



French Société Anonyme (joint stock company) with share capital of €517,619.54  
Registered office: 259/261 Avenue Jean Jaurès – Immeuble le Sunway – 69007 LYON  
Lyon Trade And Companies Registry 510 970 817

## 2018 DOCUMENT DE RÉFÉRENCE



AUTORITÉ  
DES MARCHÉS FINANCIERS

This *document de référence* was filed with the *Autorité des Marchés Financiers* (the “AMF”) on April 8, 2019 under the number D.19-0289, in accordance with Article 212-13 of its General Regulation. It may be used to support a financial transaction if completed by an offering circular approved by the AMF. This document was prepared by the issuer and is the responsibility of its signatories.

In accordance with Article 28 of Commission Regulation (EC) No. 809/2004, the Poxel restated financial statements for financial years 2016 and 2017, prepared in accordance with IFRS as adopted by the European Union, as well as the related statutory auditors’ report set out in Sections 20.1 “IFRS financial statements prepared for the financial years ended December 31, 2016 and December 31, 2017” and 20.2 “Verification of Annual Historical Financial Information” of the *documents de référence* registered with the AMF respectively on April 24, 2017 and on April 27, 2018 under numbers R.17-020 and R.18-0035, are included for reference purposes in this *document de référence*. “

This document is available free of charge at the Company’s registered office, and in electronic form on the website of the *Autorité des Marchés Financiers* ([www.amf-france.org](http://www.amf-france.org)) and on the Company’s website ([www.poxel.com](http://www.poxel.com)).

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## GENERAL REMARKS

### *Note*

In this *document de référence*, and unless otherwise indicated:

- The terms the “**Company**” or “**Poxel**” refer to Poxel, a French société anonyme (public limited company) with share capital of €517,619.54, whose registered office is at 259/261 Avenue Jean Jaurès – Immeuble le Sunway – 69007 Lyon, France, and which is registered with the Lyon Trade and Companies Registry under number 510 970 817.
- The term the “**Group**” refers to the Company and to all companies falling within its scope of consolidation.

The financial statements prepared in accordance with French accounting standards for the financial year ended December 31, 2018 are set out in Section 26.1 “Statutory financial statements prepared for the year ended December 31, 2018” of this *document de référence*.

### *Warning*

This *document de référence* contains information relating to the business activities of the Company and the market in which it operates. This information derives from studies attributable to internal or external sources (e.g. industry publications, specialized studies, information published by market research companies, analysts’ reports). The Company believes that as of the date of this document, this information provides a true and fair view of its reference market and its competitive position in this market. However, this information has not been verified by an independent expert and the Company cannot guarantee that a third party using different methods to gather, analyze or calculate market data would obtain the same results.

### *Forward-looking statements*

This *document de référence* also contains information on the Company’s objectives and development priorities. This information is sometimes identified by the use of the future or conditional tense and forward-looking terms such as “estimate,” “consider,” “aim,” “expect,” “intend,” “should,” “would” and “could,” or any other variant or similar terminology. The reader's attention is drawn to the fact that these objectives and development priorities are not historical data and must not be interpreted as a guarantee that the facts and data mentioned will occur, that the assumptions will be verified or that the objectives will be achieved. These are objectives which by nature might not be achieved and the information provided in this *document de référence* may be incorrect without the Company’s being required to update it, subject to applicable regulations, including the General Regulation of the *Autorité des Marchés Financiers*.

### *Risk factors*

Investors are invited to consider the risk factors described in Section 4 “Risk factors” of this *document de référence* before making any investment decision. The realization of any or all of these risks could have a negative effect on the business, position, financial results or objectives of the Company. In addition, other risks not yet identified or considered immaterial by the Company could have the same negative effect and investors could lose all or part of their investment.

## 1. INDIVIDUALS RESPONSIBLE

### 1.1. Person in charge of the document de référence

Mr. Thomas Kuhn, Chief Executive Officer

### 1.2. Certification by the person in charge

I certify, after having taken all reasonable measures to this effect, that the information contained in this *document de référence* is, to my knowledge, consistent with reality and there is no omission likely to affect its impact.

I certify that, to my knowledge, the financial statements have been prepared in accordance with the applicable accounting standards and give a true and fair view of the Company's assets and liabilities, financial position and operating results, and that the management report, the table of concordance for which is set out on page 328, gives a reliable account of the developments in business activities, the operating results and the financial position of the Company and all companies included in the scope of consolidation, as well as a description of the main risks and uncertainties they face.

