		€3,500.00
5	Compensation per meeting of the Board attended in person	6	€4,300.00
6	Compensation per meeting of the Board attended via Video or TeleConference	3	€1,400.00
7	Compensation per meeting of the Board attended via e-mail	4	€250.00
8	Compensation per meeting of the Committee attended in person	3	€1,000.00
9	Compensation per meeting of the Committee attended via Teleconference	2	€700.00

The Fixed Compensation, which shall be determined annually by the Company's shareholders at the General Shareholders' Meeting for the financial year in which it is adopted, shall remain in force until a change thereof is approved. The determination of the exact amount to pay within such maximum amount, as well as the distribution thereof among the various directors, shall be established by decision of the Board of Directors. Such Fixed Compensation may be different for

the directors and shall be made up of: (i) a fixed allocation for simply holding the position; (ii) compensation for belonging to any existing committees; (iii) compensation for holding positions (Chair and/or Vice-Chair) on the Board of Directors and Committees, although the compensation provided in (ii) and (iii) may not be cumulative and only the higher of them shall be received; and (iv) if applicable, any severance payments agreed to with the directors.

Unless the shareholders determine otherwise, the distribution of the compensation among the directors shall be established by resolution of the Board of Directors, which must take into consideration the duties and responsibilities assigned to each director, membership on committees of the Board of Directors and other circumstances they deem relevant.

For so long as the shareholders have not set the Fixed Compensation approved for the preceding fiscal year, adjusted up or down, as applicable, from January of each fiscal year in accordance with the Consumer Price Index (CPI) published by the National Statistics Institute (*Instituto Nacional de Estadística*) or any other agency that replaces it, shall be received on a provisional basis; the compensation thus received shall be adjusted up or down within the first ten (10) days of the calendar month following the month in which the shareholders at a General Shareholders' Meeting have approved the Fixed Compensation for the fiscal year in question.

The Fixed Compensation shall be deemed established for the fiscal year of twelve (12) months in which the resolution is adopted by the shareholders at a General Shareholders' Meeting; thus, if a fiscal year lasts less than twelve (12) months, the amount of such compensation shall be reduced proportionally.

In addition, regardless of the compensation provided for in the preceding sections, the members of the Board of Directors shall be entitled to: (i) the attendance fees approved by the shareholders for attending meetings of the Board of Directors and its Committees, which amount shall remain in effect for so long as the shareholders do not approve a modification thereof; and (ii) the reimbursement of any reasonable duly justified expense that is directly related to the discharge of their duties as a director of the Company.

Furthermore, without prejudice to all of the foregoing, the Company shall have civil liability insurance for its directors and officers that may be updated and adjusted from time to time by the Board of Directors to the needs and circumstances of the Company, the directors, and the officers covered.

The Board of Directors and the Appointments and Compensation Committee shall adopt all measures available to them in order to ensure that the compensation of the directors is that which is necessary to attract and retain directors with the desired profile and to provide compensation for the dedication, qualifications and responsibilities demanded by the position, but not so high as to compromise the independent judgment of the non-executive directors.

The compensation of the directors must in any case be reasonably proportional to the size of the Company, its financial situation at each moment, and market standards for comparable companies. The compensation system that is established must be focused on promoting the long-term profitability and sustainability of the Company and include the safeguards necessary to avoid the excessive assumption of risks and the reward of unfavorable results.

In accordance with the provisions of Section 529 *novodecies* of the Companies Act, the shareholders acting at the General Shareholders' Meeting of ORYZON held on April 4, 2018 approved the Compensation Policy for the directors of the Issuer, which shall remain in effect during fiscal years 2019, 2020 and 2021 and which was made available to the shareholders of the Company upon the call to said General Shareholders' Meeting and which is available at ORYZON's corporate website (www.oryzon.com).

Said policy establishes a series of general principles applicable both to the system for compensating directors in their capacity as such and to the additional compensation system for the performance of executive duties.

With respect to the general principles of the Compensation Policy, the guiding principle thereof is the search for reciprocal generation of value for the Company and for the employees, and the alignment of its interests with those of the shareholders.

As regards the principles applicable to the system for compensating directors in their capacity as such, the following are of note:

- The compensation must be sufficient and adjusted to the dedication, qualification and responsibilities of the directors, but without the possibility that it may compromise their independence of judgment;
- The compensation must be in line with the market rate;
- The compensation should not include variable components;
- The Compensation Policy shall be compatible with appropriate and efficient risk management, promoting this kind of management and not offering incentives to assume risks that exceed the risk level tolerated by the Company;
- The Board of Directors, in its supervisory function, shall adopt and periodically review the general principles of the Compensation Policy and shall be responsible for supervising the implementation thereof, ensuring its effective and proper application; and
- The rules for managing compensation shall be clearly and concisely drafted, simplifying as far as possible both the description thereof and the calculation methods and conditions applicable to receipt thereof.

Similarly, the principles applicable to the additional compensation system for the performance of executive duties are listed below:

- The structure and overall amount of the compensation must comply with best practices and be competitive in relation to other comparable entities in order to attract, retain and motivate the best professionals;
- The compensation must be established with objective criteria relating to the individual performance of the executive directors and the achievement of the Company's corporate goals;
- The annual variable component must be linked to the achievement of specific and quantifiable goals, in line with the corporate interest, with control and measurement systems that determine the receipt of the variable compensation based on evaluations that measure individual performance and personal contribution to the achievement of the established goals;
- Medium/long-term multiyear variable compensation systems must be incorporated that foster the sustained achievement of goals over time and the retention of key staff;
- The configuration of the compensation package shall be made up of a range of instruments that facilitate the adjustment of compensation to the needs of both the Company and its professionals in terms of content (pecuniary and non-pecuniary), timeline (short, medium and long-term), security (fixed and variable) and goals;

- Maintain alignment of the Compensation Policy of the executive directors and that of senior management; and
- Introduce into the contracts a clause that permits the Company to make payment of a part of the accrued variable compensation subject to the non-occurrence of certain circumstances established by the Company's Board of Directors.

Moreover, regarding the compensation system of the Board of Directors for their collective decision-making duties, the Compensation Policy establishes a system to compensate directors for their supervisory and collective decision-making duties, made up of the components described in article 40 of the Bylaws and article 23 of the Regulations of the Board of Directors described above.

Likewise, in order for the compensation to be reasonably proportionate to the Company's situation at any time and not to reward unfavorable outcomes, the Board of Directors may waive the compensation corresponding thereto by up to 20% in the event that the circumstances established by the Board of Directors occur or do not occur.

ORYZON may partially or totally recover the compensation already paid to each one of the directors if the director has seriously and willfully breached any of the Company's applicable internal rules during the two (2) years immediately subsequent to the payment thereof.

The shareholders acting at the General Shareholders' Meetings held on June 14, 2017 and April 4, 2018 set the compensation of the Board of Directors for fiscal years 2017 and 2018, respectively, at the maximum amount of EUR 525,000 for each of such fiscal years.

The compensation actually received by the members of the Board of Directors of the Company in fiscal year 2015, 2016 and 2017 was EUR 306,297, EUR 371,100 and EUR 456,900, respectively, excluding the salaries of the executive directors.

Pursuant to the resolution regarding the Compensation Policy, the executive directors are also entitled to receive the following for the performance of their executive duties:

- Fixed compensation:

  Directors performing executive duties also receive fixed compensation for the higher level of dedication and responsibility involved in the performance of their duties and which, pursuant to the Compensation Policy, should be competitive with respect to customary standards in the industry for the positions of higher responsibility that they hold.

  The Executive Chairman received annual gross fixed compensation in 2017 in the amount of EUR 274,222, distributed and paid in twelve (12) equal monthly payments at the end of each month. Pursuant to his contract, such amount will hereafter be updated annually by resolution of the Board of Directors, which update may in no case be less than the amount based on the applicable annual CPI. Pursuant to the foregoing, such annual gross fixed compensation will be a total of EUR 279,045 in 2018.

  For her part, the executive director received annual gross fixed compensation in 2017 in the amount of EUR 191,176, distributed and paid in twelve (12) equal monthly amounts at the end of each month. Pursuant to her contract, such amount will be updated annually by resolution of the Board of Directors, which update may in no case be less than the amount based on the applicable annual CPI. Pursuant to

the foregoing, such annual gross fixed compensation will be a total of EUR 194,339 in 2018.

- Annual variable compensation:

The main goal of variable compensation is to incentivize performance, focusing i ton the goals set by the Company, while at the same time promoting strong and effective risk management that avoids the variable compensation creating incentives towards individual behavior with an excessive assumption of risks.

Variable compensation is additional and supplemental to fixed compensation. It is contingent compensation that cannot be consolidated and that is linked to meeting targets in accordance with the guidelines approved by the Board of Directors. Such compensation annually weighs the contribution of each director to the achievement of the Company's goals, which are pre-determined, specific and quantifiable.

Along these lines, the amount of the variable compensation will be established based on the level of achievement of the objectives set at the beginning of each fiscal year. In this way, it is a completely flexible system that determines the existence of fiscal years in which there might not be variable compensation if the level of achievement of the objectives is below minimum established levels or if the results of ORYZON overall do not justify the accrual thereof.

These objectives are related to financial and non-financial metrics under the Company's Strategic Plan, as well as the achievement of certain R&D milestones under the approved Scientific Plan.

The weighting of the various objectives are different for the Executive Chairman and the executive director, as described below:

Executive Chairman:

- 20% corporate financial objectives
- 70% R&D objectives
- 10% corporate non-financial objectives

Executive director:

- 90% R&D objectives
- 10% corporate non-financial objectives

Achievement of the objectives of the executive directors will be evaluated by the Appointments and Compensation Committee.

In addition, if there is a material adverse event, the Board of Directors may decide to reduce or not make variable payments. In fiscal year 2018, there have been three (3) adverse events that would activate this clause relating to financial, R&D and Company-related value objectives.

In the case of the Executive Chairman, for achieving 100% of the established objectives, annual variable gross compensation in 2017 was 45% of the

corresponding annual gross fixed salary. The same proportion of 45% of the corresponding annual gross fixed salary is maintained for 2018.

As regards the executive director, for achieving 100% of the established objectives, annual variable gross compensation in 2017 was 30% of the corresponding annual gross fixed salary. The same proportion of 30% of the corresponding annual gross fixed salary is maintained for 2018.

The Executive Chairman and the executive director received annual variable gross remuneration in 2017 in the amount of EUR 61,554 and EUR 28,579, respectively.

- Long-term variable compensation:

  The executive directors also benefit from an LTI that has been approved by the Board of Directors and which will be received in 2020. The accrual and payment of the LTI is subject in all cases to corporate, clinical and financial objectives for the 2017-2019 period with an impact on the income levels and valuation of the Company.

The maximum amounts for 100% achievement of the established objectives are EUR 228,683 and EUR 140,417 for the Executive Chairman and the executive director, respectively.

Set out below is a table showing the individual accrued compensation of the directors for 2017, including the compensation received by senior executive officers of the Company, as appropriate:

	Fiscal Year 2017			
	Item			
	Per executive officer [2]	Fixed compensation	For attending Board and Committee meetings	Total Compensation
Mr. Carlos Manuel Buesa Arjol	€335,776	€11,500	€39,000	€386,276
Ms. Tamara Maes	€219,755	€11,500	€36,100	€267,355
NAJETI CAPITAL, S.A.[1]		€11,500	€36,100	€47,600
NAJETI, S.L.[1]		€3,500	€39,000	€42,500
Mr. José María Echarri Torres		€3,500	€39,000	€42,500
NAJETI, S.A.S.[1]		€3,500	€39,000	€42,500
Mr. Antonio Fornieles Melero		€11,500	€50,700	€62,200
Ms. Isabel Aguilera Navarro		€11,500	€47,800	€59,300
Mr. Ramón Adell Ramón		€11,500	€50,700	€62,200
TOTAL	**€555,531**	**€79,500**	**€377,400**	**€1,012,431**

[1] NAJETI CAPITAL, S.A., NAJETI, S.L. and NAJETI, S.A.S tendered their resignations as members of the Company's Board of Directors on February 19, 2018.

[2] Does not include the provision for LTI in fiscal year 2017 corresponding to the compensation accrued by Mr. Carlos Manuel Buesa Arjol or Ms. Tamara Maes for performing executive duties, in order to maintain consistency with the Annual Director Remuneration Report prepared with tax accrual standards. However, it is stated for the record that for accounting purposes the formulation of annual financial statements includes the provision relating to the cash LTI approved by the Board of Directors and which will be received in 2020. The accrual and payment of the LTI is subject

in any case to corporate, clinical and financial objectives for the 2017-2019 period with an impact on income levels and the valuation of the Company. The amounts accrued for contingent LTI during 2017 were EUR 76,228 with respect to Mr. D. Carlos Buesa and EUR 46,806 with respect to Ms. Tamara Maes; therefore, the amounts accrued by Mr. Carlos Manuel Buesa Arjol and Ms. Tamara Maes for performing executive duties under accounting principles aggregating the contingent provisions for LTI accrued in fiscal year 2017 are EUR 412,004 and EUR 266,561, respectively.

The estimated compensation of the members of the Company's Board of Directors for all of fiscal year 2018 is EUR 1,086,638, of which EUR 781,585 represents compensation for holding office as executive officers, broken down as: EUR 658,552 as executive officers and EUR 123,033 as the provision for contingent LTI.

15.1.2. Compensation accrued by senior executive officers of the Company

The compensation of the senior executive officers of the Company, excluding compensation as members of the Board of Directors, accrued during fiscal years 2015, 2016 and 2017 for Mr. Carlos Buesa was EUR 186,070, 256,910 and 335,776 and for Ms. Tamara Maes was EUR 173,571, 186,786 and 219,755, respectively.

Below is a table showing the breakdown of the compensation accrued in favor of members of Company management who are not members of the Board of Directors during fiscal years 2015, 2016 and 2017:

	Fiscal year		
Item	**2017**	**2016**	**2015**
Compensation	**566,268**	**479,146**	**€378,136**
Fixed	522,395	403,604	€378,136
Variable	43,872	75,540	-
In kind	2,618	3,015	€2,817
Stock Options	11,880	335,518	-
Total	**580,765**	**817,678**	**€380,953**

15.2. Total amounts set aside or accrued by the issuer or its subsidiaries to provide pension, retirement or similar benefits

There are no outstanding advances or loans to the members of the Board of Directors or of management, nor are there any pension or life insurance obligations in respect of former and current members of the Board of Directors, and no obligations have been guaranteed on their behalf.

16. BOARD PRACTICES

16.1. Date of expiration of the current term of office, if applicable, and the period during which the person has served in that office

Pursuant to article 36 of the Bylaws and article 16 of the Regulations of the Board of Directors, directors shall serve in their position for a term of four (4) years and may be re-elected on one or more occasions for terms of the same maximum length.

Based on the foregoing, below is a table showing the period during which the directors of the Company hold their respective offices according to the date of their appointment:

Name	Date of appointment	Date of expiration of term of office
Mr. Carlos Manuel Buesa Arjol	11/03/2015	11/03/2019
Ms. Tamara Maes	11/03/2015	11/03/2019
Mr. José María Echarri Torres	11/03/2015	11/03/2019
Mr. Antonio Fornieles Melero	11/03/2015	11/03/2019
Mr. Ramón Adell Ramón	11/03/2015	11/03/2019
Ms. Isabel Aguilera Navarro	11/03/2015	11/03/2019
Mr. José Carlos Gutiérrez Ramos	02/19/2018	11/03/2019

16.2. Information about members of the administrative, management or supervisory bodies' service contracts with the issuer or any of its subsidiaries providing for benefits upon termination of employment, or an appropriate negative statement

The executive director, Mr. Carlos Manuel Buesa Arjol, is entitled to benefits upon termination of his duties, in accordance with the contract in effect executed by him and the Company.

If such contract is terminated at the request of ORYZON for any reason, including those established in the Bylaws, and which is not with respect to a serious or negligent breach of the duties of the executive director, the director shall have the right to receive a severance payment in an amount equal to two (2) times the total annual salary (fixed compensation and annual variable compensation) in effect at the time of termination of the relationship. The amount of the last annual variable compensation actual received shall be taken into account for these purposes.

Furthermore, if ORYZON does not give notice of the termination of employment within the time and upon the terms set out in the contract, the Company must pay Mr. Carlos Manuel Buesa Arjol severance compensation equal to six (6) times his monthly salary for the then-current year.

Mr. Carlos Manuel Buesa Arjol would have the right to the severance set out in the preceding paragraph if he decides to terminate his contract unilaterally as a result of a change in control (whatever the form thereof) or change in the current shareholders of the Company entailing a change in control thereof, as well as in the case of termination of the contract by unilateral decision thereof if the decision to terminate such relationship is based on a serious or negligent breach by ORYZON of the duties incurred with respect to his position or if there is a material reduction in the duties or powers thereof.

In addition, Mr. Carlos Manuel Buesa Arjol is subject to a non-compete agreement both during the term of the employment contract as well as after termination thereof for a period of twelve (12) months from the date he ceases to provide services as executive director. The consideration

for signing the non-compete agreement will be 75% of the overall compensation of the executive director during the fiscal year in which the termination of his services occurs, and must be paid at the time of termination of the employment contract. Without prejudice to the foregoing, the Company reserves the right to release the executive director from the application of this clause within a period of thirty (30) days following the termination of the contract, without the application of any indemnification.

The executive director Ms. Tamara Maes also has benefits upon the termination of her duties in accordance with the contracts in effect signed by her and the Company.

If such contract is terminated by ORYZON for any reason, including those set forth in the Bylaws, and is not related to a serious or willful breach by the executive director, she shall have the right to receive severance pay in an amount equal to the maximum to which she would have been entitled in the event of a termination declared to be improper under an ordinary labor relationship.

Furthermore, if ORYZON does not give notice of termination of the relationship within the period and upon the terms set forth in the contract, the Company must pay the executive director compensation equal to three (3) monthly payments of her compensation.

The executive director would have the right to the severance pay indicated in the preceding paragraph if she decides to terminate her contract unilaterally as a result of a change in control (whatever the form thereof) or change in the current shareholders of the Company entailing a change in control thereof, as well as in the case of termination of the contract by unilateral decision thereof if the decision to terminate such relationship is based on a serious or negligent breach by ORYZON of the duties incurred with respect to her position or if there is a material reduction in the duties or powers thereof.

Finally, severance pay equal to 75% of the overall compensation of the executive director is established for the post-contractual non-compete agreement for twelve (12) months from the date of termination of the relationship.

16.3. Information about the issuer's audit committee and remuneration committee, including the names of committee members and a summary of the terms of reference under which the committee operates

The Bylaws and the Regulations of the Board of Directors of the Company provide for the creation of an Audit and Compliance Committee and an Appointments and Compensation Committee, and set the rules for the operation thereof.

Below is a description of the structure and the duties assigned to each of the aforementioned committees in accordance with the provisions of the Bylaws and the Regulations of the Board of Directors.

16.3.1. Audit and Compliance Committee

The rules for the organization and operation of the Audit and Compliance Committee, which are described below, are set out in article 42 of the Company's Bylaws and in article 28 and in article 28 *bis* of the Regulations of the Board of Directors. The Audit and Compliance Committee held six (6) meetings during 2017.

16.3.1.1. Composition

The Audit and Compliance Committee shall be made up of a minimum of three (3) and a maximum of five (5) members, at least a majority of whom must be independent, to be appointed by the Board of Directors. Diversity shall be sought in the composition of the Audit

and Compliance Committee, particularly as regards gender, professional experience, skills and industry knowledge. In any case, at least one of the members of such Committee must be appointed taking into account the knowledge and experience thereof in the areas of accounting, auditing or risk management.

Overall, the members of the Audit and Compliance Committee shall have relevant technical knowledge relating to the Company's industry.

A director who is appointed a member of the Audit and Compliance Committee shall serve for the unexpired portion of such director's term of office, without prejudice to the following grounds for cessation in office: (i) loss of status as a director of the Company; (ii) loss of status as a non-executive director; (iii) expiration of the period for which the director was appointed without being re-elected; (iv) resolution of the Board of Directors; (v) resignation from the Audit and Compliance Committee; and (vi) breach of legal provisions or the bylaws or regulations of the Company.

The Chair of the Audit and Compliance Committee must be an independent director elected from among the external directors, must be replaced every four (4) years, and may be re-elected after the passage of one year from the date when he ceased to hold office, without prejudice to the continuation or re-election thereof as a member of such Committee. The Chair shall act as the spokesperson of the Audit and Compliance Committee at meetings of the Board of Directors and, if applicable, at the General Shareholders' Meeting of the Company.

The Board of Directors may appoint a Secretary, who need not be a member of the Audit and Compliance Committee, who shall assist the Chairman and must provide for the proper operation of such Committee, duly reflecting the proceedings of meetings, the deliberations and the resolutions adopted in the minutes.