I have obtained a letter from the Statutory Auditors, stating that they have completed their engagement, which included checking the information concerning the financial situation and the accounts contained in this *document de référence* and reading all of this *document de référence*.

Signed in Lyon, on April 8, 2019

Mr. Thomas Kuhn,  
Chief Executive Officer

### 1.3. Person in charge of financial reporting

Ms. Anne Renevot,  
Director of Finances  
Address: 259/261 Avenue Jean Jaurès - Immeuble le Sunway - 69007 Lyon  
Phone: 0033 4 37 37 20 10  
Email: [investors@poxelpharma.com](mailto:investors@poxelpharma.com)

## 2. STATUTORY AUDITORS

### 2.1. Statutory auditors

MAZARS SA, member of the regional institute of statutory auditors (*compagnie régionale des commissaires aux comptes*) of Versailles, Tour Exaltis – 61 rue Henri Regnault, 92400 Courbevoie represented by Séverine HERVET

First appointment date: January 29, 2016

Term: Five years, corresponding to the remainder of the term of office of its predecessor

Term expiration date: during the General Meeting of Shareholders to approve the financial statements for the financial year ended December 31, 2020

PRICEWATERHOUSECOOPERS AUDIT, member of the regional institute of statutory auditors of Versailles, 63 rue de Villiers, 92208 Neuilly-Sur-Seine Cedex represented by Elisabeth L'HERMITE

Appointment date: January 31, 2014

Term: Six years

Term expiration date: during the General Meeting of Shareholders to approve the financial statements for the financial year ended December 31, 2019

### 2.2. Alternate statutory auditors

Emmanuel CHARNAVEL, member of the regional institute of statutory auditors of Lyon, Le Premium, 131 Boulevard Stalingrad, 69624 Villeurbanne Cedex

Alternate for MAZARS SA

Appointment date: January 29, 2016

Term: Five years, corresponding to the remainder of the term of office of its predecessor

Term expiration date: during the General Meeting of Shareholders to approve the financial statements for the financial year ended December 31, 2020

Jean-Christophe GEORGHIU, member of the regional institute of statutory auditors of Versailles, 63 rue de Villiers, 92208 Neuilly-Sur-Seine Cedex

Alternate for PRICEWATERHOUSECOOPERS AUDIT

Appointment date: January 31, 2014

Term: Six years

Term expiration date: during the General Meeting of Shareholders to approve the financial statements for the financial year ended December 31, 2019

### 2.3. Information on auditors who have resigned, have been removed or have not been renewed

None.

### 3. SELECTED FINANCIAL INFORMATION

The selected financial information presented below is extracted from the Company's consolidated financial statements prepared in accordance with IFRS for the fiscal years ended December 31, 2017 and 2018, set out in Section 20.1 of this *document de référence*.

This selected accounting and operating data should be read in conjunction with the information contained in Sections 9 "Operating and Financial Review" and 10 "Liquidity and Capital Resources" of this *document de référence*.

Simplified balance sheets in K€ IFRS standards	12/31/2018 Audited 12 months	12/31/2017 Audited 12 months	12/31/2016 Audited 12 months
<b>TOTAL ASSETS</b>	<b>105 516</b>	<b>66 752</b>	<b>50 304</b>
<b>Non-current assets</b>	<b>17 246</b>	<b>500</b>	<b>703</b>
<i>of which intangible assets</i>	16 577		
<i>of which tangible fixed assets</i>	296	143	145
<i>of which of which other non-current financial assets</i>	372	356	557
<b>Current assets</b>	<b>88 270</b>	<b>66 253</b>	<b>49 601</b>
<i>of which trade receivables and related receivables</i>	14 262	4 902	36
<i>of which other receivables</i>	7 271	7 187	3 997
<i>of which cash and cash equivalents</i>	66 737	54 163	45 569
<b>TOTAL LIABILITIES</b>	<b>105 516</b>	<b>66 752</b>	<b>50 304</b>
<b>Shareholders' equity</b>	<b>55 782</b>	<b>19 327</b>	<b>39 385</b>
<b>Non-current liabilities</b>	<b>638</b>	<b>785</b>	<b>840</b>
<i>of which commitments to employees</i>	279	230	131
<i>of which non-current financial debts</i>	359	555	709
<b>Current liabilities</b>	<b>49 096</b>	<b>46 640</b>	<b>10 079</b>
<i>of which current financial debts</i>	13 873	936	1 017
<i>of which provisions</i>	18	84	
<i>of which trade payables and related accounts</i>	20 742	9 008	8 547
<i>of which tax and social security liabilities</i>	1 129	899	460
<i>of which other creditors and accrued liabilities</i>	13 334	35 714	55

Simplified income statements in K€ IFRS standards	12/31/2018 Audited 12 months	12/31/2017 Audited 12 months	12/31/2016 Audited 12 months
<b>Revenue</b>	<b>74 605</b>	<b>5 290</b>	<b>70</b>
<i>Net research and development costs of the RTC</i>	-54 540	-20 973	-17 675
<i>General and administrative expenses</i>	-7 527	-6 219	-6 678
<b>Operating income</b>	<b>12 538</b>	<b>-21 902</b>	<b>-24 282</b>
<i>Financial expenses</i>	-28	-81	-505
<i>Financial income</i>	1 092	-315	304
<b>Net income</b>	<b>13 525</b>	<b>-22 298</b>	<b>-24 483</b>
<i>Earnings per share</i>	0,54	(0,97)	(1,16)

<b>Simplified cash flow statements (in K€ Consolidated financial statements - IFRS standards]</b>	<b>12/31/2018 Audited 12 months</b>	<b>12/31/2017 Audited 12 months</b>	<b>12/31/2016 Audited 12 months</b>
<b>Cash flow from operating activities</b>	<b>-4 744</b>	<b>8 126</b>	<b>-18 849</b>
<i>of which self-financing capacity</i>	<i>15 116</i>	<i>-20 377</i>	<i>-22 886</i>
<i>of which change in WCR]</i>	<i>-19 860</i>	<i>28 503</i>	<i>4 037</i>
<b>Cash flows from investing activities</b>	<b>-7 608</b>	<b>213</b>	<b>180</b>
<b>Cash flows from financing activities</b>	<b>25 676</b>	<b>-496</b>	<b>21 824</b>
<b>Change in cash position and cash equivalents</b>	<b>13 325</b>	<b>7 843</b>	<b>3 155</b>
Cash position and cash equivalents at the beginning of the year	53 412	45 569	42 413
Cash position and cash equivalents at the end of the year	66 737	53 412	45 569

<b>Level of the Company's net debt (in K€) IFRS standards</b>	<b>12/31/2018 Audited 12 months</b>	<b>12/31/2017 Audited 12 months</b>	<b>12/31/2016 Audited 12 months</b>
+ Non-current financial liabilities	359	555	709
+ Current financial liabilities	13 827	936	1 017
- Cash and cash equivalents	66 737	54 163	45 569
<b>Total net debt (1)</b>	<b>-52 505</b>	<b>-52 589</b>	<b>-43 843</b>

(1) Net debt is the sum of financial debt, less net cash (active cash flow, less passive cash flow)

## 4. RISK FACTORS

*Any investment in a Company involves a degree of risk. Potential investors are asked to read attentively all the information contained in this document de référence, and especially consider all the risks associated with such an investment, including the risk factors described in this section, before deciding to subscribe or acquire Company shares.*

*The Company performed a review of risks that could have an unfavorable effect on the Company, its business, prospects, capacity to meet its objectives, financial position, cash flows or operating results.*

*The attention of potential investors is drawn to the fact that the list of risks and uncertainties given below is not exhaustive. The risks discussed below are those that the Company considers significant. Other risks or uncertainties that are unknown or have not been considered, as of the date of this document de référence, as likely to have a significant unfavorable effect may exist, and the manifestation of one or more of these risks could have a significant unfavorable result on the Company, its business, prospects, capacity to meet its objectives, financial position, cash flows or operating results.*

### 4.1. Risks related to the Company's drug candidate portfolio

- 4.1.1.** Drug candidates under development must undergo costly, rigorous and highly regulated preclinical studies and clinical trials, whose time of completion, number and outcomes are uncertain.

The Company is engaged in preclinical studies and clinical trials, with the primary objective of developing and marketing drug therapies aimed at combating metabolic pathologies, including type 2 diabetes and non-alcoholic steatohepatitis (NASH). Preclinical studies and clinical trials are generally expensive, are difficult to design and implement, can take many years to complete and are inherently uncertain as to outcome. The Company cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, if at all. It may take several years to complete the preclinical studies and clinical development necessary to commercialize a drug candidate, and delays or failure can occur at any stage. Interim results of clinical trials do not necessarily predict final results, and success in preclinical studies and early clinical trials does not ensure that later clinical trials will be successful. A number of companies in the pharmaceutical, biopharmaceutical and biotechnology industries have suffered significant setbacks in advanced clinical trials even after promising results in earlier trials, and the Company cannot be certain that it will not face similar setbacks. The design of a clinical trial can determine whether its results will support approval of a product, and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced. An unfavorable outcome in one or more trials would be a major setback for the Company and its drug candidates. Due to the Company's limited financial resources, an unfavorable outcome in one or more trials may require it to delay, reduce the scope of, or eliminate one or more product development programs, which could have a material adverse effect on its business and financial position and on the value of its securities.