As of the date of this document, the composition of the Audit and Compliance Committee is as follows:

Name	Position	Nature
Mr. Ramón Adell Ramón	Chair	Independent
Mr. Antonio Fornieles Melero	Member	Independent
Ms. Isabel Aguilera Navarro	Member	Independent

16.3.1.2. Operation

Pursuant to the provisions of article 42 of the Bylaws and article 28 of the Regulations of the Board of Directors, the rules of operation of the Audit and Compliance Committee may be summarized as follows:

- The Audit and Compliance Committee shall ordinarily meet on a quarterly basis in order to review the periodic financial information that must be sent to stock exchange authorities as well as the information that the Board of Directors must approve and include within its annual public documentation. It shall also meet whenever its members so request and whenever called by the Chair, who must do so whenever the Board or its Chair requests the issuance of a report or the adoption of proposals, and in any event when appropriate for the proper performance of its duties.
- The Audit and Compliance Committee must report on its activities and answer for the work performed at the first meeting of the full Board of Directors after its meetings. The Audit and Compliance Committee must also keep minutes of its meetings and send

a copy thereof to all members of the Board of Directors. The Board of Directors shall deliberate on the proposals and reports submitted thereto by the Audit and Compliance Committee.

- A valid quorum for Audit and Compliance Committee meetings shall be established with the attendance, in person or by proxy, of one half plus one of its members. Unless the Companies Act (*Ley de Sociedades de Capital*), the Bylaws or the Regulations of the Board provide otherwise based on the nature of the resolutions to be adopted, the resolutions of the Audit and Compliance Committee shall be adopted with the favorable vote of one half plus one of its members present in person or by proxy at the meeting. In the event of a tie, the Chair of the Audit and Compliance Committee shall have the tie-breaking vote.

- To best perform its duties and the objectives assigned thereto efficiently, the Audit and Compliance Committee shall have the resources necessary to satisfactorily achieve them, which shall be provided by the Company. The Audit and Compliance Committee may obtain the advice of external advisors regarding legal, accounting, valuation, risk or any other matter if it so deems necessary. It may also call to the meeting any employee or officer of the Company, and even provide that they appear without the presence of any other officer. Along these lines, the attendance thereof or of other persons at meetings of the Audit and Compliance Committee must be preceded by an invitation sent by the Chair thereof and be limited only to those items on the agenda for which they are called. Furthermore, the Audit and Compliance Committee shall establish an annual working plan including, among other things, an annual meeting schedule, the planning thereof and channels for regular communication with the officers of the Company, the Director of Internal Audit and the statutory auditor, and the provision, to the extent possible, of having external experts to advise on the performance of any of the duties of the Audit and Compliance Committee. The planning of the meetings of the Audit and Compliance Committee must take into account that the members thereof mainly have supervisory and advisory duties and should not intervene in execution or management proper to the management and the executive bodies of the Company.

- The members of the Audit and Compliance Committee shall engage in sufficient questioning of the data, the evaluation processes and the conclusions previously reached by the executives and officers of the Company. This means a critical attitude, not automatically accepting the opinions thereof, acknowledging the arguments for and against and forming their own position both at the individual level of each of its members and at the group level. They must also act with independent judgement and action and must perform their work with the maximum diligence and professional competence possible. In particular, attendance at the meetings of such committee shall be preceded by sufficient dedication of its members to analyzing and evaluating the information received, which shall be made available thereto by the Chair of the Audit and Compliance Committee with the help of the Secretary sufficiently in advance of each meeting for them to properly analyze it and prepare for the meeting unless the meeting is held or called urgently on an exceptional basis.

- The Board of Directors may approve the performance of the work of internal auditing by a specific manager. In such event, it shall appoint a Director of Internal Audit and head of such function, taking into account the knowledge and experience thereof in the areas of accounting, auditing or risk management. In such case, the Director of Internal Audit must: (i) submit to the Audit and Compliance Committee a working plan

and report directly thereto on the events occurring during the preparation thereof; and (ii) at the end of each fiscal year submit an annual report on its activities to the Audit and Compliance Committee.

16.3.1.3. Duties

The Audit and Compliance Committee shall have at least the following basic duties:

- To inform the shareholders at the General Shareholders' Meeting about issues that arise in relation to matters within the purview of the Audit and Compliance Committee, and particularly regarding the results of the audit, explaining how it has contributed to the integrity of the financial information and the function that the Company has performed in such process.
- To supervise the effectiveness of the internal control of the Company, internal audit, and risk management systems, as well as to discuss with the auditor any significant weaknesses in the internal control system detected during the course of the audit, all without diminishing the independence thereof. For such purposes, they may submit recommendations or proposals to the Board of Directors and the corresponding period for follow-up.
- To supervise the process of preparing and presenting mandatory financial information and to submit recommendations or proposals to the Board of Directors to protect the integrity thereof.
- To make proposals to the Board of Directors to select, appoint, re-elect and replace the statutory auditor, taking charge of the selection pursuant to the applicable legal provisions in this regard, as well as the conditions for engaging the auditor, including regularly reviewing information relating to the audit plan and its execution with the auditor, as well as ensuring its independence in the performance of its duties.
- To establish appropriate relationships with the external auditor in order to receive information about any issues that might entail a threat to its independence, so that these may be examined by the Audit and Compliance Committee, and any other matters related to the process of auditing the accounts, and, when applicable, the approval of services other than those that are prohibited upon the terms contemplated in applicable legal provisions on the rules for independence, as well as any other communications required under the laws on auditing and audit regulations. In any event, it must receive the auditor's annual declaration of independence in relation to the Company or entities directly or indirectly associated therewith, as well as detailed and individualized information about any type of additional services provided by it and the corresponding fees received from these entities by the external auditor or by the persons or entities associated therewith, in accordance with the laws on auditing, all without prejudice to the laws and regulations governing audits.
- To issue on an annual basis, prior to the issuance of the audit report, a report expressing an opinion on whether the independence of the statutory auditors or audit firms has been compromised. This report must in all cases contain an reasoned assessment of the provision of each and every one of the additional services referred to in the preceding letter, considered both individually and collectively, other than the statutory audit services, and in relation to the system of independence or the legal provisions governing auditing, all without prejudice to the laws on the activity of auditing of accounts.

- To inform the Board of Directors, in advance, about all of the issues required by law, the Bylaws and these Regulations, and particularly regarding: (i) the financial information that the Company must periodically publish; (ii) the creation or acquisition of equity interests in special purpose entities or entities domiciled in countries or territories that are considered to be tax havens; and (iii) related-party transactions.
- To perform those duties assigned thereto in the Internal Regulations for Conduct, as head of compliance thereof, receiving the reports and notices resulting from the provisions of such Internal Regulations for Conduct.
- To examine compliance with the Internal Regulations for Conduct, the Regulations of the Board of Directors, and the Company's governance rules generally, and make such proposals as are deemed necessary for the improvement thereof.
- To receive information and, if applicable, issue reports on disciplinary measures to be imposed on the members of the Company's senior management team.

Additionally, the Audit and Compliance Committee shall have the following duties:

1. With relation to the internal information and control systems:

- To supervise the preparation process and integrity of the financial information relating to the Company and, if applicable, to the group, reviewing compliance with regulatory requirements, the proper definition of the consolidation perimeter and the correct application of accounting criteria.
- To ensure the independence of the unit that assumes the internal audit duty, if applicable; to propose the selection, appointment, re-election and removal of the head of the internal audit service; to propose the budget for such service; to approve its orientation and working plans, ensuring that its activity is mainly focused on the significant risks that the Company faces; to receive regular information regarding its activities; and to verify that senior management takes into account the conclusions and recommendations of its reports.
- To establish and supervise a mechanism that permits employees to confidentially and, if possible and deemed appropriate, anonymously, report potentially significant irregularities, especially financial and accounting, that arise within the company.

2. With relation to the external auditor:

- In the case of withdrawal of the external auditor, to examine the circumstances that gave rise to it.
- To ensure that the remuneration of the external auditor for its work does not compromise its quality or independence.
- To oversee the Company notifying the CNMV of the change of auditor as a significant event (*hecho relevante*) and attaching thereto a statement on the possible existence of discrepancies with the outgoing auditor and, if any exist, their content.
- To ensure that the external auditor holds an annual meeting with the full board of directors to report on the work it has carried out and on the evolution of the Company's accounting and risk situation.
- To ensure that the Company and the external auditor respect applicable law regarding the provision of services other than audit services, the limits on concentration of the auditor's business and, in general, the other regulation on independence of auditors.

3. To assess everything relating to non-financial risks of the company, including operational, technological, legal, social, environmental, political and reputational risks.

The Audit and Compliance Committee must in all cases be informed regarding operations involving structural and corporate modification that the Company plans to undertake, in order for it to analyze them and make a prior report to the Board of Directors on their financial conditions and accounting impact and particularly, where applicable, on the proposed exchange ratio.

It should be noted that at its meeting held on April 4, 2018, after a favorable proposal from the Chair, the Board of Directors resolved to amend the Regulations of the Board of Directors to conform them to the amendments of the Bylaws approved by the shareholders at the Ordinary General Shareholders' Meeting held on April 4, 2018. Such amendments, which are reflected in this Registration Document, were converted into a public instrument by deed executed before the Notary of Madrid, Ms. Eloísa López-Monís Gallego, on May 20, 2018 and recorded in her notarial book of records under number 932 and 934, respectively, and registered with the Commercial Registry of Madrid on June 18, 2018 in Volume 36,533, Folios 137 and 138, respectively, Sheet M-656493, Entries 7 and 9.

16.3.2. Appointments and Compensation Committee

The rules of organization and operation of the Appointments and Compensation Committee described below are set out in article 43 of the Bylaws of the Company and in article 27 and article 27 *bis* of the Regulations of the Board of Directors. The Appointments and Compensation Committee held six (6) meetings during 2017.

16.3.2.1. Composition

The Appointments and Compensation Committee shall be made up of a minimum of three (3) and a maximum of five (5) directors, all non-executive (and at least two (2) of whom must be independent), to be appointed by the Board of Directors.

The members of the Appointments and Compensation Committee shall be appointed taking into account their expertise, qualifications and experience and the objectives of the Committee.

A director who is appointed as a member of the Appointments and Compensation Committee shall serve for the unexpired portion of such director's term of office, without prejudice to the Board of Directors' power of revocation, and which shall in any event become ineffective due to cessation in office as a director of the Company.

The Chair of the Appointments and Compensation Committee must be an independent director elected from among the external directors, must be replaced every four (4) years, and may be re-elected after the passage of one (1) year from the date when he ceased to hold office.

The Board of Directors may appoint a Secretary, who need not be a member of the Appointments and Compensation Committee, who shall assist the Chair and must provide for the proper operation of such Committee, duly reflecting the proceedings of meetings, the deliberations and the resolutions adopted in the minutes.

As of the date of this document, the composition of the Appointments and Compensation Committee is as follows:

Name	Position	Nature
Ms. Isabel Aguilera Navarro	Chair	Independent
Mr. Ramón Adell Ramón	Member	Independent

Mr. Antonio Fornieles Melero	Member	Independent
Mr. José Carlos Gutiérrez Ramos	Member	Independent

16.3.2.2. Operation

Pursuant to the provisions of article 43 of the Bylaws and article 27 of the Regulations of the Board of Directors, the rules of operation of the Appointments and Compensation Committee may be summarized as follows:

- The Appointments and Compensation Committee shall ordinarily meet on a quarterly basis. It shall also meet whenever called by its Chair, who must do so whenever the Board of Directors or its Chair requests the issuance of a report or the adoption of proposals, and in any event when appropriate for the proper performance of its duties.
- The Appointments and Compensation Committee must report on its activities and answer for the work performed at the first meeting of the full Board of Directors after its meetings. The Appointments and Compensation Committee must also keep minutes of its meetings, and send a copy thereof to all members of the Board of Directors. The Board of Directors shall deliberate on the proposals and reports submitted thereto by the Committee.
- A valid quorum for Appointments and Compensation Committee meetings shall be established with the attendance, in person or by proxy, of one-half plus one of its members. Unless the Companies Act, the Bylaws or the Regulations of the Board of Directors provide otherwise based on the nature of the resolutions to be adopted, the resolutions of the Appointments and Compensation Committee shall be adopted with the favorable vote of more than one-half of its members present in person or by proxy at the meeting. In the event of a tie, the Chair of the Appointments and Compensation Committee shall have the tie-breaking vote.
- The Appointments and Compensation Committee may obtain the advice of external experts if it so deems necessary for the better performance of its duties.
- A request for information from the Appointments and Compensation Committee shall be made by the Board of Directors or the Chair thereof.
- Any director may request that the Appointments and Compensation Committee consider potential candidates to fill vacancies if they find them to be appropriate. The Appointments and Compensation Committee must also consider the suggestions made thereto by the members of the Board of Directors, the officers, or the shareholders of the Company.

16.3.2.3. Duties

Without prejudice to the other duties assigned to it by the law, the Bylaws or the Regulations of the Board of Directors, the Appointments and Compensation Committee shall have at the least the following powers:

- To assess the skills, knowledge and experience required by the Board of Directors. For such purposes, the Committee shall define the functions and skills required by candidates for each vacancy and assess the time and dedication required for the role to be efficiently performed.
- To establish a goal for representation by the less represented gender on the Board of Directors and prepare guidance on how to reach this objective.

- To bring proposed appointments of independent directors to the Board of Directors for appointment on an interim basis to fill a vacancy or for submission of such proposals to a decision by the shareholders at the General Shareholders' Meeting, as well as proposals for the re-election or removal of such directors by the shareholders at the General Shareholders' Meeting.
- To report on proposed appointments of the other directors for appointment on an interim basis to fill a vacancy or for submission of such proposals to a decision by the shareholders at the General Shareholders' Meeting, as well as proposals for the re-election or removal thereof by the shareholders at the General Shareholders' Meeting.
- To report on proposals for the appointment and separation of the members of senior management and the basic terms of their contracts.
- To analyze and organize the succession of the Chair of the Board of Directors and the chief executive officer of the Company, and make proposals to the Board of Directors so that this succession occurs in an organized and planned way, as appropriate.
- To propose to the Board of Directors the compensation policy for directors and general managers or of those people that perform senior management functions reporting directly to the Board of Directors, the executive committees or the chief executive officers, as well as the individual compensation and other contractual conditions of executive directors, ensuring that these conditions are fulfilled.

The Appointments and Compensation Committee shall also have the following duties:

- To propose to the Board of Directors the basic conditions of the contracts of senior management.
- To confirm observance of the Compensation Policy established by the Company.
- To periodically review the compensation policy applicable to directors and senior management, including share compensation systems and their application, as well as to ensure that their individual compensation is proportionate to that paid to the Company's other directors and senior management.
- To ensure that potential conflicts of interest do not prejudice the independence of the external advice provided to the committee.
- To verify the information on compensation of directors and senior management contained in the various corporate documents, including the annual director compensation report.
- To oversee compliance with the Company's internal codes of conduct and corporate governance rules.
- To oversee the shareholder and investor communication and relations strategy, including small and midsize shareholders.
- To periodically assess the adequacy of the Company's corporate governance system, in order for it to meet its purpose of promoting the corporate interest and to take into account the legitimate interests of the other stakeholders, as applicable.
- To review the Company's corporate responsibility policy, ensuring that it is focused on the creation of value.
- To monitor corporate social responsibility strategy and practices and to assess levels of compliance therewith.

- To supervise and assess processes involving relations with the various stakeholders.
- To coordinate the non-financial and diversity information reporting process, in accordance with applicable law and with international standards.

16.4. A statement as to whether or not the issuer complies with its country's of incorporation corporate governance regime(s). In the event that the issuer does not comply with such a regime, a statement to that effect must be included together with an explanation regarding why the issuer does not comply with such regime

ORYZON complies with currently applicable Spanish legal provisions regarding corporate governance. The Company reports on its level of compliance with the recommendations on an annual basis in the Annual Corporate Governance Report. Pursuant to the Annual Corporate Governance Report for fiscal year 2017, which is incorporated by reference in this document, of the total of sixty-four (64) recommendations of the Good Governance Code, at the time of publication of such report, the Company met thirty-nine (39) recommendations, eleven (11) were not applicable thereto (recommendations 2, 10, 11, 19, 23, 24, 37, 38, 48, 52 and 62), six (6) were partially met (recommendations 4, 5, 20, 46, 54 and 55) and eight (8) recommendations were explained (recommendations 1, 7, 16, 59, 60, 61, 63 and 64).

Except as expressly provided, the recommendations set out below are partially met or are not met by the Company as of the date of this document:

- Recommendation 1, regarding bylaw restrictions that limit the casting of a maximum number of votes or hinder a takeover of the Company through the acquisition of its shares on the market: the Company did not comply with such recommendation because existing shareholder agreements in effect at that time, the Bylaws and the Regulations of the Board of Directors required a majority of four-fifths of the directors for approval of certain resolutions.

  Notwithstanding the foregoing, as of the date of registration of this document, the Company complies with such recommendation given that the shareholders acting at the Ordinary General Shareholders' Meeting held on April 4, 2018 approved an amendment to the Bylaws for purposes of eliminating the heightened quorum and voting requirements with respect to the Board of Directors. Likewise, at its meeting held on April 4, 2018, the Board of Directors resolved to amend the Regulations of the Board of Directors to conform them to the aforementioned amendments of the Bylaws. Both the amendment of the Bylaws and the amendment of the Regulations of the Board of Directors are registered with the Commercial Registry of Madrid and contained in this Registration Document.
- Recommendation 4, regarding the policy for communication and contacts with shareholders, institutional investors and proxy advisors: the Company complies with the aforementioned recommendation in part because, although it is governed by the principles of: (i) transparency, ensuring similar treatment to shareholders in the same position; (ii) development of reporting channels; and (iii) regulatory compliance, given its capitalization and nature, for the time it is not deemed necessary to formalize a specific policy and proceed to the publication thereof. In turn, for purposes of the principle of transparency, the Company inserted press releases and corporate presentations for the general knowledge of its shareholders on its corporate website (www.oryzon.com) throughout the year.
- Recommendation 5, regarding the proposed delegation of powers to issue shares or convertible securities without pre-emptive subscription rights for an amount

exceeding 20% of capital at the time of such delegation. The Company complies partially because, during the single capital increase that occurred in fiscal year 2017, the Board of Directors used a delegation of powers from the shareholders that was limited to an amount of no more than 20% of capital at the time of the delegation. In addition, during such capital increase with the exclusion of pre-emptive subscription rights, the Company immediately published on its corporate website (www.oryzon.com) the reports relating to such referred to in commercial legislation. However, on April 4, 2018, the shareholders acting at the Ordinary General Shareholders' Meeting approved a delegation of powers to issue shares or convertible securities with the exclusion of pre-emptive subscription rights in an amount greater than 20% of the capital at the time of such delegation.

- Recommendation 7, regarding the broadcast of the General Meetings live on its website: given its size and capitalization, the Company does not broadcast the General Meetings live.

- Recommendation 16, regarding the percentage of proprietary directors out of all non-executive directors: the Company does not comply with this recommendation, given the percentage of proprietary directors out of all non-executive directors of ORYZON is greater than the existing proportion between the capital of the Company represented by such directors and the rest of the capital, because Mr. José María Echarri Torres was appointed as a proprietary director of the Company when he became a shareholder thereof.

- Recommendation 20, regarding the resignation of proprietary directors when the shareholder they represent disposes of its ownership in its entirety or reduces its stake to a level requiring a reduction in the number of its proprietary directors: the Company complies in part, since although the Regulations of the Board of Directors contains such a provision, article 16 thereof provides that a director who loses their proprietary status will not be removed if the Board of Directors finds, after a report of the Appointments and Compensation Committee, that there are grounds for such director to remain, without prejudice to the impact that the new prevailing circumstances may have on the classification of the director. Based on the foregoing, ORYZON partially complies as it has deemed it appropriate to exclude the obligation of the director to resign in the instances provided for in such recommendation, because it is clear that the high level of awareness of ORYZON and of the industry in which it operates may in certain cases justify their remaining on the Board of Directors. However, the decision must be made by the Board of Directors after a favorable report from the Appointments and Compensation Committee, which must find the occurrence of the grounds in favor of remaining.

- Recommendation 46, regarding the existence of a specialized committee of the Board of Directors with internal control and risk management duties: the Company partially complies with this recommendation given that, due to its size, such duty is currently delegated to the internal audit unit, which reports to the Audit and Compliance Committee.

- Recommendation 54, regarding the corporate social responsibility policy: the Company partially complies with this recommendation, given that the Company's corporate social responsibility policy does not include all of the principles contained in this recommendation - in particular, it does not include methods for monitoring the results of corporate social responsibility practices. In addition, the Company is not

currently required to report non-financial information, given its status as a public interest entity with an average of less than five (500) employees, for which reason the size of the Company and the costs that it would incur to establish analysis methods for monitoring the results of corporate social responsibility activities would go against the principle of financial viability, which should prevail in the management of financial resources.

- Recommendation 55, regarding the methodologies for preparing the report on corporate social responsibility developments, the Company partially complies with this recommendation, because although the Company is not currently required to report non-financial information given its status as a public interest entity with less than five hundred (500) employees, it has prepared a report on corporate social responsibility issues that does not only follow internationally accepted methodologies in this area. The size of ORYZON and the costs that it would incur to issue a report prepared only following internationally accepted methodologies in the area of corporate social responsibility would go against the principle of financial viability, which should prevail in the management of financial resources.

- Recommendation 59, regarding the deferral of payment of a major part of variable remuneration components for a long enough period to ensure that predetermined performance criteria have effectively been met, the Company does not comply with such recommendation because the variable component of the compensation of the executive directors is currently made up of a short-term element and a medium-term element, for which reason, through the multi-annual incentive, ORYZON measures the achievement of the executive directors' performance over a period greater than one year. The executive are also fully aligned with the evolution and solvency of the entity due to their high percentage interest in the share capital due to their status as founding shareholders of the Company.

- Recommendation 60, that remuneration linked to Company earnings should bear in mind any qualifications stated in the external auditor's report that reduce their amount: the Company does not comply with such recommendation because the system for variable compensation of the executive directors does not expressly contemplate it, although the Appointments and Compensation Committee evaluates the level of achievement of the incentive once it has the audited financial statements of the Company, such that it bears in mind such qualifications when determining the level of achievement of the objectives and the percentage of variable compensation achieved.

- Recommendation 61, regarding the linking of executive directors' variable compensation to the delivery of shares: the Company does not comply with such recommendation because, owing to the dual nature of executive directors as founding shareholders, they hold a sufficiently large shareholding. However, ORYZON does not rule out the use of these forms of compensation in the future if it is appropriate.

- Recommendation 63, regarding the reimbursement of the variable components of compensation, given that although ORYZON has included clauses for the recovery of compensation received by the directors for their collective duties, taking into account their particular circumstances, the Company believes that it has not be necessary to include this clause within the executive director variable compensation system, to the extent that they have a high interest in the share capital due to their status as founding shareholders of the Company, for which reason they are not in any case incentivized

to assume risks that exceed the level tolerated thereby. Furthermore, the executive director annual variable compensation system includes specific clauses that allow the Company not to pay a portion of the accrued variable compensation if certain circumstances determined by the Board of Directors do/do not occur.

- Recommendation 64, regarding payments upon termination of the agreement do not exceed an amount equal to two (2) years of total annual compensation and are not paid until the Company has been able to verify that the director has met previously-established performance criteria: the Company does not comply with this recommendation because such severance payment is not subject to the Company verifying that the Director has met the previously-established performance criteria..

On an annual basis, the Board of Directors of the Company shall, upon a prior report of the Audit and Compliance Committee, prepare the Annual Corporate Governance Report, to be approved by the shareholders at the General Shareholders' Meeting.

The Company also has a corporate website (www.oryzon.com) through which it keeps its shareholders and the market in general apprised of any significant events that may occur in connection with the Company. The contents and structure of such website complies with applicable laws and regulations.

17. EMPLOYEES

17.1. Number of employees at the end of the period or the average for each financial year for the period covered by the historical financial information and a breakdown of persons employed by main category of activity and geographic location.

The following table shows the final number of employees broken down by professional categories during the fiscal years ended on December 31, 2015, 2016 and 2017:

Professional category	03.31.2018	12.31.2017	12.31.2016	12.31.2015	% change 12.31.2017/2016	% change 12.31.2016/2015
Directors	2	2	2	2	0%	0%
Area managers	4	4	4	4	0%	0%
Researchers	16	16	13	11	23.1%	18.1%
Laboratory technicians	10	10	11	7	(9.1)%	57.1%
Staff	8	7	7	4	0%	75%
Total	**40**	**39**	**37**	**28**	**5.4%**	**32.1%**

The average number of temporary employees during fiscal years 2015, 2016 and 2017 was as follows:

Temporary employees	03.31.2018	12.31.2017	12.31.2016	12.31.2015
Temporary employees	5	4.8	3.3	2.1

17.1.1. Restructuring Plans

As of the date of registration of this document, there are no restructuring plans, nor are any such plans foreseen.

17.1.2. Pension Plans

As of the date of registration of this document, the Company does not offer, nor does it plan to offer its employees, the possibility of subscribing to pension plans.

17.2. Shareholdings and stock options

In 2007, the Company approved a compensation system for its executive officers and directors based on the delivery of stock or of stock options of the Company. The stock option plan was initially approved by the Board of Directors of the Company on September 26, 2007 and amended by the Board of Directors of the Company on August 1, 2014. On September 18, 2014, the shareholders at the General Shareholders' Meeting approved the restated text of the stock option plan.

During 2016, stock options were exercised for the first time by four (4) beneficiaries of the stock option plan. A total of 126,212 shares were delivered in the exercise of such rights.

During 2017, stock options were exercised by one (1) of the beneficiaries of the stock option plan. A total of 5,500 shares were delivered in the exercise of such rights.

At the date of registration of this document, there are no stock options offered to the beneficiaries of such compensation system, as the term for executive officers and directors to exercise their rights under such system has expired.

17.2.1. ORYZON shares held by executive officers

The following table shows the number of ordinary shares of the Company owned by executive officers of the Company who are not members of the Board of Directors.

Direct shares	Indirect shares	% capital
54,510	-	0.15%

17.2.2. ORYZON shares held by the directors

The following table shows the number of ordinary shares of the Company controlled by the directors of the Company who are shareholders of the Company as of the date of registration of the document:

Director	Direct shares	Indirect shares	% capital [(1)]
Mr. Carlos Manuel Buesa Arjol	3,742,530	-	10.96%
Ms. Tamara Maes	3,742,530	-	10.96%
Mr. José María Echarri Torres	1,026,928	-	3.01%
Mr. Ramón Adell Ramón	20,000	-	0.06%
Total	**8,531,988**	**-**	**24.99%**

[(1)] Percentages have been obtained from the website of the CNMV (www.cnmv.es) and recalculated by the Company pursuant to information from the latest capital increase implemented by the Company in April 2017.

17.3. Description of any arrangements for involving the employees in the capital of the issuer

There is no arrangement for involving the employees in the capital of ORYZON.

18. MAJOR SHAREHOLDERS

18.1. In so far as is known to the issuer, the name of any person other than a member of the administrative, management or supervisory bodies who, directly or indirectly, has an interest in the issuer's capital or voting rights which is notifiable under the issuer's national law, together with the amount of each such person's interest or, if there are no such persons, an appropriate negative statement

Below are the names of the persons or entities which, while not belonging to the administrative, management or supervisory bodies, directly or indirectly have a notifiable interest in the Issuer's capital or voting rights:

Shareholder	Direct shares	Indirect shares	% capital
Mr. José María Ventura Ferrero [(1)]	-	2,004,723	5.87%
Total	**-**	**2,004,723**	**5.87%**

[(1)] Through ARRIENDOS VENFERCA, S.L., a company indirectly controlled by Mr. José María Ventura Ferrero through VENAR FILLS, S.L. and EUROPE FOOD, S.L., which hold an interest of 73.12% and 4.23%, respectively, in ARRIENDOS VENFERCA, S.L.

18.2. Whether the issuer's major shareholders have different voting rights, or an appropriate negative statement

All shares representing the share capital of ORYZON are ordinary book-entry shares of the same class and series and grant the holders thereof the same voting, economic and like rights. Each share carries the right to one vote, and there are no preferred shares.

18.3. To the extent known to the issuer, state whether the issuer is directly or indirectly owned or controlled and by whom, and describe the nature of such control, and describe the measures in place to ensure that such control is not abused

There is no individual or legal entity that exercises direct or indirect control over the Company.

18.4. A description of any arrangements, known to the issuer, the operation of which may at a subsequent date result in a change in control of the issuer

The Company is not aware of the existence of any agreement, the operation of which may at a subsequent date give rise to a change in control of ORYZON.

19. RELATED PARTY TRANSACTIONS

The terms and conditions of related party transactions, as defined in Order EHA/3050/2004 of September 15, which must be reported by issuers of securities admitted to trading on official secondary markets pursuant to such Order, are the same as those for arm's-length transactions.

Below is a description of the transactions by ORYZON with related parties as of December 31, 2013, 2014, 2015 and as of June 30, 2016. It is also stated for the record that there have been no other related party transactions as of the date of this document.

19.1. Transactions with significant shareholders

In 2013 and within the framework of a process of reorganization of the Company's activity, the two (2) activities that the Company had been carrying out within a single structure, therapy and diagnosis, were segregated, giving rise to a new company named OGDSL.

During 2014, the Company divested OGDSL by means of the sale of shares representing 75.01% of OGDSL's share capital, and the remaining stake (24.99%) was reclassified to financial investment available for sale. The value of such shares was reviewed at fair value (such value corresponding to the most recent transaction regarding the sale of the 75.01% stake). Subsequently, on June 30, 2015, the remaining stake was fully impaired.

The sale of 75.01% of OGDSL's share capital was made to the ODSL BIOTECH investment consortium. The divestment did not amount to 100% of OGDSL due to the fact that such consortium was unable to secure financing for the acquisition of 100% of OGDSL.

Such consortium was made up of, among others, INVEREADY CAPITAL COMPANY, S.L., a company with a 43.98% interest in such consortium, of which Mr. José María Echarri Torres, a member of the Board of Directors of ORYZON and holder of 3.01% of the shares of the Company, is Chairman and Chief Executive Officer. The book value of ORYZON's 100% interest in OGDSL was EUR 526,139, and accordingly, following the sale of 75.01% for an amount of EUR 1,187,500, ORYZON obtained a capital gain of EUR 792,843.

Of the total amount of the transaction, i.e., EUR 1,187,500, EUR 1,050,000 was paid in cash, while payment of the balance, EUR 137,500, was deferred through promissory notes payable in twenty-four (24) months, with monthly due dates, and which had been fully collected as of June 30, 2016. All payments of the matured promissory notes were made on the due date of each of such notes. In the same manner, on carrying out the sale of 75.01% of OGDSL, the Company simultaneously effected an increase in the share capital of OGDSL in the total amount of EUR 150,000, of which EUR 37,485 corresponded to 24.99% of the interest (contributed by ORYZON) and the remaining amount was contributed by the purchaser of the 75.01% (investment consortium ODSL BIOTECH). As a result, the interest had a recorded book value in ORYZON of EUR 168,967.

The fair value of this interest was established on the basis of the last available transaction, corresponding to the amount of the sale of 75.01%, generating an net asset value adjustment in the amount of EUR 169,991 (75% of the increase in value) and a deferred tax liability in the amount of EUR 56,664 (25% of the increase in value). ORYZON's 24.99% interest in OGDSL was impaired in its entirety in 2015 as a result of the reduction in such company's financial capacity and in its cash assets. Such impairment entailed a depreciation of EUR 168,967 for ORYZON in 2015, which was charged to income, as well as the cancellation of the value included in value adjustments of EUR 169,991 and the cancellation of deferred tax liabilities in the amount of EUR 56,664.

During the first half of 2016, the remaining 24.99% was sold for the amount of EUR 150,000, recording this amount in the profit and loss statement under impairment and gains or losses from disposal of financial instruments, for which reason, as of the date hereof, ORYZON has no influence on and no link to this entity, nor does it hold any interest therein.

On March 2017, within the framework of the Company's capital increase in April 2017, an agreement was executed for the loan of shares by the shareholders Mr. Carlos Buesa (229,000 shares) and NAJETI CAPITAL S.A. (4,100,000 shares) to INVEREADY VENTURE FINANCE II SCR PYME, S.A. (an entity of the INVEREADY Financial Group, of which the shareholder and member of the Board of Directors Mr. José María Echarri Torres is the Chair), as a mechanism to facilitate the placement of shares among qualified investors in the U.S., pursuant to which the Company gave various indemnities to Mr. Carlos Manuel Buesa Arjol and to NAJETI CAPITAL, S.A. for a period of four (4) years (until July 25, 2022) and with a maximum limit of 615,000 in both cases.

INVEREADY VENTURE FINANCE II SCR, PYME, S.A. also signed a financial intermediation agreement with the Company, for which it received a fee of EUR 103,896.

In addition, INVEREADY INNVIERTE BIOTECH II SCR, S.A. (an entity of the INVEREADY Financial Group, of which the shareholder and member of the Board of Directors Mr. José María Echarri Torres is the Chair) subscribed 200,000 new shares of the Company for EUR 640,000 within the framework of the 2017 capital increase described in section 10.1.1.1 of Section II of this document.

It should be noted that such transactions were the subject of a favorable report by the Audit and Compliance Committee and were approved by the Board of Directors with the corresponding abstention by the directors affected by such transactions.

Notwithstanding the foregoing, the terms and conditions of the transactions by the Company with related parties, as defined in Order EHA/3050/2004 of September 15 and which must be reported pursuant to the aforementioned Order by the issuers of securities admitted to trading on official secondary markets, are equivalent to those of transactions made on an arm's-length basis.

19.2. Transactions by members of the Board of Directors who are members of the senior management of ORYZON

The only transactions by the members of the Board of Directors who are also members of the Company's senior management are collection of the compensation described in section 15.1.2 of Section II of this document.

With the exceptions described above, during the period covered by the historical financial information of this document, no member of the Board of Directors or any other member of the Company's senior management, none of their close relatives (within the meaning of Order EHA/3050/2004 of September 15, 2004 concerning information on related party transactions) or any other company controlled by such persons or in which such persons exercise a significant influence has engaged in unusual or significant transactions with the Company, aside from the compensation accrued in favor of the members of the Board of Directors and of senior officers, which expense is reported in detail in section 15 of Section II of this document.

As of December 31, 2015, 2016 and 2017, no advances or loans had been provided to senior officers or to the members of the Board of Directors, nor had any obligations been guaranteed on their behalf.

19.3. Transactions between persons, companies or entities of the group

During fiscal years 2017, 2016 and 2015, there were transactions with the following related parties:

Company	2017	2016	2015
ORYZON CORP	-	Company of the Group	Company of the Group

The following is a description of transactions with related parties:

Related Party Transactions						
	2017		2016		2015	
	Sales/ (purchases)	Financial Income	Sales/ (purchases)	Financial Income	Sales/ (purchases)	Financial income
Group companies	-	-	(101,105)	19,226	(362,059)	18,722
Related entities	-	-	-	-	-	-
Total	**-**	**-**	**(101,105)**	**19,226**	**(362,059)**	**18,722**

The pricing policy followed in all transactions results from the application of the normal market value, pursuant to section 16 of the Corporate Income Tax Act (*Ley de Impuestos de Sociedades*).

The table below shows the breakdown of balances with related parties:

Balances with related parties						
	12.31.2017		12.31.2016		12.31.2015	
	Assets	Liabilities	Assets	Liabilities	Assets	Liabilities
	Debit bal.	Credit bal.	Debit bal.	Credit bal.	Debit bal.	Credit bal.
	Loan & int.	Purchases & serv.	Loan & int.	Purchases & serv.	Sales & serv.	Debts
Group company	-	-	-	-	293,296	(65,613)
Related entity	-	-	-	-	-	-
Total	-	-	-	-	**293,296**	**(65,613)**

As of December 31, 2015, loans and interest in the amount of EUR 293,296 were made up of a loan provided by the Issuer to ORYZON CORP. in the amount of EUR 274,574 and EUR 18,722 in accrued interest. As of December 31, 2017, interest for loans provided by the Issuer to ORYZON CORP. was EUR 19,226 and there were no loan balances with such entity, as it was resolved to dissolve and liquidate ORYZON CORP., which was duly recorded with the Secretary of State of the State of Delaware on December 29, 2016, causing a partial recovery of the loan in the amount of EUR 251,775. There were no balances with related parties as of December 31, 2017.

20. FINANCIAL INFORMATION CONCERNING THE ISSUER'S ASSETS AND LIABILITIES, FINANCIAL POSITION AND PROFITS AND LOSSES

20.1. Historical financial information

Basis of presentation and accounting principles

The historical financial information included in this section refers to the financial statements ended December 31, 2017, 2016 and 2015, prepared in accordance with the National Chart of Accounts (*Plan General de Contabilidad*), and which are incorporated by reference into this document.

GRANT THORNTON, S.L.P. audited the financial statements, which consist of the balance sheet and the statement of changes in equity at December 31, 2017, 2016 and 2015, the income statement and statement of cash flows for 2017, 2016 and 2015, and the notes to the financial statements for the years ended on such dates, as well as the special-purpose financial statements prepared by the Issuer in the context of the admission to trading of the Company's shares on the continuous market in December 2015.

For purposes of comparison, the financial information for the years ended December 31, 2017, 2016 and 2015 is shown with each item of the balance sheet, income statement, statement of cash flows and statement of changes in equity.

20.1.1. Balance Sheets

The table below shows the balance sheets at December 31, 2017, 2016 and 2015:

Balance sheet					
€	**12.31.2017**	**12.31.2016**	**12.31.2015**	***Chg. 16/17***	***Chg. 15/16***
Non-current assets					
Intangible assets	22,457,756	18,810,398	15,188,231	*19.4%*	*23.8%*
Property, plant and equipment	638,279	695,870	853,561	*(8.3)%*	*(18.5)%*
Long-term investment in group companies and associates	-	-	280,293	*-*	*(100)%*
Non-current financial assets	66,748	66,682	64,000	*0.1%*	*4.2%*
Deferred tax assets	1,750,862	1,695,820	1,664,245	*3.2%*	*1.9%*
Total non-current assets	24,913,645	21,268,770	18,050,330	*17.1%*	*17.8%*
Current assets					
Inventories	7,276	8,331	3,935	*(12.7)%*	*111.7%*
Trade and other receivables	856,696	978,059	940,051	*(12.4)%*	*4.0%*
Short-term investments in group companies and associates	-	-	18,722	*-*	*(100)%*
Current financial assets	213,183	5,241,556	2,241,556	*(95.9)%*	*133.8%*
Current prepayments and accrued income	102,604	219,320	9,197	*(53.2)%*	*2,284.6%*
Cash and cash equivalents	34,950,334	22,028,192	19,467,099	*58.7%*	*13.2%*
Total current assets	36,130,093	28,475,457	22,680,560	*26.9%*	*25.6%*
Total assets	**61,043,737**	**49,744,228**	**40,730,890**	***22.7%***	***22.1%***
Equity					
Shareholders' equity					

Capital	1,708,070	1,423,391	1,138,713	*20.0%*	*25.0%*
Share premium	47,760,319	29,825,590	30,110,268	*60.1%*	*(0.9)%*
Reserves	(4,009,184)	(2,288,463)	(2,765,905)	*75.2%*	*(17.3)%*
(Treasury shares and interests)	(1,539,745)	(1,791,234)	(1,711,290)	*(14.0)%*	*4.7%*
Profit/(loss) from previous years	(9,542,866)	(4,094,609)	(3,102,706)	*133.1%*	*32.0%*
Profit/(loss) for the year	(5,197,159)	(5,448,257)	(991,903)	*(4.6)%*	*449.3%*
Other equity instruments	-	-	(76,964)	-	*100%*
Total shareholders' equity	29,179,435	17,626,418	22,600,213	*65.5%*	*(22.0)%*
Grants, gifts and bequests received	5,252,585	5,102,360	4,992,734	*2.9%*	*2.2%*
Total equity	**34,432,020**	**22,728,779**	**27,592,947**	***51.5%***	***(17.6)%***
Non-current liabilities					
Long-term provisions	123,033	-	-	*100%*	-
Non-current payables					
Bank borrowings	13,107,596	14,933,811	3,069,763	*(12.2)%*	*386.5%*
Other financial liabilities	2,933,984	2,789,310	3,107,008	*5.2%*	*(10.2)%*
Total non-current payables	16,041,579	17,723,121	6,176,771	*(9.5)%*	*186.9%*
Deferred tax liabilities	1,750,862	1,695,820	1,664,245	*3.2%*	*1.9%*
Total non-current liabilities	17,915,474	19,418,941	7,841,016	*(7.7)%*	*147.7%*
Current liabilities					
Current payables					
Bank borrowings	6,385,271	4,250,423	1,403,060	*50.2%*	*202.9%*
Other financial liabilities	968,348	1,226,971	1,492,330	*(21.1)%*	*(17.8)%*
Total current payables	7,353,619	5,477,394	2,895,390	*34.3%*	*89.2%*
Trade and other payables					
Payable to Suppliers	820,250	1,602,694	1,614,132	*(48.8)%*	*3.5%*
Other creditors	522,374	516,420	427,368	*1.2%*	*20.8%*
Total trade and other payables	1,342,624	2,119,114	2,041,499	*(36.6)%*	*3.8%*
Current prepayments and accrued income	-	-	360,038	-	*(100)%*
Total current liabilities	8,696,243	7,596,508	5,296,927	*14.5%*	*43.4%*
Total equity and liabilities	**61,043,737**	**49,744,228**	**40,730,890**	***22.7%***	***22.1%***

20.1.1.1. Assets

The composition of the assets on the Issuer's balance sheets is as follows:

Balance sheet			
%	**12.31.2017**	**12.31.2016**	**12.31.2015**
Non-current assets			
Intangible assets	36.8%	37.8%	37.3%
Property, plant and equipment	1.0%	1.4%	2.1%
Long-term investment in group companies and associates	0.0%	0.0%	0.7%
Non-current financial assets	0.1%	0.1%	0.2%
Deferred tax assets	2.9%	3.4%	4.1%
Total non-current assets	40.8%	42.8%	44.3%
Current assets			
Inventories	0.0%	0.0%	0.0%
Trade and other receivables			

Trade and other receivables	1.4%	2.0%	2.3%
Short-term investments in group companies and associates	0.0%	0.0%	0.0%
Current financial assets	0.3%	10.5%	5.5%
Current prepayments and accrued income	0.2%	0.4%	0.0%
Cash and cash equivalents	57.3%	44.3%	47.8%
Total current assets	59.2%	57.2%	55.7%
Total assets	**100.0%**	**100.0%**	**100.0%**

Intangible assets

Intangible assets include amounts relating to development, patents, licenses, trademarks and software:

Intangible assets			
€	**12.31.2017**	**12.31.2016**	**12.31.2015**
Neurodegenerative Epigenetics	16,356,118	13,869,429	11,013,668
Oncological Epigenetics	-	657,400	1,314,801
New Epigenetic Therapies	5,903,735	4,259,300	2,840,999
Oncological Epigenetic - New Therapies	169,351	-	-
Total development expenses	22,429,203	18,786,129	15,169,469
Software	28,553	24,270	18,763
Total	**22,457,756**	**18,810,398**	**15,188,231**

This is the most important item of balance sheet assets, accounting at December 31, 2015, 2016 and 2017 for 37.3%, 37.8% and 36.8%, respectively. The value of these intangibles is fundamental, given their potential for generating income and positive cash flow.

As noted in section 20.1.2.2 above, since 2014, research expenses incurred during the year are booked in the income statement, with those that meet certain requirements of the National Chart of Accounts not being capitalized, adopting for this purpose standards closer to those established by International Financial Reporting Standards.

However, development expenses for the year will be capitalized once all the following conditions are met:

- Existence of a specific individual project that allows a reasonable valuation of the outlay attributable to the implementation of the project;
- The allocation, attribution and distribution over time of the costs of each project must be clearly established;
- At all times there must be duly founded reasons to believe in the technical success of the project, whether the company intends to exploit it directly or to sell the results of the project to a third party once concluded, if there is a market;
- The financial and commercial profitability of the project must be reasonably assured;
- The funding for the completion of the various projects must be reasonably assured. Moreover, the availability of adequate technical and other resources for the completion of the project and to exploit or sell the intangible asset must be reasonably assured; and

- There must be an intention to complete the intangible asset in question, in order to use or sell it.

Standard measures are used for this purpose to evaluate the technological risks of the various phases of development and to establish a reasonable and soundly based forecast of technical, commercial and financial success. Taking account of the Company's business model, the estimates are made separately for each molecule.

The costs considered to be capitalizable development expenses, valued at production cost, are all those directly attributable and necessary to create, produce and prepare the asset to operate as planned, including the costs of the staff involved, materials and services used directly in the projects, depreciation of the fixed assets used and the portion of the indirect costs that may reasonably be allocated to the development project, as long as it represents a rational allocation of such costs.

The development phase begins once the Company has defined a few molecules (usually between one (1) and five (5)), which have the elements necessary to be nominated as pre-clinical candidates. In this phase, the various refining or final optimization tasks are begun, together with the regulatory toxicological assessment that will be necessary to obtain the authorization of the regulatory bodies to begin the Phase I studies.

In accordance with the Company's business model, the patent families of experimental molecules are licensed to large corporations in their early phases (normally during Phase I or Phase II), although there is no current license agreement as of the date of this document.

Once a decision to license is made, the depreciation of the development project begins at an annual rate of 20%.

Additional extraordinary depreciation (impairment write-down) is applied if the project's viability is considered to be compromised, if it is decided to cancel the project, or if the net book value of the project exceeds its recoverable value with regard to expectations for future generation of income.

A description of the development expenses is set forth below:

Development expenses			
€	**12.31.2017**	**12.31.2016**	**12.31.2015**
Cost			
Initial balance	34,116,412	29,842,350	26,911,133
Inflows	4,300,475	4,274,062	2,931,017
Outflows	-	-	-
Final balance	38,416,887	34,116,412	29,842,350
Depreciation, amortization and impairment losses			
Initial balance	(15,330,283)	(14,672,881)	(14,015,481)
Depreciation and amortization charges	(657,400)	(657,401)	(657,400)
Assets retired on spin-off	-	-	-
Impairment	-	-	-
Final balance	(15,987,683)	(15,330,283)	(14,672,881)
Net book value	**22,429,203**	**18,786,129**	**15,169,469**

The oncological epigenetics development line began to be depreciated in fiscal year 2013, having accumulated a level of systematic impairment at December 31, 2017 equal to 100% of the acquisition or production value, with a net book value of EUR 0 at December 31, 2017. The other

development lines have not been subject to systematic impairments, as they are assets under development and were not subject to impairment, or to impairments in value.

Fixed assets

As noted in section 8.1 of Section II of this document, fixed assets essentially consist of machinery, facilities, furniture and laboratory equipment for the purposes of carrying out the development work which gives rise to the intangible assets. The Company has high-level technologically advanced equipment, acquired in 2009 and 2010, for which reason significant investment has not been required under this heading.

Fixed assets			
€	**12.31.2017**	**31.12.1016**	**12.31.2015**
Technical facilities and machinery	259,008	329,707	433,143
Other fixed assets	379,271	366,163	420,418
Total	**638,279**	**695,870**	**853,561**

Long-term investment in group companies and associates

The Company had no equity instruments of this kind at December 31, 2017 and December 31, 2016.

At December 31, 2015, investments in group companies and associates was EUR 280,293, as a result of a EUR 274,574 loan by the Company to ORYZON CORP., with a term of one (1) year and an annual interest rate of 7%. It is booked as long-term, as it was expected to be renewed on maturity.

On December 20, 2016, ORYZON CORP. resolved to dissolve and liquidate, terminating the loan provided by the Company, for which reason the Company had no investments in group companies and associates at March 31, 2018.

Non-current financial assets

Non-current financial assets include the following items:

Financial assets			
€	**12.31.2017**	**12.31.2016**	**12.31.2015**
Assets at fair value through profit and loss	41,000	41,000	41,000
Investments held to maturity	25,748	25,682	23,000
Total	**66,748**	**66,682**	**64,000**

Assets at fair value through profit and loss and Investments held to maturity correspond to equity interests in the mutual guarantee company AVALIS and bank guarantees deposited for the lease of the building in which are located the registered office, in Madrid at Carrera de San Jerónimo, nº 15, 28014, and laboratories, in Barcelona at Cornellà de Llobregat, calle Sant Ferran 74.

Deferred tax assets

Deferred tax assets correspond to activated tax losses (100% at December 31, 2017, 100% at December 31, 2016 and 97% at December 31, 2015). Historically, the Company has activated tax losses and deductions for R&D, limited to the maximum equivalent amount of deferred tax liabilities, with the variations in 2015, 2016 and 2017 being EUR 19,712, EUR 31,575 and EUR 55,042, respectively, all due to the change in liabilities due to deferred taxes, in relation to the change in the balance for grants, gifts and bequests.

Inventories

Inventories represent supplies for the laboratory, the value of which is immaterial. No impairment due to loss of value has been booked.

Trade and other receivables

The composition of Trade and other receivables is as follows:

Trade and other receivables			
€	**12.31.2017**	**12.31.2016**	**12.31.2015**
Trade receivables for sales and services	-	-	-
Other accounts receivable	310,010	437,869	412,270
Other credits/loans from public administrations	546,686	540,190	527,780
Total	**856,696**	**978,059**	**940,051**

Trade receivables for sales and services are composed of the outstanding balances relating to agreements for the provision of R&D services. The amount thereof is zero (0) at December 31, 2015 and 2016, as on the first day of each quarter the revenues corresponding thereto are billed, which may be deferred, and the amount thereof collected during the quarter itself. There was no new recognition of sales or services in 2017 giving rise to balances in the trade receivables accounts.

At December 31, 2015, a provision was made for impairment due to the possibility of an uncollectible credit of EUR 59,574, which was reverted during the first months of fiscal year 2016 as the provisioned debt was completely collected.

Other accounts receivable are composed mainly of accrued grants payable, while other credits/loans from public administrations mainly include the amounts corresponding to pending returns of value added tax.

Current financial assets, cash and cash equivalents

The aggregate amount of Current financial assets, Cash and cash equivalents at December 31, 2017 is EUR 35,163,517.

The increase of EUR 7,893,769 between December 31, 2017 and December 31, 2016 mainly corresponds to the funds contributed in the capital increase by the Issuer, after covering R&D investments, structuring costs and debt service.

The increase of EUR 5,561,093 at December 31, 2016 compared to December 31, 2015 is mainly due to the funds from the round of bank financing during such fiscal year, after covering R&D investments, structuring costs and debt service.

20.1.1.2. Shareholders' equity and liabilities

Equity

The composition of this item is described in section 10.1 of Section II of this document.

Financial liabilities

The composition of this item is described in section 10.1 of Section II of this document.

Deferred tax liabilities

The composition of this item is described in the table below:

Deferred tax liabilities

€	12.31.2017	12.31.2016	12.31.2015
For interest-free and soft loans	289,303	303,363	231,596
For capital grants	1,461,559	1,392,457	1,432,649
Total deferred tax liabilities	**1,750,862**	**1,695,820**	**1,664,245**

Deferred tax liabilities include the timing differences identified as those amounts expected to be recovered arising from the differences between the book value of assets and liabilities and their tax value. These amounts are booked by applying the timing difference corresponding to the legally established tax rate. From the amounts to be booked directly in equity under Valuation adjustments and Grants, donations and bequests, the amount corresponding to the tax rate applicable to these items is subtracted from these items and booked as deferred tax liabilities.

Trade and other payables

This item is described in the table below:

Trade and other payables			
€	**12.31.2017**	**12.31.2016**	**12.31.2015**
Payable to Suppliers	820,250	1,602,694	1,614,132
Staff (accrued salaries)	278,203	292,120	311,032
Other accounts payable to public administrations	244,171	224,300	116,336
Total	**1,342,624**	**2,119,114**	**2,041,499**

Current prepayments and accrued income

At December 31, 2017, 2016 and 2015, there were no balances corresponding to anticipated deferred income.

20.1.2. Income statements

The Income statements for fiscal years 2017, 2016 and 2015 are detailed below:

Income statement					
€	**2017**	**2016**	**2015**	***Chg. FY16-17***	***Chg. FY15-16***
Net revenues	16,764	735,312	4,253,586	*(97.7)%*	*(82.7)%*
In-house work on non-current assets	4,300,475	4,274,062	2,931,017	*0.6%*	*45.8%*
Procurement	(271,987)	(370,975)	(357,523)	*(26.7)%*	*3.8%*
Other operating income	14,264	10,827	32,007	*31.7)%*	*(66.2)%*
Staff expenses	(2,949,277)	(2,481,768)	(1,962,043)	*18.8%*	*26.5%*
Other operating expenses	(5,011,979)	(6,255,216)	(4,755,478)	*(19.9)%*	*31.5%*
Depreciation and amortization charge	(826,738)	(852,682)	(896,633)	*(3.0)%*	*(4.9)%*
Allocation of grants for non-financial non-current assets	403,830	366,466	491,225	*10.2%*	*(25.4)%*
Impairment losses and gains or losses on disposal of assets	-	(3,748)	(24,271)	*(100.0)%*	*(84.6)%*
Other gains or losses	407	50	55,179	*714.9%*	*(99.9)%*

Operating income	**(4,324,240)**	**(4,577,673)**	**(232,933)**	***(5.5)%***	***1,865.2%***
Financial income	46,587	41,655	37,924	*11.8%*	*9.8%*
Financial expenses	(816,494)	(936,883)	(652,517)	*(12.8)%*	*43.6%*
Exchange rate differences	(158,054)	50,952	61,543	*(410.2)%*	*(17.2)%*
Impairment losses and gains or losses on disposal of fin. instruments	-	(57,884)	(168,967)	*(100.0)%*	*(65.7)%*
Financial income	(927,961)	(902,159)	(722,018)	*2.9%*	*24.9%*
Profit/(loss) before tax	(5,252,201)	(5,479,832)	(954,951)	*(4.2)%*	*473.8%*
Income tax	55,042	31,575	(36,952)	*74.3%*	*(185.4)%*
Profit/(loss) for the year	**(5,197,159)**	**(5,448,257)**	**(991,903)**	***(4.6)%***	***449.3%***

20.1.2.1. Net revenues

At the end of 2018, the Company made a change in strategic focus, from a company providing services to third parties, with the participation of different consortia, to one focusing on the development of its own products. The exit from service provision was gradual, given that contracts remained in force, and the first revenue from the new business model was obtained beginning in April 2014 with the signing of the License Agreement with Roche.

This Agreement entailed an initial payment when the contract was signed of USD 17,000,000 (EUR 12,347,500), which was recognized as income in the first half of 2014. In June 2015 a milestone was reached corresponding to the end of the multiple ascending dose (MAD) stage of its clinical testing of Phase I to evaluate the safety, tolerability and pharmacokinetics of ORY-1001 in patients with acute leukemia (AML), by the establishment of a recommended dose of ORY-1001, which achieved a non-refundable milestone in the amount of USD 4,000,000 (EUR 3,636,363.64). The income recognized as net revenue from fiscal years 2015, 2016 and 2017 was EUR 4,253,586, EUR 735,312 and EUR 16,764, respectively, and corresponds to the accrual of revenue from licensing and the provision of R&D services from the Agreement signed with Roche.

At December 31, 2017 and 2016, there were no balances for anticipated revenues and at December 31, 2015 the amount thereof was EUR 360,038.27.

The Agreement with Roche has provided cumulative revenue to the Company in the amount of EUR 17,957. On July 19, 2017, Roche gave notice of the discontinuation of clinical development of ORY-1001, and as a result the Company will not receive new collections under such license agreement.

The license agreement was discontinued during 2017, with the resulting recovery by ORYZON in January 2018 of the rights to develop and sell the licensed product.

20.1.2.2. In-house work on non-current assets

This corresponds to the expenses capitalized as development expenses. The expenses capitalized for each line of research are described in the following table, in which epigenetics plays a notable role in neurodegenerative therapies.

In-house work on non-current assets			
€	**12.31.2017**	**12.31.2016**	**12.31.2015**
Neurodegenerative Epigenetics	2,486,689	2,855,761	2,077,694
New Epigenetic Therapies	1,644,435	1,418,301	853,323

Oncological Epigenetic - New Therapies	169,351	-	-
Total	**4,300,475**	**4,274,062**	**2,931,017**

The Company's in-house work on non-current assets is booked in the income statement, and corresponds to the development expenses incurred each year when they are broken down by project and their cost is clearly established so that it can be distributed over time, and they also generate well-reasoned expectations of technical success and financial and commercial profitability.

In-house work on non-current assets during the period analyzed is based on the number of development projects estimated to be viable and their current stage or phase, both of which are always dependent on the financial resources available to the Company. The Company has increased its development spending, reflecting the strategy adopted by management and the greater available financial capacity deriving from rounds of equity and debt financing. In-house work by the Company on its assets has been mainly in the area of neurodegenerative epigenetics and for fiscal years 2015, 2016 and 2017 represented an investment of EUR 2,078, EUR 2,856 and EUR 2,487 thousand, respectively.

20.1.2.3. Procurement

Procurement refers mainly to the purchase of laboratory materials (molecules, reagents, etc.). It is not directly correlated with in-house work on non-current assets, as each line of investigation is different and therefore so are the requirements for laboratory materials.

Procurement			
€	**2017**	**2016**	**2015**
Domestic procurement	200,194	303,152	245,555
EU procurement	37,442	49,673	61,646
Imports	33,296	22,546	45,317
Changes in inventory	1,055	(4,396)	5,005
Total procurement	**271,987**	**370,975**	**357,523**

20.1.2.4. Other operating income

Other operating income includes:

- Income for expenses paid by the Company on behalf of third parties and for staff services. At December 31, 2017, 2016 and 2015, this income stood at EUR 2,783, EUR 9,570 and EUR 21,183, respectively;
- Operating grants received, which at December 31, 2017, 2016 and 2015, stood at EUR 11,481, EUR 1,257 and EUR 10,824, respectively.

20.1.2.5. Staff expenses

In 2014, staff expenses rose due to new recruitment after the Roche Agreement was signed, which has entailed the inclusion of new profiles and the rehiring of staff who had been laid off.

The increase in staff expenses during fiscal year 2017 compared to fiscal year 2016 was mainly the result of an increase in average staff in 2017. Average staff relative to researchers increased by 23%. The staff increases have allowed for adjustment of the operating structure to increase the Company’s level of compliance and internal control. Also in 2017, staff expenses includes a provision in the amount of EUR 123,034 regarding an LTI approved by the Board of Directors and that will be received in 2020. The accrual and payment of the LIT are subject in any case to corporate, clinical and financial objectives for the 2017-2019 period with an impact on revenue levels and on the valuation of the Company. The amounts accrued for contingent LTI in 2017

were EUR 76,228 with respect to Mr. Carlos Buesa and EUR 46,806 with respect to Ms. Tamara Maes.

Costs relating to social security contributions in 2017, 2016 and 2015 represent 17%, 14% and 14%, respectively of total salaries.

Progress on the R&D projects as well as the growth in the size thereof, ORYZON's status as a listed company, and its advances in corporate governance and compliance, have required an increase in personnel, which has entailed an increase in expenses for this item.

Staff expenses			
€	**2017**	**2016**	**2015**
Wages and salaries	2,528,083	2,178,168	1,737,033
Social security contributions	421,193	303,601	225,010
Total staff expenses	**2,949,277**	**2,481,768**	**1,962,043**

20.1.2.6. Other operating expenses

This is the largest category of expenses in every year of the period covered. The table below shows the main items under this heading:

Other operating expenses			
€	**2017**	**2016**	**2015**
External services			
Independent professional services	1,302,224	1,678,853	1,420,202
Research and development services	2,788,714	3,616,825	2,639,174
Leases	188,673	155,132	43,119
Other services	706,806	792,898	588,495
Total external services	4,986,417	6,243,708	4,690,990
Taxes	25,562	69,023	2,457
Losses, impairment and variation in provisions for commercial trans.	-	(59,574)	59,574
Other current management expenses	-	2,059	2,457
Total procurement	**5,011,979**	**6,255,216**	**4,755,478**

Fiscal year 2017

During 2017, the Company engaged in various recurring activities relating to independent professional services in the amount of EUR 1,203 thousand (securities market transactions of EUR 344 thousand, professional fees relating to strategic, legal, sales, tax, audit and compliance and criminal risk prevention advice in the amount of EUR 482 thousand, and compensation for membership on the Board of Directors in the amount of EUR 457 thousand and the Scientific Committee and others for EUR 19 thousand).

Activities relating to the scientific programs of the Company carried out externally are included under external R&D and patent services and are mainly for the provision of services through CROs, such as the subcontracting of the clinical development of ORY-2001 for Phase I (hospital research, monitoring costs and pharmacokinetic analysis), as well as prior work to commence

the Phase II studies (new experimental models in other indications of interest, manufacture of drug lots, studies of chronic toxicology and preparation of the design for new studies and regulatory documentation, engagement of CROs for monitoring and first contacts with researchers involved in the study). Furthermore, the Phase I study of ORY-1001 has been formally finalized with the regulatory authorities upon completion of the study and preparation of the corresponding final report. In addition, there have been preclinical development activities for the ORY-3001 candidate (including toxicology and regulatory studies), and finally, Discovery activities for earlier projects on additional inhibitors.

The chapter corresponding to other services shows an 11% reduction at December 31, 2017 compared to December 31, 2016. The chapter includes, among other things, maintenance, repair and conservation expenses, expenses for travel and expenses for representation of the ordinary activities of the Company, which do not follow a standard line but rather are subject to non-standard spikes during different time periods.

Fiscal year 2016

The Company significantly intensified its professional services activities during fiscal year 2016. There have been strategic consulting and investor relations activities in the amount of EUR 535 thousand, activities of representation and promotion of the Company in the USA by ORYZON CORP. in the amount of EUR 101 thousand, stock exchange activities in the amount of EUR 231 thousand, professional fees for legal, sales, tax, audit and criminal risk compliance and prevention consulting in the amount of EUR 318 thousand, and compensation to the members of the Board of Directors in the amount of EUR 371 thousand and to the Scientific Committee and others in the amount of EUR 122 thousand (of which EUR 34,204 correspond to expenses of the Scientific Advisory Committee and EUR 87.800 are for expenses relating to miscellaneous strategic advice and consulting). The most significant change for fiscal year 2015 corresponds to strategic studies of a corporate nature requested by the Board of Directors.

Activities relating to scientific programs of the Company through external engagement are included under external R&D and patent services and mainly correspond to the provision of services through CROs and research bodies, such as the subcontracting of the preclinical development activities for ORY-2001 (manufacture of the drugs to be administered, and the chronic toxicology studies needed for the clinical Phase II) and ORY-3001 (GMP synthesis of the compound, preclinical regulatory activities and safety studies required to begin Phase I), the latter activities relating to the monitoring and closing of the clinical trial of ORY-1001 with leukemia patients and activities relating to the Phase I Clinical Study of healthy persons for the ORY-2001 program (hospital, monitoring, analysis laboratories, etc.). Finally, there have also been various Discovery activities for earlier projects or for preliminary exploration of new indications.

Other services shows an increase over the prior year as a result of the Company's internationalization and promotion efforts in the domestic and North American market, which has required higher investment in advertising and an increased presence and travel to conferences and meetings.

Fiscal year 2015

In 2015, Independent professional services increased compared to 2014, because during the first eight (8) months of fiscal year 2014 there was no compensation for the members of the Board of Directors and a total of EUR 94 thousand accrued during the last four (4) months of 2014; in 2015 the compensation of the members of the Board of Directors rose to EUR 306 thousand. 2015 also includes services related to the raising, negotiation and assistance of

financial funds and representation and promotion of the Company in the USA, amounting to EUR 362 thousand, which services were provided by ORYZON CORP.

As regards R&D services, the substantial increase at December 31, 2015 compared to the same period of 2014 is mainly due to completion of significant scientific programs of the Company through CROs, the subcontracting of the preclinical development of ORY-2001, the synthesis of compounds of new targets and backups of ORY-1001 and ORY-2001, bio-analysis of samples for the clinical study of ORY-1001, and various analysis sampling methods, as well as other costs relating to the monitoring of the clinical study, regulatory procedures for ORY-1001 and the hospital clinical trials which contributed to the increase in expenses for development services provided by third parties.

As to Leases, during the first half of 2015 the Company formalized a new agreement for the lease of the laboratory building in which the Company's registered office was located, and which was a significant decrease from the prior year as a result of the negotiation process. The new agreement, which reduced the rent being paid to a third party, was negotiated by the Finance Department and was signed for a period of ten (10) years, with the first two (2) being mandatory.

20.1.2.7. Depreciation and amortization charge

Depreciation mainly corresponds to intangible assets, which are subject to a 20% straight line depreciation. The Company applies impairment when it considers that the viability of any project is compromised or if the net book value of the project exceeds its recoverable value with regard to the future generation of income. In 2013, this item increased substantially because the intangible asset represented by the ORY-1001 molecule began to be depreciated and the frequency of depreciation was maintained through December 31, 2017, at which time the intangible was completely depreciated with a net book value of EUR 0. Therefore, depreciation has been stable for the fiscal years ended December 31, 2017, 2016 and 2015.

20.1.2.8. Allocation to profit or loss of grants related to non-financial non-current assets and other

Non-refundable grants, gifts and bequests are initially booked as income directly attributable to shareholders' equity after subtracting amounts corresponding to deferred tax liabilities, and are recognized in the income statement in line with the amortization or, if appropriate, when the intangible assets recognized on the balance sheet are disposed of, corrected for impairment or written off.

20.1.2.9. Impairment losses and gains or losses on disposal of assets

The Company rejects any project that does not form part of its main business of neurodegenerative and oncological epigenetics. Impairment losses and gains or losses on disposal of assets at December 31, 2017, 2016 and 2015 have been immaterial, totaling EUR 0, EUR 3,748 and EUR 24,271, respectively, mainly corresponding to the impairment of rights acquired through a license that is no longer deemed viable.

20.1.2.10. Financial income

Financial income has a correlation with both the cash position and the interest rates available in the market, the amounts thereof are immaterial and cash positions are held in products with low yields but that ensure the principle thereof to a greater extent.

20.1.2.11. Financial expenses

This includes both interest actually paid to financing institutions and interest linked to the restatements of capital grants relating to reimbursable aid, which in the latter case do not result in cash outflows for the Company.

At December 31, 2017, financial expenses were EUR 816 thousand (EUR 210 thousand less than the cost recorded at December 31, 2016), corresponding to interest actually paid in the amount of EUR 447 thousand and recorded interest corresponding to the actual value of the debt regarding subsidized interest rates in the amount of EUR 369 thousand.

At December 31, 2016, financial expenses were EUR 963 thousand, corresponding to interest actually paid in the amount of EUR 612 thousand and interest recorded corresponding to the actual value of the debt regarding subsidized interest rates in the amount of EUR 449 thousand.

At December 31, 2015, financial expenses were EUR 653 thousand, corresponding to interest actually paid in the amount of EUR 204 thousand and interest recorded corresponding to the actual value of the debt regarding subsidized interest rates in the amount of EUR 449 thousand.

There has been a reduction in market interest rates in recent years.

Historical indebtedness at higher interest rates has been replaced by new indebtedness at lower interest rates, as a result of adding to the market trend the Company's increased ability to negotiate, which has allowed for an improvement in financial expenses when comparing financial cost to indebtedness.

Amortization of the principal of historical loans, replaced by new indebtedness at lower interest rates, has led to better financial costs than would be expected from a simple proportional change in the volume of growth in indebtedness.

20.1.2.12. Exchange rate differences

Active positions in currencies (US dollars) are maintained in order to meet future payment commitments.

Exchange differences in fiscal years 2017, 2016 and 2015 were EUR 158 thousand in losses and EUR 51 thousand and EUR 62 thousand in gains, respectively, as a result of changes in the market price of the US dollar on bank balances and payables in foreign currency.

A change in currency rates of +/- 3% on balances held at December 31, 2017, 2016 and 2015 would involve a potential change with a positive or negative impact of EUR 21 thousand, EUR 51 thousand and EUR 72 thousand, respectively.

20.1.2.13. Impairment losses and gains or losses on disposal of financial instruments

There were no impairment losses or gains or losses on disposal of financial instruments in 2017.

In 2016 there were losses in the amount of EUR 59 thousand as a result of:

- Losses from financial divestments in the amount of EUR 40 thousand, mainly from the dissolution and liquidation of ORYZON CORP., a Company in which there was an investment of EUR 4,718 and a loan with a remaining balance of EUR 282 thousand. This generated a loss of EUR 40 thousand at the time of liquidation;
- Losses from disposals and other in the amount of EUR 18 thousand, based on the net effect of: (i) gains of EUR 150 thousand from the sale of 24.99% of the remaining interest in OGDSL (in 2015 there was an impairment of the value of the Company's

interest in OGDSL in the amount of EUR 169 thousand); and (ii) losses from financial investments in third party companies in the amount of EUR 168 thousand.

20.1.3. Statement of changes in equity

Statements of changes in equity for fiscal years 2017, 2016 and 2015 are shown below:

Statement of changes in total equity

€	Authorized capital	Share premium	Reserves	Treasury shares and interests	Results from previous years	Profit/(loss) for the year	Other equity instruments	Valuation adjustments	Grants, gifts and bequests received	Total
Balance start 2015	**235,907**	**14,479,772**	**(1,112,179)**	**(1,711,290)**	**(9,753,210)**	**6,650,504**	**-**	**169,991**	**4,933,597**	**13,893,092**
Total recognized income and expenses	-	-	-	-	-	(991,903)	(76,964)	(169,991)	59,137	(1,179,721)
Transactions in treasury shares	902,806	15,630,496	(1,808,442)	-	-	-	-	-	-	14,724,860
Other changes in equity	-	-	154,716	-	6,650,504	(6,650,504)	-	-	-	154,716
Other changes in equity	-	-	-	-	-	-	-	-	-	-
Balance end 2015	**1,138,713**	**30,110,268**	**(2,765,905)**	**(1,711,290)**	**(3,102,706)**	**(991,903)**	**(76,964)**	**-**	**4,992,734**	**27,592,947**
Adjusted balance start 2016	**1,138,713**	**30,110,268**	**(2,765,905)**	**(1,711,290)**	**(3,102,706)**	**(991,903)**	**(76,964)**	**-**	**4,992,734**	**27,592,947**
Total recognized income and expenses			-	-	-	(5,448,257)	76,964	-	109,627	(5,261,666)
Capital increases	284,678	(284,678)	-	-	-		-	-	-	-
Transactions in treasury shares			398,082	(79,944)						318,148
Other changes in equity		-	79,350		(991,903)	991,903	-	-	-	79,350
Balance end 2016	**1,423,391**	**29,825,590**	**(2,288,463)**	**(1,791,234)**	**(4,094,609)**	**(5,448,257)**	**-**	**-**	**5,102,360**	**22,728,779**
Adjusted balance start 2017	**1,423,391**	**29,825,590**	**(2,288,463)**	**(1,791,234)**	**(4,094,609)**	**(5,448,257)**	**-**	**-**	**5,102,360**	**22,728,779**
Total recognized income and expenses			**-**	**-**	**-**	**(5,197,159)**	**-**	**-**	**150,225**	**(5,046,934)**
Capital increases	284,678	17,934,730	(1,732,121)	-	-	-	-	-	-	16,487,287
Transactions in treasury shares			11,400	251,489	-	-	-	-	-	262,889
Other changes in equity		-	-	-	(5,448,257)	5,448,257	-	-	-	-
Balance end 2017	**1,708,070**	**47,760,319**	**(4,009,184)**	**(1,539,745)**	**(9,542,866)**	**(5,197,159)**	**-**	**-**	**5,252,585**	**34,432,020**

Section 10.1 of Section II of this document includes a summary of the Company's shareholders' equity.

20.1.4. Statement of cash flows

The statements of cash flows for fiscal years 2017, 2016 and 2015 are shown below:

Statement of Cash Flows			
€	**2017**	**2016**	**2015**
Cash flows from operating activities			
Profit/(loss) for the year before tax	(5,252,201)	(5,479,832)	(954,951)
Adjustments to income			
Depreciation and amortization charge	826,738	852,682	896,633
Impairment losses	-	(59,574)	228,541
Allocation of grants	(403,830)	(366,466)	(491,225)
Impairment losses and gains or losses on disposal of non-current assets	-	3,748	-
Impairment losses and gains or losses on disposal of financial instruments	-	57,884	24,271
Financial income	(46,587)	(41,655)	(37,924)
Financial expenses	816,494	936,883	652,517
Exchange rate differences	-	-	(61,543)
Valuation of fair value of financial instruments	-	-	-
Other revenue and expenses	11,880	(343,115)	23,263
Total adjustments to income	1,204,695	1,040,387	1,234,533
Changes in working capital			
Inventories	1,055	(4,396)	5,006
Trade and other receivables	301,736	40,288	(295,476)
Other current assets	116,716	(210,123)	2,785
Trade and other payables	(653,456)	77,623	798,756
Other non-current assets and liabilities	-	-	(55,778)
Total changes in working capital	(233,949)	(96,608)	455,293
Interest payments	(473,026)	(512,903)	(652,517)
Collections of interest	46,586	41,655	80,745
Other payments/collections	-	-	360,038
Total other cash flows from operating activities	(426,440)	(471,248)	(211,734)
Total cash flows from operating activities	**(4,707,895)**	**(5,007,301)**	**523,141**
Total cash flows from investment activities			
Payments due to investments			
Group companies and associates	-	-	(274,575)
Intangible assets	(4,311,489)	(4,292,425)	(2,966,531)
Property, plant and equipment	(105,015)	(28,485)	(87,650)
Other financial assets	(40,555)	(3,500,556)	-
Total payments due to investments	(4,457,059)	(7,821,466)	(3,328,756)
Proceeds from disposals			
Group companies and associates	-	240,615	-
Other financial assets	5,100,000	479,667	3,440,230
Total proceeds from disposals	5,100,000	720,282	3,440,230
Total cash flows from investment activities	**642,941**	**(7,101,184)**	**111,474**
Cash flows from financing activities			
Proceeds and payments relating to equity instruments			
Issuance of equity instruments	18,219,408	(12,741)	14,724,860

Cancellation of equity instruments	-	-	-
Acquisition of equity instruments	(3,084,400)	(1,891,444)	-
Disposal of equity instruments	1,323,514	1,683,528	
Grants, gifts and bequests received	428,778	507,663	570,074
Total collections and payments for equity instruments	16,887,299	287,006	15,294,934
Proceeds and payments relating to financial liability instruments:			
Issuance			
Bank borrowings	5,351,901	15,750,000	1,750,000
Other debts	279,719	972,974	336,939
Total issuance	5,631,620	16,722,974	2,086,939
Repayment and cancellation of:			
Bank borrowings	(5,531,823)	(1,351,948)	(1,356,960)
Borrowings from group companies and associates	-	-	-
Other debts	-	(988,454)	(824,946)
Total repayments and cancellation	(5,531,823)	(2,340,402)	(2,181,906)
Total collections and payments for financial liability instruments	99,797	14,382,572	(94,967)
Total cash flows from financing activities	**16,987,096**	**14,669,578**	**15,199,967**
Effect of exchange rate changes			-
Net increase/decrease in cash and equivalents	**12,922,142**	**2,561,093**	**15,834,582**
Cash or equivalents at start of year	22,028,192	19,467,099	3,632,517
Cash or equivalents at end of year	34,950,334	22,028,192	19,467,099

The more significant changes in the Statement of Cash Flows between fiscal years 2015 and 2017 correspond to the following:

It should be noted that c ash flows from operating activities decreased mainly as a result of lower pre-tax results for the year as a result of the decrease in income generated by the Roche Agreement. In 2015, the flow was positive at EUR 523,141, but negative at EUR (5,007,301) and EUR (4,707,895), respectively, for fiscal years 2016 and 2017.

There was an increase in cash flows from investment activities from EUR 111,474 in 2015 to EUR 642,941 in 2017, due mainly to the cancellation of cash surpluses placed in term deposits held by the Company charged in 2017 to proceeds from disposals of other financial assets in the amount of EUR 5,100,000, offsetting the payments due to investments of EUR 4,457,059..

Cash flows from financing activities increased from EUR 15,199,967 in 2015 to EUR 16,987,096 in 2017, due mainly to capital increases and rounds of bank financing by the Company.

During the period between December 31, 2017 and December 31, 2015, there was a net increase in cash or cash equivalents from EUR 19,467,099 to EUR 34,950,334, a net increase of EUR 15,483,235 after accounting for contributions made to R&D activities and to cover structuring costs and debt service, all as a result of the contributions from financial indebtedness and increase in shareholders' equity.

20.2. Pro forma financial information

Not applicable.

20.3. Financial statements

At the date of registration of this document, ORYZON is an individual company and does not formulate consolidated financial statements. Furthermore, as regards fiscal years 2016 and 2015, pursuant to Sections 7.1.a and 7.1.c of Royal Decree 1159/2010 of September 17 approving the standards for the preparation of consolidated financial statements and amending

the National Chart of Accounts and the Chart of Accounts for Small and Medium-sized Enterprises approved by Royal Decree 1515/2007 of November 16, ORYZON was exempt from the obligation to consolidate the financial statements of ORYZON CORP. because it does not exceed the minimum limits in this respect. It should also be noted that such company was liquidated in December 2016.

20.4. Auditing of historical annual financial information

20.4.1. Statement that the historical financial information has been audited

GRANT THORNTON, S.L.P. has audited the special-purpose financial statements for the years ended December 31, 2015, 2016 and 2017. The audit reports for these fiscal years contain a favorable opinion.

20.4.2. Indication of any other information in the registration document which has been audited by the auditors

There is no information other than as stated in the preceding section that has been audited by the auditors.

20.4.3. Where financial data in the registration document is not extracted from the issuer's audited financial statements state the source of the data and state that the data is unaudited

All data and information contained in this document for the years ended December 31, 2015, 2016 and 2017 have been extracted from the financial statements audited by GRANT THORNTON, S.L.P.

20.5. Age of latest financial information

The latest audited financial information included in this document corresponds to December 31, 2017.

20.6. Interim information and other financial information

The Company's unaudited balance sheet and income statement for the first quarter of 2017, which is incorporated by reference herein and which can be viewed on the website of the CNMV (www.cnmv.es) and on the Company's corporate website (www.oryzon.com) is included below.

Balance Sheet

Balance sheet			
€	**03.31.2018**	**12.31.2017**	**Chg. %**
Non-current assets			
Intangible assets	24,234,680	22,457,756	*7.9%*
Property, plant and equipment	657,262	638,279	*3.0*
Non-current financial assets	66,742	66,748	*(0.0)%*
Deferred tax assets	1,709,455	1,750,862	*(2.4)%*
Total non-current assets	26,668,139	24,913,645	*7.0%*
Current assets			
Inventories	10,436	7,276	*43.4%*
Trade and other receivables	1,125,142	856,696	*31.3%*
Current financial assets	182,046	213,183	*(14.6)%*
Current prepayments and accrued income	316,480	102,604	*208.4%*
Cash and cash equivalents	30,718,596	34,950,334	*(12.1)%*
Total current assets	32,352,699	36,130,093	*(10.5)%*
Total assets	**59,020,838**	**61,043,737**	*(3.3)%*

Equity			
Shareholders' equity			
Capital	1,708,070	1,708,070	-
Share premium	47,760,319	47,760,319	-
Reserves	(4,009,184)	(4,009,184)	-
(Treasury shares and interests)	(1,539,745)	(1,539,745)	-
Profit/(loss) from previous years	(14,740,025)	(9,542,866)	*54.5%*
Profit/(loss) for the year	(1,024,241)	(5,179,159)	*(80.2)%*
Other equity instruments	-	-	-
Total shareholders' equity	28,155,194	29,179,435	*(3.5)%*
Valuation adjustments	-	-	-
Grants, gifts and bequests received	5,128,366	5,252,585	*(2.4)%*
Total equity	33,283,560	34,432,020	*(3.3)%*
Non-current liabilities			
Long-term provisions	142,553	123,033	*15.9%*
Non-current payables			
Bank borrowings	11,232,036	13,107,596	*(14.3)%*
Other financial liabilities	2,647,505	2,933,984	*(9.8)%*
Total non-current payables	13,879,542	16,041,579	*(13.5)%*
Long-term borrowings from group companies and associates		-	-
Deferred tax liabilities	1,709,455	1,750,862	*(2.5)%*
Total non-current liabilities	15,731,550	17,915,474	*(12.2)%*
Current liabilities			
Short-term provisions		-	-
Current payables			
Bank borrowings	6,859,936	6,385,271	*7.4%*
Other financial liabilities	1,016,915	968,348	*5.0%*
Total current payables	7,876,851	7,353,619	*7.1%*
Trade and other payables			
Payable to Suppliers	1,650,419	820,250	*101.2%*
Other creditors	478,458	522,374	*(8.4)%*
Total trade and other payables	2,128,878	1,342,624	*58.6%*
Current prepayments and accrued income		-	
Total current liabilities	10,005,728	8,696,243	*15.1%*
Total equity and liabilities	**59,020,838**	**61,043,737**	***(3.3)%***

The Company's balance sheet at March 31, 2018 shows an increase in non-current assets in the amount of EUR 1,754 thousand, mainly relating to the capitalization of development expenses and systematic impairments of other intangibles. Also, in current assets, there is a reduction in cash and other liquid assets and cash equivalents in the amount of EUR 4,232 thousand, which was mainly used to pay research and development expenses, structuring costs and debt service.

Furthermore, payables to suppliers increased to EUR 1,650,419 at March 31, 2018 (EUR 820,250 at December 31, 2017) as a result of the increase in the services activity, which have been accrued but not yet paid.

The Company has continued to regularly pay the debt service and there have been reclassifications in accordance with the loan repayment schedules, reducing long-term bank borrowings to EUR 11,232,036 at March 31, 2018 (EUR 13,107,596 at December 31, 2017), with no significant change in short-term bank borrowings in the amount of EUR 6,859,936 at March 31, 2018 (EUR 6,385,271 at December 31, 2017), with short-term maturities being paid on a regular basis.

On the other hand, losses (EUR 1,024 thousand) and changes in capital grants (EUR 124 thousand) obtained in the first three (3) months of 2018 have caused a decrease in equity in the amount of EUR 1,148 thousand compared to December 31, 2017 as a result of structuring costs, financial costs and research expenses that have not been capitalized as intangible assets.

Income statement for the three (3) months to March 31, 2018

Income statement at 03.31.18			
€	**2018 (3 m)**	**2017 (3 m)**	**Change %**
Net revenues	-	16,764	(100.0)%
In-house work on non-current assets	1,778,620	1,189,636	49.5%
Procurement	(48,296)	(77,984)	(38.1)%
Other operating income	456	-	100.0%
Staff expenses	(784,005)	(776,553)	1.0%
Other operating expenses	(1,747,808)	(1,305,496)	33.9%
Depreciation and amortization charge	(34,463)	(207,706)	(83.4)%
Allocation of grants for non-financial non-current assets	216,139	222,237	(2.7)%
Other gains or losses	366	254	44.1%
Operating income	**(618,993)**	**(938,848)**	**(34.1)%**
Financial income	1,522	5,304	(71.3)%
Financial expenses[(1)]	(350,054)	(347,780)	0.7%
Exchange rate differences	(15,311)	(31,109)	(50.8)%
Financial income	(363,843)	(373,586)	(2.6)%
Profit/(loss) before tax	(982,836)	(1,312,434)	(25.1)%
Income tax	(41,406)	23,944	(272.9)%
Profit/(loss) for the year	**(1,024,242)**	**(1,288,490)**	**(20.5)%**

[(1)] Apart from nominal interest corresponding to loans accruing a market interest rate, this item includes interest accruing each fiscal year on loans at a zero interest rate or at an interest less than the market rate, the annual change in the fair value of such loans, the amount of expenses recognized in such item, which has a neutral effect on the income statement, due to the recognition of income from the allocation of grants arising from aid or subsidies granted to the Company.

The Company continued its R&D activities during the first quarter of 2018, which has allowed for significant advances in its portfolio, positioning itself with two (2) clinical studies in Phase IIa with ORY-2001, one for AD (ETHEREAL), and the other for Multiple Sclerosis (SATEEN). In addition, the Company has worked intensely on finalizing the preparations for the Phase IIa clinical studies with ORY-1001 in LMA and in SCLC, after recovering all rights to the molecule at no cost at the end of January.

As a result of this activity, the costs of external collaboration has increased, as reflected in "other operating expenses", which have reached EUR 1,747,808 (EUR 1,305,496 in the first quarter of 2017).

20.7. Dividend policy

20.7.1. The amount of the dividend per share for each financial year for the period covered by the historical financial information adjusted, where the number of shares in the issuer has changed, to make it comparable

The Company has not distributed a dividend since incorporation.

Regardless of the legal limitations on the distribution of dividends established in the Companies Act, there is no restriction on the distribution of dividends as there has been full repayment of the loan provided in fiscal year 2008 by the Institut Català de Finances (ICF) and the loan

provided during fiscal year 2010 by EMPRESA NACIONAL DE INNOVACIÓN, S.A. (ENISA) and repayment of more than 50% of the principal provided during fiscal year 2009 by the Institut Català de Finances (ICF).

In this context, the possibility is not ruled out that dividends will be distributed in the future as a consequence of excess cash flows after compliance with all prior requirements deriving from private agreements and/or requirements established in the Companies Act.

20.8. Legal and arbitration proceedings

At the registration date of this document, there is no litigation that might have a material adverse effect on the Company.

20.9. Significant change in the issuer's financial or trading position

There were no significant changes in financial position at December 31, 2017.

21. ADDITIONAL INFORMATION

21.1. Share capital

21.1.1. Amount of issued capital, and for each class of share capital

On March 10, 2017, the Board of Directors, in exercise of the delegation granted by the shareholders at the General Shareholders' Meeting of June 29, 2016, resolved to increase the share capital with the exclusion of preemptive subscription rights in the maximum nominal amount of EUR 284,678.25 through the issuance and placement into circulation of a maximum of 5,693,565 ordinary shares, par value EUR 0.05, at a minimum share price of EUR 3.06, with 5,693,565 shares subscribed through a private placement procedure at a share price of EUR 3.20. As a result, the capital was increased by EUR 18,217,408, of which EUR 284,678.25 correspond to share capital and EUR 17,934,729.75 correspond to the share premium through the issuance of 5,693,565 ordinary shares with a par value of EUR 0.05, pursuant to a public instrument executed before the Notary of Barcelona, Mr. Francisco Armas Omedes, on April 4, 2017, recorded in his notarial book of records under number 894, and registered with the Commercial Registry of Barcelona on that same date at Volume 45,267, Folio 74, Sheet B-221174.

Consequently, as of the date of this document, the par value of the issued share capital is EUR 1,708,069.55 divided into 34,161,391 shares with a par value of EUR 0.05 each, all of the same class and series, fully subscribed and paid up, and represented by book entries.

21.1.1.1. Number of shares authorised

The shareholders at the General Shareholders' Meeting held on April 4, 2018 approved the delegation to the Board of Directors of the Company of the power to increase the Company's share capital, on one or more occasions, by a maximum amount of up to 50% of the subscribed and paid up capital as of the date of such authorization, as well as the power to partly or wholly exclude the right of pre-emption as provided by Section 506 of the Companies Act. As of the date of registration of this document, the delegated powers have not been used.

21.1.1.2. Number of shares issued and fully paid up and issued but not fully paid up

There are no capital calls, as the share capital of ORYZON is entirely subscribed and paid up.

21.1.1.3. Par value per share, or that the shares have no par value

All the shares into which ORYZON's share capital is divided have a par value of EUR 0.05 each.

21.1.1.4. Reconciliation of the number of shares outstanding at the beginning and end of the year. If more than 10% of capital has been paid for with assets other than cash within the period covered by the historical financial information, state that fact.

There were 34,161,391 shares outstanding as of December 31, 2017, which figure corresponds to the number of shares outstanding on the date of registration of this document.

21.1.2. If there are shares not representing capital, state the number and main characteristics of such shares

There are no shares not representing capital.

21.1.3. Number, book value and face value of shares in the issuer held by or on behalf of the issuer itself, or by subsidiaries of the issuer

As at the date of this document, the Company holds 668,578 shares of its own stock representing 1.95% of ORYZON's current share capital.

21.1.4. Amount of any convertible securities, exchangeable securities or securities with warrants, with an indication of the conditions governing and the procedures for conversion, exchange or subscription

ADDF is a U.S. foundation fighting against AD, the goals of which include financing drug research programs at academic centers and biotechnology companies.

Various experiments corresponding to the ORY-2001 program for the treatment of AD have been financed by ADDF, as indicated in section 10.1.2 of this document.

ADDF had the right to acquire shares of the Company under certain conditions pursuant to the First ADDF Loan and the Second ADDF Loan. As for the conditions for the exercise of the right to acquire the shares by ADDF, the latter is entitled to request the acquisition of shares upon expiration of a five (5)-year period as from the drawdown date of each of the tranches of the First ADDF Loan and from the drawdown date of the Second ADDF Loan, at an exercise price of EUR 2.43 per share for the first loan, and of EUR 2.54 per share in the event that it exercises the right to acquire shares under the second loan, with respect to the amounts actually drawn down.

Along these lines, it should be emphasized that the ADDF has exercised all of its rights to acquire shares on April 26, 2016 and September 26, 2016, having acquired 4,423 shares and 175,071 shares, respectively, representing in the aggregate 0.63% of the share capital of the Company, with no rights remaining to exercise with respect to such loans.

In 2017, ADDF approved aid of USD 300,000 to support the ORYZON project called "*Clinical development of a supplemental biomarker for use with the dual inhibitor LSD1/MAOB ORY-2001*" and according to the terms of the agreement received 82,029 ordinary shares of ORYZON at a price of EUR 3.41 per share, reaching a 0.86% interest in the share capital of the Company. At the date of registration of this document, ADDF has no rights to convertible securities.

21.1.5. Information about and terms of any acquisition rights and or obligations over authorised but unissued capital or an undertaking to increase capital

The Company has not issued (nor has it adopted any resolution to issue) acquisition rights and/or obligations with respect to authorized capital, and there is no commitment to increase the Company's share capital.

21.1.6. Information about any capital of any member of the group which is under option or agreed conditionally or unconditionally to be put under option and details of such options, including those persons to whom such options relate

As of the date of registration of this document, there is no option agreement on the capital of the Company, except as described in section 22.2 of Section II of this document.

21.1.7. A history of share capital, highlighting information about any changes, for the period covered by the historical financial information

Below is a description of the most recent changes in the share capital and in the par value of the shares of ORYZON during the period covered by the historical financial information:

- At the Ordinary General Shareholders' Meeting of the company held on first call on June 30, 2015, the shareholders approved an increase in the Company's share capital by means of an increase in the par value of the outstanding shares, from EUR 0.01 to EUR 0.04, charged to the share premium account, in the amount of EUR 707,722.38, increasing the Company's capital to EUR 943,629.84.
- The shareholders at the Annual General Shareholders' Meeting held on first call on June 30, 2015 resolved to increase the share capital of the Company by means of

monetary contributions and excluding pre-emptive rights, by a nominal amount of EUR 300,000 through the issuance and placement into circulation of a maximum of 7,500,000 new ordinary shares with a par value of EUR 0.04 each, and with a minimum share premium of EUR 2.61 per share, delegating the respective powers to the Board of Directors pursuant to the provisions of Section 297.1.a) of the Companies Act.

In this connection, the Board of Directors of the Company, at its meeting held on July 19, 2015, in writing and without a meeting, pursuant to the powers delegated by the shareholders at the Annual General Shareholders' Meeting mentioned in the preceding paragraph, resolved that upon expiration of the subscription and placement period of the increase effected by the Company and after setting the total price per share at EUR 3.39, the share capital be increased by a nominal amount of EUR 156,342.2, through the issuance and placement into circulation of 3,908,555 ordinary shares with a par value of EUR 0.04 each, of the same class and series as the shares of the Company currently outstanding, and represented by book entries.

- The Board of Directors of the Company, at its meeting held on August 7, 2015, acting under the powers delegated to it by the shareholders at the Extraordinary General Shareholders' Meeting of June 6, 2001, adopted a resolution to increase the share capital of the Company by issuing 1,964,236 new shares with a par value of EUR 0.04 each, at a total price per share of EUR 3.39. Such capital increase was effected on October 13, 2015, in the amount of EUR 38,741, through the issuance of 968,525 new shares.

- At the Ordinary General Shareholders' Meeting of the Company held on first call on June 29, 2016, the shareholders approved an increase in capital by means of an increase in the par value of the outstanding shares, from EUR 0.04 to EUR 0.05, charged to the share premium account, in the amount of EUR 284,678.26, increasing the Company's capital to EUR 1,423,391.3.

- At the Ordinary General Shareholders' meeting of the Company held on first call on June 29, 2016, the shareholders resolved to delegate to the Board of Directors the power to increase share capital by up to one half of the share capital by means of cash contributions and the exclusion of preemptive subscription rights for a maximum period of five (5) years, although this right was limited to capital increases with the exclusion of preemptive subscription rights under such authorization up to a maximum aggregate amount of 20% of the Company's share capital at such time, pursuant to the provisions of section 297.1.b) of the Companies Act.

- Within this context, at its meeting held on March 10, 2017, and pursuant to the delegation made by the shareholders referred to in the preceding paragraph, the Board of Directors resolved to increase the share capital, with the exclusion of preemptive subscription rights, by a maximum nominal amount of EUR 284,678.25 through the issuance and placement into circulation of a maximum of 5,693,565 ordinary shares with a par value of EUR 0.05 at a share price of EUR 3.06. At the end of the period for subscribing and placing the increase implemented by the Company and after setting the total price per share at EUR 3.20, the share capital was increased by the nominal amount of EUR 284,678.25, by means of the issuance and placement into circulation of 5,693,565 ordinary shares with a par value of EUR 0.05 each, of the same class and series as the outstanding shares of the Company, represented by book entries.

The table below shows the main features of the increases through the issuance of new shares:

	Capital increase July 2015	Capital increase October 2015	Capital increase March-April 2017
Equivalent value of the increase	Monetary contributions	Monetary contributions	Monetary contributions
Share capital prior to the increase	€943,629.84	€1,099,972.04	€1,423,391.30
Number of shares prior to the increase	23,590,746	27,499,301	28,467,826
Par value per share	€0.04	€0.04	€0.05
Share premium per share	€3.35	€3.35	€3.15
Total price per share	€3.39	€3.39	€3.20
Number of new shares issued	3,908,555	968,525	5,693,565
Nominal amount of the increase	156,342.2	38,741	284,678.25
Share premium	13,093,659.25	3,244,558.75	17,934,729.75
Total amount of the increase	€13,250,001.45	3,283,299.75	18,217,408
Share capital following the increase	€1,099,972.04	1,138,713.04	1,708,069.55
Number of shares following the increase	27,499,301	28,467,826	34,161,391

Set out below is a table summarizing the changes in the Company's share capital from January 1, 2015 to the date of registration of this document.

DATE	EVENT	CHANGE DUE TO CAPITAL INCREASE (€)	No. RESULTING SHARES	RESULTING UNIT PAR VALUE (€)	RESULTING SHARE CAPITAL (€)
01/01/2015	Capital prior to increases		23,590,746	0.01	235,907.46
30/06/2015	Capital increase	707,722.38	23,590,746	0.04	943,629.84
24/07/2015	Capital increase	156,342.20	27,499,301	0.04	1,099,972.04
13/10/2015	Capital increase	38,741	28,467,826	0.04	1,138,713.04

06/29/2016	Capital increase	284,678.26	28,467,826	€0.05	1,423,391.3
04/04/2017	Capital increase	284,678.25	34,161,391	€0.05	1,708,069.55

21.2. Memorandum and Articles of Association

21.2.1. A description of the issuer's objects and purposes and where they can be found in the memorandum and articles of association

Article 2 of the Bylaws provides as follows:

"Article 2.- The purpose of the Company is as follows:

a) the discovery, development and application of genomic, molecular and genetic biomarkers and tools to obtain personalized medical products or acquire modified organisms of pharmaceutical, industrial or agricultural interest.

b) the performance of clinical tests in the fields of diagnosis and prognosis in humans or in other organisms of health-related or industrial interest.

c) the provision of various scientific research services, such as pharmacological, chemical, biological, industrial, nutritional and other services of interest in human beings, animals and organisms or model systems.

d) the development of chemical molecules, peptides, proteins or antibodies with therapeutic applications in humans and other organisms and clinical research into new human therapies.

d) research/investigation and development/discovery of new pharmaceutical products, provision of scientific, technical or business consulting and advice in the area of biotechnology, pharmaceutics and medicine.

f) manufacturing in general of software tools for diagnostic use, of health-related in vitro diagnostic products, and of human health therapeutic products.

The activities listed above may be carried out by the Company, in whole or in part, indirectly through ownership of shares or interests in companies with an identical or similar purpose.

The National Classification of Economic Activities (Clasificación Nacional de Actividades Económicas) (CNAE) corresponding to the activities covered by the corporate purpose is 7211 - Experimental research and development in biotechnology.

Excluded are all those activities for which the Law has special requirements that cannot be met by this Company.

If legal provisions require a professional degree or government authorization or registration in Public Registries for the exercise for any of the activities included in the corporate purpose, such activities must be performed through persons who hold such degree and may not be commenced prior to meeting any applicable governmental requirements.

Notwithstanding the foregoing, as indicated in subsection 5.1.4.2 of Section II of this document, the corporate purpose and ends of the Company have been focused in recent years, and are so contemplated in its future business plan, on the research/investigation and development/discovery of new pharmaceutical products through the development of chemical molecules with therapeutic applications in humans and clinical research into new human

therapies. The Company's field of activity is primarily focused on the area of epigenetics in diverse indications, with a particular emphasis on oncology and neurodegenerative diseases. The Company can support itself selectively using alliances with academic institutions and other companies to explore the potential of epigenetic drugs in other indications (such as viral or inflammatory diseases).

The Bylaws, the Regulations for the General Shareholders' Meeting, the Regulations of the Board of Directors and the Internal Regulations for Conduct of ORYZON are available to the public and may be viewed at the registered office located in in Madrid, at Carrera de San Jerónimo 15, 28014, as well as through the corporate website of the Company (www.oryzon.com). The Regulations for the General Shareholders' Meeting, the Regulations of the Board of Directors and the Internal Regulations for Conduct may also be viewed on the website of the CNMV (www.cnmv.es). The Bylaws, the Regulations for the General Shareholders' Meeting and the Regulations of the Board of Directors may also be viewed at the Commercial Registry of Barcelona.

21.2.2. A summary of any provisions of the issuer's articles of association, statutes, charter or bylaws with respect to the members of the administrative, management and supervisory bodies.

The operation and composition of the Board of Directors of ORYZON is governed by articles 33 to 40 of the Bylaws and in the Regulations of the Board of Directors. The operation of the Committees of the Board of Directors is set out in articles 41 to 43 of the Bylaws and in articles 25 to 30 of the Regulations of the Board of Directors.

Set forth below is a brief description of the main provisions of the Bylaws and of the Regulations of the Board of Directors containing the rules for the Board of Directors. A description of the rules of operation and of the composition of the Audit and Compliance Committee and of the Appointments and Compensation Committee is set forth in subsection 16.3 of Section II of this document.

21.2.2.1. Duties and responsibilities

The Board of Directors reserves to itself, as the core of its mission, the definition of a corporate governance system that ensures the sound and prudent management of the Company and that includes a proper distribution of duties within the organization and the prevention of conflicts of interest, as well as approval of the Company's strategy and the specific organization required to put that strategy into practice. In turn, the Board of Directors shall oversee and monitor the senior officers, especially endeavoring to ensure compliance with the goals set and observance of the corporate purpose and interest of the Company, which is understood as the common interest of all shareholders.

The Board of Directors shall act with unity of purpose and independent judgment, ensuring that no shareholder receives privileged or unequal treatment with respect to the others and that in its relations with other stakeholders, the Company abides by the law, fulfils in good faith its obligations and contracts, observes the customs and good practices of the industries in which it does business, and complies with the standards of responsibility to which it has adhered.

For the purposes described in the preceding paragraphs, the Board of Directors shall have the following non-delegable powers in addition to any such non-delegable powers as may be provided for in the Companies Act and/or the Bylaws:

(i) The preparation of the annual financial statements, the management report, and the proposed allocation of the Company's profits, as well as any consolidated annual

financial statement, and the submission thereof for approval by the shareholders at a General Shareholders' Meeting.

(ii) The call of the General Shareholders' Meeting, as well as the publication of the notices relating thereto and the preparation of the agenda, making the proposed resolutions it deems to be appropriate based on the nature of each General Shareholders' Meeting.

(iii) The appointment of directors on an interim basis and the submission of proposals to the shareholders regarding the appointment, ratification, re-election or removal of directors, upon a proposal of the Appointments and Compensation Committee, if applicable.

(iv) The appointment and renewal of positions within the Board of Directors and of the members of the committees, after a report from the Appointments and Compensation Committee.

(v) The distribution of director compensation among its members, upon a proposal of the Appointments and Compensation Committee.

(vi) The declaration of its position regarding all tender offers for securities issued by the Company.

(vii) The assessment of the quality and operation of the Board of Directors, of the Committees, of the Chair, and of any CEO, obtaining the reports it needs from the Committees themselves and from the Appointments and Compensation Committee.

(viii) The determination and approval of the general policies and strategies of the Company, particularly:

(a) The strategic or business plan, as well as the annual management goals and budget.

(b) The investment and financing policy.

(c) The definition of the structure and administration of the group of companies of which the Company is the controlling entity, if applicable.

(d) The corporate governance policy of the Company and any controlled companies, the organization and operation thereof, and particularly the approval and amendment of the Regulations of the Board of Directors.

(e) The corporate social responsibility policy.

(f) The dividend policy.

(g) The compensation policy and evaluation of the performance of the senior officers, upon a proposal of the Appointments and Compensation Committee.

(h) The policy for the control and management of risks, including tax risks, as well as the regular monitoring of the internal information and control systems.

(i) The Company’s treasury stock policy within the framework of the authorization provided by the shareholders.

(j) The determination of the Company’s tax strategy.

(ix) The approval of the following operational decisions:

(a) Appointment and dismissal of the senior officers that report directly to the Board of Directors or to any of the members thereof, after a report from the Appointments and Compensation Committee, and the establishment of the basic terms of their contracts, including their compensation.

(b) Investments, including investments in subsidiaries or acquiring interests in companies both within and outside of Spain, or transactions of a strategic nature or having a special tax risk due to the high amount or special nature thereof, unless approval thereof is vested within the shareholders acting at a General Shareholders' Meeting.

(c) The creation or acquisition of equity interests in special purpose entities or entities domiciled in countries or territories that are considered to be tax havens or similar transactions that, due to the particular complexity thereof might affect the transparency of the Company and, if applicable, of the group.

(x) The approval, after a report from the Audit and Compliance Committee, of transactions that the Company or any companies in its group engage in with directors or with shareholders that individually or collectively with others have a significant shareholding as defined by applicable law, including shareholders represented on the Board of Directors of the Company or of other companies forming part of the same group, or with parties related thereto.

(xi) The approval or waiver of obligations arising from the duty of loyalty when approval is vested in the Board of Directors, pursuant to the provisions of applicable law.

(xii) The preparation of any type of report that the Board of Directors is required to prepare by law, provided that the transaction referred to by the report cannot be delegated.

(xiii) The powers that the shareholders acting at a General Shareholders' Meeting may have delegated to the Board of Directors, unless it has been expressly authorized thereby to sub-delegate them.

(xiv) Any other matter that the Regulations of the Board of Directors reserve to a hearing by the full Board.

Furthermore, the Board of Directors may not delegate the decision-making powers referred to in Section 249 *bis* or those listed in Section 529 *ter* of the Companies Act.

21.2.2.2. Structure and composition

The Board of Directors shall be made up of a minimum of five (5) and a maximum of twelve (12) directors, who shall be appointed or ratified by the shareholders at a General Shareholders' Meeting subject to applicable legal and bylaw requirements.

The shareholders acting at a General Shareholders' Meeting shall determine the exact number of directors between the limits stated above either by express resolution or indirectly by filling vacancies or appointing new directors.

The Board of Directors must propose to the shareholders acting at a General Shareholders' Meeting the number of directors within such limits that, given the circumstances affecting the Company, is most appropriate to the situation thereof and ensures the effectiveness and due representative capacity of such body.

The members of the Board of Directors shall be appointed by the shareholders acting at a General Shareholders' Meeting, without prejudice to the power of the Board of Directors to appoint members on an interim basis in the event of a vacancy and without prejudice to the

system of proportional representation to which the shareholders are entitled under the provisions of law.

The Chair of the Board of Directors shall be elected from among the members thereof (and removed when appropriate) with the favorable vote of an absolute majority of the members of the Board of Directors present at the meeting after a report from the Appointments and Compensation Committee and, as the person responsible for the effective operation of the Board of Directors, shall assume the duties vested therein by law and the Bylaws, and shall particularly ensure that the directors receive sufficient information in advance to analyze, deliberate and vote on the items on the agenda; shall direct and stimulate debate and participation during the meetings of the Board of Directors, safeguarding their freedom to take positions and express opinions; and shall organize and coordinate with the chairs of any Committees that have been created on the regular evaluation of the Board of Directors as well as any Chief Executive Officer.

Therefore, the Chair shall have the following powers, in addition to all those powers that may be vested therein by the Companies Act, the Bylaws, the Regulations for the General Shareholders' Meeting, the Internal Regulations for Conduct in the Securities Markets and the Regulations of the Board of Directors:

(i) The ordinary power to call and preside over meetings of the Board of Directors, setting the agenda and directing the discussion and debate.

(ii) To preside over the General Shareholders' Meeting, upon the terms set forth in the Bylaws and in the Regulations for the General Shareholders' Meeting, exercising the powers inherent to such position.

(iii) To bring to the Board of Directors those proposals that the Chair deems appropriate for the progress of the Company, particularly those corresponding to the operation of the Board of Directors itself and other corporate decision-making bodies.

(iv) To coordinate the regular evaluation of the Chief Executive Officer, if any.

The position of Chair of the Board of Directors may be held by an executive director.

If the Chair of the Board of Directors is also the chief executive of the Company, the Board of Directors, with the abstention of the executive directors and upon a proposal of the Appointments and Compensation Committee, shall appoint a lead director (*consejero coordinador*) from among the independent directors, who shall be especially empowered to request a call to meeting of the Board of Directors or the inclusion of new items on the agenda of a Board meeting that has already been called; coordinate and meet with the non-executive directors; if applicable, direct the regular evaluation of the Chair of the Board of Directors; preside over meetings of the Board of Directors in the absence of the Chair and the Vice Chairs; reflect the concerns of the non-executive directors; maintain contacts with investors and shareholders to be aware of their viewpoints for purposes of forming an opinion regarding their concerns, particularly with respect to the Company’s corporate governance; and coordinate a succession plan for the Chair.

The Board of Directors, after a report from the Appointments and Compensation Committee, must appoint from among its members one or more Vice Chairs and shall replace the Chair in case of absence or illness.

If there are several Vice Chairs, they shall replace the Chair in the order established for such purpose by the Board of Directors.

The Board of Directors, after a report from the Appointments and Compensation Committee, and with the favorable vote of an absolute majority of the members of the Board of Directors present at the meeting, shall elect (and shall remove when appropriate) a Secretary, who need not be a director, with the skills to perform the duties of such position. If the Secretary of the Board of Directors is not a director, the Secretary shall have the right to be heard but not to vote.

Apart from the actions corresponding thereto by law, the Bylaws, the Regulations for the General Shareholders' Meeting and the Regulations of the Board of Directors, the Secretary shall ensure that the actions of the Board of Directors:

(i) Conform to the letter and spirit of the law and the regulations thereunder, including those approved by regulatory bodies.

(ii) Conform to the Bylaws, the Regulations of the Board of Directors, the Regulations for the General Shareholders' Meeting, the Internal Regulations for Conduct in the Securities Markets and other regulations of the Company:

(iii) Conform to the good governance recommendations contained in the CBGSC that the Company has accepted, based on the circumstances.

The Secretary shall also be responsible for maintaining the documentation of the Board of Directors, keeping the minutes of the meetings and certifying their content and the resolutions adopted. The Secretary shall also assist the Chair so that the directors receive information relevant to the exercise of their duties sufficiently in advance and in the proper format.

The Secretary shall also prepare and approve a summary in English of the minutes and other working documents attached to the documentation.

The Board of Directors may, after a report from the Appointments and Compensation Committee, appoint (and remove when appropriate) an Assistant Secretary, who need not be a director, in order to assist the Secretary of the Board of Directors or replace him in the event of non-performance of the duties thereof.

Unless otherwise decided by the Board of Directors, the Assistant Secretary may attend the meetings thereof to assist the Secretary in drafting the minutes of the meeting and with the Secretary's other duties.

The removal of the Secretary and Assistant Secretary shall also require a prior report of the Appointments and Compensation Committee.

21.2.2.3. Duties of directors

In the performance of their duties, the members of the Board of Directors must comply with the duties imposed by applicable law, the Bylaws, the Internal Regulations for Conduct in the Securities Markets, the Regulations for the General Shareholders' Meeting and the Regulations of the Board of Directors, with the diligence of any ordinary businessman and the loyalty of a faithful representative, acting in good faith and in protection of the best interests of the Company, taking into account the nature of the position and the duties attributed to each of them. The members of the Board of Directors, and to a greater extent the independent directors, shall at all times contribute their strategic vision, as well as the ideas, standards and innovative measures for the development and evolution of the Company.

In the area of strategic and business decisions, subject to business discretion, the standard of diligence of an ordinary businessman shall be deemed met if the director has acted in good faith

without personal interest in the matter being decided, with sufficient information and pursuant to an appropriate decision-making process.

In particular, and by way of example only, directors shall be required to:

(i) Diligently inform themselves regarding the progress of the Company and adequately prepare for the meetings of the Board of Directors and of the committees to which they belong.

(ii) Attend the meetings of the decision-making bodies of which they are members and actively participate in deliberations, in order for their opinions to contribute effectively to the decision-making process, and take responsibility for them.

(iii) Carry out any specific duty assigned to them by the Board of Directors that reasonably falls within the scope of their commitments.

(iv) Prompt the investigation of any irregularity in the management of the Company which may have come to their attention and procure the adoption of appropriate measures to control any situation of risk.

(v) Request that a meeting of the Board of Directors be called whenever they consider it necessary, or that the items they deem appropriate be included in the agenda.

(vi) Clearly express their objection if they deem a proposed decision submitted to the Board of Directors to be contrary to applicable law, to the Bylaws, to the Internal Regulations for Conduct in the Securities Markets, to the Regulations for the General Shareholders' Meeting, to the Regulations of the Board of Directors or to the corporate interest, and request that such objection be recorded in the minutes. In particular, independent directors and other directors not affected by a potential conflict of interest must also object if dealing with decisions that might prejudice shareholders that are not represented on the Board of Directors.

Directors must devote the time and efforts required to perform their duties and, to such end, must report to the Appointments and Compensation Committee on their other professional obligations if they might interfere with the performance of their duties as directors.

In addition, pursuant to the provisions of article 20 of the Regulations of the Board of Directors, the directors shall be subject to a duty of secrecy even after cessation in office.

An exception to the duty referred to in the preceding paragraph is made for instances in which the law permits the communication or disclosure of the information to third parties or they are required to do so or must respond to the respective supervisory authorities, in which case the release of information must comply with the provisions of law.

If a director is a legal entity, the duty of secrecy shall lie with its representative, without prejudice to the representative’s obligation to report thereto.

Directors must also comply with the duties imposed by applicable law, the Bylaws, the Internal Regulations for Conduct in the Securities Markets, the Regulations for the General Shareholders' Meeting and the Regulations of the Board of Directors with fidelity to the corporate interest, which is understood as the interest of the Company.

Directors must carry out their office with the loyalty of a faithful representative, acting in good faith and in the best corporate interest of the Company. To that end, directors must comply with the following obligations and observe the following prohibitions:

(i) Directors may not exercise their powers for purposes other than those for which they were given.

(ii) Directors may not use the name of the Company or invoke their status as a member of the Board of Directors to unduly influence transactions for their own account or that of related persons.

(iii) Directors may not, for their own benefit or for the benefit of related persons, make investments or enter into transactions relating to the assets of the Company of which they have become aware based on their position if such transactions have been offered to the Company, or make use of corporate assets, including the Company's confidential information, for private purposes, nor may they exploit the Company's business opportunities.

(iv) No director or person related thereto may obtain advantages or compensation from third parties other than the Company and its group related to the performance of their duties, except for tokens received merely as a gesture of courtesy.

(v) No director or person related thereto may undertake activities personally or for third parties that effectively compete with the Company, whether actually or potentially, or that in any other way places them in permanent conflict with the interests of the Company.

(vi) No director may hold positions or provide services to entities that have a corporate purpose that is completely or significantly analogous to that of the Company or that are direct competitors of the Company and/or the companies in which it holds an interest. The Board of Directors may, if it deems it appropriate, relieve the affected director from this restriction, after a report from the Appointments and Compensation Committee.

(vii) Directors must refrain from participating in the deliberations and voting on resolutions or decisions in which they or a related person have a direct or indirect conflict of interest, other than those resolutions or decisions that affect their status as a director, such as their appointment to or removal from positions on the Board of Directors or other situations of similar significance.

(viii) Directors must perform their duties under the principle of personal responsibility with freedom of judgment and independence from third-party instructions or associations.

(ix) Directors must inform the Board of Directors of any situation of direct or indirect conflict they may have with the interests of the Company. In the event of conflict, the affected director shall refrain from participating in the transaction to which the conflict refers.

(x) Directors must disclose to the Company through the Appointments and Compensation Committee all the positions they hold and the activities they carry out at other companies or entities, as well as any significant change in their professional status.

(xi) Directors must also disclose to the Company through the Appointments and Compensation Committee all criminal complaints and government or any other type of claims that due to the significance thereof may have a serious impact on the reputation of the Company, or if they are involved in any of the instances of disqualification or legal prohibition, and generally any fact or situation that might be relevant to their actions as a director of the Company.

For purposes of the provisions of the preceding paragraphs, related persons are understood as the persons referred to in Section 231 of the Companies Act.

Notwithstanding the foregoing, pursuant to the provisions of article 22 of the Regulations of the Board of Directors, the Board of Directors, after a report from the Audit and Compliance Committee, may in individual cases waive the prohibitions contained in paragraphs (i) through (ii) above, authorizing the directors or a person related thereto, provided that there are assurances as to the independence of the members providing the waiver with respect to the director, guarantees as to the harmlessness of the transaction to corporate assets, or if applicable, the performance thereof on market terms and the transparency of the process.

21.2.2.4. Meeting and call to meeting

The Board of Directors, upon the terms provided by law, the Bylaws and the Regulations of the Board of Directors, shall meet with the frequency required to effectively perform its duties, and at least eight (8) times per year (with a meeting having to take place at least once per quarter in any case), and, at the initiative of the Chair or the lead director (*consejero coordinador*), if any, as many times as they deem appropriate for the proper operation of the Company.

The Board of Directors must meet within the first three (3) months of each fiscal year in order to formulate the financial statements for the preceding year, and whenever it must call a General Shareholders' Meeting.

Directors making up at least one-third of the members of the Board of Directors may also call a meeting, establishing the agenda thereof, in order for the meeting to be held at the place where the registered office is located, if a prior petition has been submitted to the Chair and the Chair has failed without well-founded reasons to call the meeting within a period of one month.

The Chair of the Board of Directors, with the assistance of the Secretary, must endeavor to ensure that the directors are provided sufficiently in advance with the information necessary for deliberation on and the adoption of resolutions regarding the matters to be dealt with that have been described in the agenda, unless the Board of Directors meets or has been called on an exceptional basis for reasons of urgency.

The agenda for the meetings shall clearly indicate those items for which the Board of Directors must adopt a decision or resolution so that the directors can first examine or obtain the information required for the adoption thereof.

Notwithstanding the foregoing, if the Chair wants to submit decisions or resolutions that do not appear on the agenda for approval by the Board of Directors on an exceptional basis for reasons of urgency, the prior express consent of directors representing at least four-fifths of the members of the Board of Directors shall be required, which consent must be recorded in the minutes.

The call to meeting must be provided by certified mail or any other means of individual written communication that can ensure the receipt thereof (including email sent to the address customarily used with the receiving director), sent at least seven (7) days prior to the date for holding the meeting, to the address that each director communicates to the Company for such purpose.

The Chair may call extraordinary meetings of the Board of Directors by telephone if the Chair believes the circumstances so warrant. Notwithstanding the foregoing, the Chair shall endeavor to ensure that any documentation that must be provided to the directors is delivered sufficiently in advance. A meeting of the Board of Directors shall also be deemed to be validly held without

a call if all of its members represented in person or by proxy unanimously agree to the holding of the meeting.

Meetings of the Board of Directors may be held in several places connected to each other by a system that permits the recognition and identification of the attendees, permanent communication among the attendees regardless of their location, and participation in discussion and the casting of votes, all in real time (including videoconference or remote attendance systems or any other similar system), provided that none of them object to this procedure. The directors in attendance at any of such interconnected places shall be deemed to have attended the same meeting of the Board of Directors. The meeting shall be deemed to be held at the registered office of the Company.

The directors shall do everything possible to attend the meetings of the Board of Directors, and, if unable to attend in person, shall give their proxy in writing and specifically for each meeting to another member of the Board, including appropriate instructions and giving notice thereof to the Chair of the Board of Directors. Notwithstanding the foregoing, non-executive directors may only give their proxy to other non-executive directors.

The minutes of the meeting shall record those statements by the directors or the Secretary expressing their concern for the performance of the Company with respect to a particular matter or proposal, respectively, if such matter or proposal is not decided by the Board of Directors and such recording is expressly requested.

At the initiative of the Chair, the Board of Directors may adopt resolutions in writing and without a meeting if no director objects thereto. If this voting procedure is followed, the Secretary of the Board of Directors shall record the resolutions adopted in the minutes, stating the names of the directors and the system used to determine the decision of the Board of Directors, with a statement of the vote cast by each director. In this case, it shall be deemed that the resolutions have been adopted at the place of the registered office and on the date of receipt of the last of the votes cast. It shall also be stated that no member of the Board of Directors has objected to this procedure.

A valid quorum of the Board of Directors shall exist with the presence, in person or by proxy, of directors representing at least a majority of the members of the Board of Directors.

21.2.2.5. Majorities required to adopt resolutions

Resolutions shall be adopted by absolute majority of the directors attending the meeting, except for the inclusion of issues not included on the agenda, which shall require the prior express consent of directors representing at least four-fifths of the members of the Board of Directors and for those instances in which applicable law provides for a specific majority.

The Board of Directors, upon the terms set forth in article 31 of the Regulations of the Board of Directors, shall strengthen the Company's communication with its shareholders, using appropriate channels to hear proposals that the shareholders might make in connection with the management of the Company.

For such purposes, it shall also promote the holding of informational meetings by the directors and/or members of senior management it deems appropriate regarding the progress of the Company and its group, particularly for shareholders residing in areas with more significant financial markets in Spain and abroad, as well as with institutional investors. In no event shall such meetings entail the delivery of any information that provides a privileged or advantageous position vis-à-vis the other shareholders. The Board of Directors shall ensure equality of treatment, simultaneously providing the presentations used at public informational meetings to the CNMV and publishing them on the Company's corporate website (www.oryzon.com).

The Board of Directors shall also establish appropriate mechanisms for the regular exchange of information with those institutional investors that are holders of shares of the Company in accordance with the provisions of article 32 of the Regulations of the Board of Directors.

In no event shall the relations between the Board of Directors and the institutional shareholders entail the delivery to them of any information that might place them in a privileged or advantageous position vis-à-vis the other shareholders.

21.2.2.6. Relationships with the Securities Markets

The Board of Directors, through notices of significant events (*hechos relevantes*) to the CNMV and the corporate website (www.oryzon.com), shall immediately inform the public regarding all significant information upon the terms provided by the Securities Market Act and the laws in implementation thereof.

The Board of Directors shall adopt the measures required to ensure that the semi-annual, quarterly, and any other financial information that it may be prudent to make available to the markets is prepared in accordance with the same principles, standards, and professional practices used to prepare the annual financial statements and is as reliable as such statements.

The Board of Directors shall include information in its annual public documentation regarding the Company's governance rules and the level of compliance therewith.

21.2.3. A description of the rights, preferences and restrictions attaching to each class of the existing shares

All shares of ORYZON currently outstanding, which are all ordinary shares belonging to a single class and series, give the holders thereof the same political and economic rights set forth in the Companies Act and in the Bylaws of ORYZON.

21.2.4. A description of what action is necessary to change the rights of holders of the shares, indicating where the conditions are more significant than is required by law

Changes in the rights of the holders of the shares into which the share capital of ORYZON is divided shall require an appropriate amendment of the bylaws, which must be approved by a majority of the shares affected if it only affects a portion of the shares and entails discriminatory treatment among them. The Bylaws of ORYZON do not include any particular rules regarding the provisions of the Companies Act.

21.2.5. A description of the conditions governing the manner in which annual general meetings and extraordinary general meetings of shareholders are called including the conditions of admission

The requirements for calling a General Shareholders' Meeting of the Company and for the shareholders to exercise their rights relating to the General Shareholders' Meeting are governed by articles 20 to 32 of the Bylaws and are developed on a detailed basis in the Regulations for the General Shareholders' Meeting of ORYZON. The Ordinary General Shareholders' Meeting shall be held within the first six (6) months of each fiscal year in order to review the corporate management, to approve the financial statements for the preceding year, if appropriate, and to decide on the application of profits, without prejudice to the power of the shareholders to entertain and decide upon any other matter appearing on the agenda. Any meeting not provided for above shall be deemed to be an Extraordinary General Shareholders' Meeting.

Pursuant to the Companies Act and the Bylaws of ORYZON, meetings shall be called by means of an announcement to be disseminated using at least the following means: (i) the Official Gazette of the Commercial Registry (*Boletín Oficial del Registro Mercantil*) or one of the more

widely circulated newspapers in Spain; (ii) the website of the CNMV (www.cnmv.es); and (iii) the official website of ORYZON (www.oryzon.com), at least one (1) month prior to the date set for the holding thereof, except for those instances in which the Companies Act provides for other specific periods. The announcement of the call to meeting shall state whether it is ordinary or extraordinary, the date and place of the meeting, and all matters to be dealt with and other issues that may be required to be included pursuant to the provisions of the Regulations for the General Shareholders' Meeting. The announcement may also state the date on which the General Shareholders' Meeting shall be held on second call, if any. At least twenty-four (24) hours must pass between the meeting on first call and second call. The provisions of the Companies Act shall also apply to court-ordered calls to meeting.

A meeting may be held on a universal basis, which shall be deemed in all cases to have been called and validly held without the need for a prior call if all of the share capital is present and the attendees unanimously agree to the holding of the meeting.

In order to attend the General Shareholders' Meeting, a shareholder must have ownership of their shares are registered in the book-entry register at least five (5) days prior to the day on which the General Shareholders' Meeting is to be held and have the corresponding attendance card up to five (5) days prior to the date of the General Shareholders' Meeting, in the form indicated in the announcement of the call to meeting and which shows the number of shares they hold and the votes corresponding thereto. If a shareholder exercises the shareholder's right to vote using remote means of communication, such shareholder must also meet this condition at the time of casting their vote.

In addition, to attend the General Shareholders' Meeting, the shareholder must have the corresponding attendance card, certificate issued by the entity in charge of the book-entry register, as applicable, or the document showing that they are a shareholder pursuant to law.

Those shareholders who attend personally or through their proxy representative at the place of the General Shareholders' Meeting on the date thereof shall present their attendance card pursuant to the provisions of the Regulations for the General Shareholders' Meeting.

In addition, those shareholders who wish to vote by remote means of communication must prove their identity and shareholder status in the manner determined by the Board of Directors in the call to meeting.

The members of the Company's Board of Directors must attend General Shareholders' Meetings, provided, however, that the absence of any of them for any reason shall in no event affect the validity of the meeting.

Without prejudice to attendance by corporate shareholders through individuals having the power to represent them, all shareholders with the right to attend may be represented at the General Shareholders' Meeting by another person, whether or not such person is a shareholder of the Company.

Voting is also permitted by mail or electronic means. The announcement must contain clear and specific information regarding the steps the shareholders must take to participate and to cast their vote at the General Shareholders' Meeting, including, among others, the system for casting votes by proxy, with a particular indication of the forms that must be used to grant proxies and the measures that must be used for the Company to be able to accept a notice of the proxies granted by electronic means, and the procedures established for casting absentee votes, whether by mail or electronic means. The Board of Directors must include in the call a mention of the specific means of long-distance communication that shareholders may use to vote or grant a proxy, as well as instructions that must be followed in order to do so. Those shareholders

who wish to vote by remote means of long-distance communication must prove their identity and shareholder status in the manner determined by the Board of Directors in the call to meeting.

21.2.6. A brief description of any provision of the issuer's articles of association, statutes, charter or bylaws that would have an effect of delaying, deferring or preventing a change in control of the issuer

There are no provisions of the current bylaws or the internal regulations that have the effect of delaying, deferring or preventing a change in control of ORYZON.

21.2.7. An indication of the articles of association, statutes, charter or bylaw provisions, if any, governing the ownership threshold above which shareholder ownership must be disclosed

The conditions to be met for changes in the share capital of ORYZON are governed by the provisions of the Companies Act. The Bylaws of ORYZON do not provide for any special condition.

21.2.8. A description of the conditions imposed by the memorandum and articles of association statutes, charter or bylaw governing changes in the capital, where such conditions are more stringent than is required by law

The conditions to be met for changes in the share capital of ORYZON and the respective rights of the shares thereof are governed by the provisions of the Companies Act; the Bylaws of the Company do not establish any special condition.

22. MATERIAL CONTRACTS

22.1. A summary of each material contract, for the two (2) years immediately preceding publication of the registration document

As regards material contracts of the Company, it has executed a first large License Agreement with Roche for its ORY-1001 molecule, pursuant to which they licensed worldwide commercial exploitation rights on an exclusive basis.

However, on July 19, 2017, Roche notified the Company that, due to a change in the strategic priorities of its portfolio, it had decided to discontinue clinical development of the experimental drug ORY-1001 (RG6016), and as a result of this decision, the development and sales rights have been recovered by ORYZON without any cost or the return of amounts received under this contract.

Pursuant to the terms of the Agreement, ORYZON recovered ORY-1001 effective January 19, 2018. This molecule is in a more advanced state than when the license was provided in 2014, which commenced Phase I, and is currently ready to begin Phase IIa studies. The Company has started work to continue with the clinical development of ORY-1001, with the goal of reaching new license agreements.

22.2. Contracts among the shareholders of the Company

Below is a description of the agreement executed by shareholders of the Company which is in force and which affects the transferability of the shares or the exercise of voting rights. It should be noted that on May 16, 2018, the Company gave notice of the termination of the shareholders' agreement signed among NAJETI CAPITAL, S.A., Mr. Carlos Buesa Ariol, Ms. Tamara Maes and Mr. Jose María Echarri Torres signed on December 2, 2015.

22.1.1. Shareholders' agreement executed among Mr. Carlos Manuel Buesa Arjol, Ms. Tamara Maes, INVERSIONES COSTEX, S.L. (currently split off in favor of ARRIENDOS VENFERCA, S.L.) and the Company

On February 22, 2008, Mr. Carlos Manuel Buesa Arjol, Ms. Tamara Maes, INVERSIONES COSTEX, S.L. and the Company signed an agreement under which INVESTIONES COSTEX, S.L. is granted a tag-along right in the event of the sale of shareholdings that entails a change of control in ORYZON, as a result of a purchase offer made by a third party or by one of the shareholders of the Company, for shares representing more than 49.99% of ORYZON.

If the purchase offer made by the third party or the shareholder comprises more than 75% of the share capital of the Company, INVERSIONES COSTEX, S.L. is guaranteed a tag-along right covering its entire interest in ORYZON.

In addition, INVERSIONES COSTEX, S.L. was given the right to appoint one (1) member of the Financial Advisory Council and one (1) member of the Scientific Advisory Committee. Notwithstanding the foregoing, on November 27, 2015, the parties executed an addendum whereby: (i) the parties represent that the appearance of the Company in the aforementioned shareholders' agreement is merely for informational purposes, and does not entail the assumption of any obligation whatsoever by the Company; (ii) they agree to revoke and terminate the provisions of the shareholders' agreement that refer to such Financial Advisory Council and declare the right given to INVERSIONES COSTEX, S.A. under the shareholders' agreement to appoint a member of such Council to have terminated; and (iii) INVERSIONES COSTEX, S.L. formally and irrevocably waives the right granted to it under the shareholders' agreement to appoint a member of the Company's Scientific Advisory Council.

It should be noted that the current interest of INVERSIONES COSTEX, S.L. in the share capital of ORYZON is owned by the company ARRIENDOS VENFERCA, S.L. pursuant to the total split-off thereby pursuant to which it transferred by global succession, among others, in favor of ARRIENDOS VENFERCA, S.L., ownership of the shares of ORYZON, thus being subrogated to the position of INVERSIONES COSTEX, S.L. in the shareholders' agreement. ARRIENDOS VENFERCA, S.L. currently has a 5.87% interest in the share capital of ORYZON. It should be noted that Mr. José María Ventura Ferrero indirectly controls ARRIENDOS VENFERCA, S.L. through VENAR FILLS, S.L. and EUROPE FOOD, S.L., which hold an interest of 73.12% and 4.23% thereof, respectively.

23. THIRD PARTY INFORMATION AND STATEMENT BY EXPERTS AND DECLARATIONS OF ANY INTEREST

23.1. Where a statement or report attributed to a person as an expert is included in the Registration Document, provide such person's name, business address, qualifications and material interest, if any, in the issuer. If the report has been produced at the issuer's request, a statement to the effect that such statement or report is included in the form and context in which it is included, with the consent of the person who has authorised the contents of that part of the Registration Document

Not applicable.

23.2. Where information has been sourced from a third party, provide a confirmation that this information has been accurately reproduced and that, as far as the issuer is aware and is able to ascertain from information published by that third party, no facts have been omitted which would render the reproduced information inaccurate or misleading. In addition, identify the source(s) of the information

Not applicable.

24. DOCUMENTS ON DISPLAY

The following documents, or copies thereof, may be inspected during the effective period of this document at the offices of the CNMV, as well as at the registered office of the Company and on its corporate website (www.oryzon.com). At the same time, the following documents (except for the articles of incorporation and the current bylaws) appear on the website of the CNMV:

- Registration Document
- Notarized articles of incorporation of ORYZON
- Current bylaws
- Regulations of the Board of Directors
- Regulations for the General Shareholders' Meeting
- Internal Regulations for Conduct
- Historical financial information:
  - Audited annual financial statements for the fiscal year ended December 31, 2015
  - Audited annual financial statements for the fiscal year ended December 31, 2016
  - Audited annual financial statements for the fiscal year ended December 31, 2017
- Interim financial information for the first quarter of fiscal year 2018

25. INFORMATION ON HOLDINGS

There are no shareholdings in other companies different than those included in section 7.2 of Section II of this document.

26. ALTERNATIVE PERFORMANCE MEASURES (APMs)

In addition to the financial information contained in this document prepared in accordance with the General Chart of Accounts, certain APMs are included based on the ESMA Guidelines on Alternative Performance Measures dated June 30, 2015 (ESMA/2015/1057) as to their compliance with ESMA recommendations.

The ESMA Guidelines define APMs as measures of financial performance that may be past or future, of financial position or of cash flows, other than a financial measure defined or specified in the applicable financial information framework.

The Company uses certain APMs, which have not been audited, and which are intended to contribute to a better understanding of the financial performance of the Company. These measures are additional information and in no case replace the financial information prepared under the General Chart of Accounts. Furthermore, both the definition and the calculation of these measures may differ from other similar measures prepared by other companies, and may therefore not be comparable.

The APMs used by the Company are described below:

- Capitalizability ratio:

  Calculated as the ratio between development expenses and the sum of development expenses and research expenses.

  It permits measurement of the intensity of accrued financial resources used for intangible asset projects of the Company that can be licensed, as compared to those accrued financial resources used for very early stage projects than cannot be licensed. Products that can be licensed are those that are at a development stage regardless of their probability or the risk level thereof.

  The closer the capitalizability ratio is to one, the greater the level of accrued financial resources used for projects that can be licensed during the specific period of analysis; on the other hand, the closer the result of the capitalization ratio to 0, the lower the level of financial resources used for projects that can be licensed.

- Scientific activity ratio:

  Calculated as the ratio between the sum of research expenses and development expenses and the Company's total expenses excluding financial expenses and income tax expenses.

  It permits measurement of the intensity of financial resources used for research and development, as compared to all operating expenses. Operating expenses are all those expenses included in the income statement except for financial expenses and income tax expenses.

  The larger the result of the ratio, the higher the level of accrued financial resources used for scientific activity; on the other hand, the lower the ratio, the higher the level of accrued financial resources used for operational structuring activities supporting the scientific activity.

- Solvency ratio:

  Calculated as the ratio between the sum of non-current assets plus current assets and the sum of non-current liabilities plus current liabilities.

  It permits measurement of the Company's ability to pay all of its debts and obligations.

The solvency ratio shows the relationship between the Euros held by the Company and its property and rights for every Euro of indebtedness. The higher the result of the solvency ratio, the greater the Company's sufficiency and strength to pay all of its debts and obligations; on the other hand, the lower the result of the solvency ratio, the lower the Company's ability to pay all of its debts and obligations.

- Liquidity ratio:

Calculated as the ratio between current assets and current liabilities. It permits the measurement of the Company's ability to cover its short-term payment commitments.

The higher the value of the liquidity ratio, the higher the Company's ability to cover its short-term payment commitments; on the other hand, the lower the liquidity ratio, the lower the Company's ability to cover its short-term payment commitments.

- Acid test ratio:

Calculated as the ratio of the sum of cash and cash equivalents plus current financial assets to current liabilities. It permits measurement of the Company's ability pay short-term debts on a more immediate basis.

The acid text shows the relationship between the Euros held by the Company in cash and financial property or rights that can be quickly converted into cash and each Euro financial or non-financial indebtedness maturing in the short term. The higher the result of the ratio, the greater the Company's sufficiency and strength to pay debts due in the short term; on the other hand, the lower the result of the ratio, the lower the Company's ability to pay debts due in the short term.

- Operating income before amortization, depreciation and impairments (EBITDA):

Calculated as operating income before provisions for amortization of assets and impairment losses and gains or losses on disposal of assets.

EBITDA provides an analysis of operating income before provisions for amortization of assets and impairment losses and gains or losses on disposal of assets, as an approximation of the company's ability to generate profits, considering only its productive activity. A positive result indicates that profits are being generated; on the other hand, a negative result indicates that losses are being generated.

RATIO	FORMULA	CALCULATION	RESULT 03/31/2018
Capitalizability	Development expenses / (development expenses and research expenses)	1,778,620 / (1,778,620 + 115,848)	0.94
Scientific activity	(Research expenses+ development expenses) / (Total expenses from Income Statement and Earnings – Financial Expenses – Expenses for Income Tax)	(115,848 + 1,778,620) / (3,021,343 - 340,054 - 41,406)	0.72
Solvency	(Non-current assets + Current assets) / (Non-current liabilities + current liabilities)	(26,668, 139 + 32,352,699)/(15,731,550 + 10,005,728)	2.29
Liquidity	Current assets / Current liabilities	32,352,699 / 10,005,728	3.23
Acid Test	(Cash and cash equivalents + current financial assets) / Current liabilities	(30,718,596 + 182,046) / 10,005,728	3.09
EBITDA	(Operating income - Amortization/depreciation - impairment losses and gains or losses on disposal of assets)	(-618,993) - (-34,463) + 0	-584,530

RATIO	FORMULA	CALCULATION	RESULT

			12/31/2017
Capitalizability	Development expenses / (development expenses and research expenses)	4,300,475 / (4,300,475 + 1,005,321)	0.81
Scientific activity	(Research expenses+ development expenses) / (Total expenses from Income Statement and Earnings – Financial Expenses – Expenses for Income Tax)	(1,005,321 + 4,300,475) / 10,089,571 – 816,494 – 55,042)	0.58
Solvency	(Non-current assets + Current assets) / (Non-current liabilities + current liabilities)	(24,913,645 + 36,130,093) / (17,915,474 + 8,696,243)	2.29
Liquidity	Current assets / Current liabilities	36,130,093 / 8,696,243	4.15
Acid Test	(Cash and cash equivalents + current financial assets) / Current liabilities	(34,950,334 + 213,183) / 8,696,243	4.04
EBITDA	(Operating income - Amortization/depreciation - impairment losses and gains or losses on disposal of assets)	(-4,342,240) – (-826,738) - 0	-3,497,502

RATIO	FORMULA	CALCULATION	RESULT 03/31/2016
Capitalizability	Development expenses / (development expenses and research expenses)	4,274,062 / (4,274,062 + 936,236)	0.82
Scientific activity	(Research expenses+ development expenses) / (Total expenses from Income Statement and Earnings – Financial Expenses – Expenses for Income Tax)	(936,236 + 4,274,062) / (10,990,731 - 936,883 - 31,575)	0.52
Solvency	(Non-current assets + Current assets) / (Non-current liabilities + current liabilities)	(21,268,770 + 28,475,457) / (19,418,941 + 7,596,508)	1.84
Liquidity	Current assets / Current liabilities	28,475,457 / 7,596,508	3.75
Acid Test	(Cash and cash equivalents + current financial assets) / Current liabilities	(22,028,192 + 5,241,556) / 7,596,508	3.59
EBITDA	(Operating income - Amortization/depreciation - impairment losses and gains or losses on disposal of assets)	(-4,577,673) - (-852,682) - (-3,748)	-3,721,243

RATIO	FORMULA	CALCULATION	RESULT 12/31/2015
Capitalizability	Development expenses / (development expenses and research expenses)	2,931,017 / (2,931,017 + 778,190)	0.79
Scientific activity	(Research expenses+ development expenses) / (Total expenses from Income Statement and Earnings – Financial Expenses – Expenses for Income Tax)	(778,190 + 2,931,017) / (8,854,384 - 652,517 - 36,952)	0.45
Solvency	(Non-current assets + Current assets) / (Non-current liabilities + current liabilities)	(18,050,330 + 22,680,560) / (7,841,016 + 5,296,927)	3.10
Liquidity	Current assets / Current liabilities	(22,680,560) / (5,296,927)	4.28
Acid Test	(Cash and cash equivalents + current financial assets) / Current liabilities	(19,467,099 + 2,241,556) / (5,296,927)	4.10
EBITDA	(Operating income - Amortization/depreciation - impairment losses and gains or losses on disposal of assets)	(-232,933) - (-896,633) - (-24,271)	687,971

27. DOCUMENTS INCORPORATED BY REFERENCE

The following documents are incorporated by reference in this Registration Document:

- Annual Corporate Governance Report for fiscal year 2017

- Historical financial information:
  - Audited annual financial statements for the fiscal year ended December 31, 2015
  - Audited annual financial statements for the fiscal year ended December 31, 2016
  - Audited annual financial statements for the fiscal year ended December 31, 2017
  - Interim financial information for the first quarter of fiscal year 2018

GLOSSARY

Agreement: means the exclusive licensing agreement signed by ORYZON GENOMICS, S.A. and F. HOFFMANN-LA ROCHE, LTD on March 28, 2014, effective as from April 1, 2014, regarding two (2) of the current nineteen (19) patent families of the Company at that time regarding the LSD1 inhibitor and that ended in January 2018.

ADDF: means the Alzheimer´s Drug Discovery Foundation, the U.S. foundation fighting Alzheimer's disease.

AEMPS: means the Spanish Medicines Agency (*Agencia Española de Medicamento*).

APMs: means Alternative Performance Measures.

ANSM: means the National Drug and Health Products Safety Agency (*Agence Nationale de Sécurité du Médicament et des Produits de Santé*).

GCP: means good clinical practice.

LBD: means Lewy body dementia.

CEDE: means the Spanish Confederation of Directors and Executives (*Confederación Española de Directivos y Ejecutivos*).

CENIT: means strategic national consortia for technical research (*consorcios estratégicos nacionales de investigación técnica*).

CNMV: means the Spanish National Securities Market Commission (*Comisión Nacional del Mercado de Valores*).

Good Governance Code: Means the Good Governance Code for Listed Companies approved by the Board of the CNMV on February 18, 2015.

CROs (Contract Research Organizations): means the group of international suppliers that gives ORYZON flexibility in managing expenses and investments, allowing for the limitation or avoidance of the company's expenses if necessary.

Crystax: means CRYSTAX PHARMACEUTICALS, S.L.

CTA: means Clinical Trial Authorization.

Registration Document: means this document, which contains information regarding the issuer, the format of which conforms to Annex I of Commission Regulation (EC) no 809/2004 of 29 April 2004 implementing Directive 2003/71/EC of the European Parliament and of the Council as regards information contained in prospectuses as well as the format, incorporation by reference and publication of such prospectuses and dissemination of advertisements.

AD: means Alzheimer's disease.

USA: means United States of America.

EMA: means European Medicines Agency.

Issuer: means ORYZON GENOMICS, S.A.

RRMS: means relapsing-remitting multiple sclerosis.

ESMA: means the European Securities and Markets Authority.

Bylaws: means the bylaws (*estatutos sociales*) of ORYZON, the restated text of which was approved by the shareholders at the General Shareholders' Meeting held on October 2, 2015, and last amended on April 4, 2018.

Risk Factors: means the risk factors listed in section II of this document regarding risk factors.

FDA: means the Food and Drug Administration, a U.S. regulatory authority.

FDCA: means the Food, Drug and Cosmetics Act.

GSK: means GlaxoSmithKline.

HDAC: means histone deacetylase.

HDAC-1: means Histone Deacetylase-1.

HDAC-2: means Histone Deacetylase-2.

Development Milestones: means payments for development milestones with respect to the Products (as defined in the Agreement).

R&D: means the activity of research and development.

ICJCE: means the Spanish Institute of Chartered Accountants (*Instituto de Censores Jurados de Cuentas de España*).

IND: means Investigational New Drug Approval as defined in the FDCA and in the applicable regulations promulgated by the FDA or an equivalent request to a corresponding agency in any other country or group of companies, the presentation of which is required to commence clinical testing of the Products in human beings.

LTI: means long-term incentive.

CNS Indication: means all the uses in disorders of Chapters V and VI of the Agreement (mental and behavioral disorders and disorders of the nervous system, respectively).

CPI: means the consumer price index.

KDMs: means histone deacetylase.

Exclusive license: means the worldwide license of all commercial rights and for all clinical indications of the ORY-1001 compound and its replacement compounds, which constituted the purpose of the Agreement signed between Roche and ORYZON.

Limited Licenses: means the limited licenses granted to Roche under the Agreement between Roche and ORYZON.

AML: means acute myeloid leukemia.

AML-MLL: means leukemia with MLL rearrangements, a particularly aggressive variety of AML.

LSD1: means lysine specific demethylase 1.

MAO-B: means monoamine oxidase B.

MHRA: means British Medicines and Healthcare products Regulatory Agency.

OGDSL: means ORYZON GENOMICS DIAGNÓSTICO, S.L.

ORYZON: means ORYZON GENOMICS, S.A.

PCT: means the Patent Cooperation Treaty.

PGC: means the National Chart of Accounts (*Plan General de Contabilidad*) approved by Royal Decree 1514/2007 of November 16.

Compensation Policy: means the compensation policy for the directors of ORYZON applicable for fiscal years 2016, 2017 and 2018, as approved by the shareholders at the General Shareholders' Meeting held on June 29, 2016.

First ADDF Loan: means the loan provided by ADDF to the Company in 2010 in the aggregate disbursed amount of USD 300,000 in 2015.

Program: means the initial 2-year collaborative development program between Oryzon, the Translational and Clinical Research Center (TCRC), and Roche's research and development center in North America (located in New York).

Regulations of the Board of Directors: means the regulations of the Board of Directors of ORYZON, the restated text of which was approved by the Board of Directors at its meeting held on October 2, 2015, and last amended on April 4, 2018.

Regulations for the General Shareholders' Meeting: means the regulations for the General Meeting of shareholders of ORYZON, the restated text of which was approved by the shareholders at the General Shareholders' Meeting held on October 2, 2015, and last amended on June 14, 2017.

Internal Regulations for Conduct: means the internal regulations for conduct in the securities markets approved by the Board of Directors of ORYZON at its meeting held on October 2, 2015, and last amended on October 24, 2016.

Fixed Compensation: means the compensation consisting of a fixed amount paid to the members of the Board of Directors of ORYZON, to be determined annually on an individual basis by the shareholders at a General Shareholders' Meeting of the Company for the fiscal year in which it is adopted.

Roche: means the multinational pharmaceutical company F. HOFFMANN-LA ROCHE, LTD.

SCLC: means small-cell lung cancer.

Second ADDF Loan: means the loan provided and disbursed by the ADDF to the Company in 2015 in the amount of USD 270,000.

Company: means ORYZON GENOMICS, S.A.

SPMS: means secondary progressive multiple sclerosis.

Third ADDF Loan: means the loan provided and disbursed by the ADDF to the Company in 2-17 in the amount of USD 300,000.

ADHD: means attention-deficit/hyperactivity disorder.

EU: means European Union.

In Madrid, on July 23, 2018

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Signed: Mr. Carlos Manuel Buesa Arjol

Attorney-in-fact of Oryzon Genomics, S.A.