In connection with clinical trials, the Company faces a number of risks, including risks that:



- a drug candidate is ineffective, inferior to existing approved medicines, unacceptably toxic or has unacceptable side effects;
- patients who take part in clinical trials may suffer severe, or even fatal, reactions for reasons that may or may not be related to the drug candidate being tested;
- studies conducted regularly on long-term tolerability could invalidate the use of the Company's product;
- the results may not confirm the positive results of earlier testing or trials; and
- the results may not meet the level of statistical significance required by the European Medicines Agency, or EMA; the U.S. Food and Drug Administration, or FDA; the Pharmaceuticals and Medical Devices Agency, or PMDA; or other regulatory authorities to establish the safety and efficacy of its drug candidates.

In addition, regulatory authorities in the jurisdictions in which the Company intends to market its drug candidates may interpret results in a different manner than the Company has. In any event, the regulatory authorities have the discretion to require further testing (including relating to research protocols, patient characteristics, durations of treatment and post-treatment monitoring) or to impose additional and unexpected conditions on the trials. The outcome of these trials is highly uncertain, and there can be no assurance that any of the Company's drug candidates will successfully complete their respective trials with marketable results or within a time frame that permits profitable marketability.

The Company cannot guarantee that the results of the clinical trials will demonstrate the tolerability, safety (including the absence or limited nature of adverse side effects or interactions with other drugs and therapies) and efficacy of one or more of its drug candidates on humans. Any failure to so demonstrate during one or more of the various clinical phases could result in a delay in the development and marketing of the product in question or result in suspension of its development.

Imeglimin, the Company's most advanced drug candidate, is currently in phase III clinical studies in Japan under the partnership agreement signed with Sumitomo Dainippon Pharma. In 2019, the Company aims to initiate phase III in the United States and in Europe, under the partnership agreement signed with Roivant Sciences LLC "Roivant Sciences" or "Roivant"). PXL770 and PXL065 (the latter initially developed by DeuteRx LLC under the name DRX-065), the Company's two other main drug candidates, are in development and are the subject of preclinical studies and clinical trials. The Company is in the process of preparing the phase IIa proof-of-concept study for the treatment of NASH patients with or without type 2 diabetes for PXL770, which should be launched in the first quarter of 2019. The Company has also begun the second part of PXL065 development phase Ia, whose results are expected in the first quarter of 2019.

Entry into more advanced clinical study phases, especially phase III, exposes broader samples of the population, and for a longer period of time, to a particular drug candidate, which could reveal previously unseen or unnoticed safety problems, adverse effects and interactions or a lack of efficacy. Moreover, clinical trials, notably phase III clinical trials, can also reveal currently unknown, but isolated, effects or trigger or aggravate currently unknown pathologies, whether pre-existing or not, which could delay or interrupt development of the drug candidate. In order to complete certain phase III and other clinical trials, the Company has entered into partnerships and, accordingly, will be subject to risks associated with its reliance on partnerships and third parties (see Section 4.2 of the present *document de référence*).

If any of the foregoing materializes, or the Company's drug candidates otherwise fail to complete, or are delayed in the completion of, their respective clinical trials, the commercialization of such drugs could be delayed or prevented, which could have a materially adverse impact on its business, prospects, financial position, cash flows or operating results.

**4.1.2.** Clinical trials are subject to prior approval by regulatory authorities, which may not be granted.

All of the Company's drug candidates are in preclinical studies or clinical trial phases and none have been submitted for final approval. Accordingly, further clinical trials will be required. All clinical trials are subject to prior approval by the regulatory authorities of the jurisdiction in which the trial is to be carried out, as well as by various ethics and similar committees. A failure to obtain an approval, or a negative opinion of a committee could delay or suspend the Company's clinical development program. Additionally, once the Company has the relevant approvals for a drug-candidate, the regulatory authorities could still subsequently suspend or terminate its development. If any of these events occur, it could have a material adverse effect on the Company's business, prospects, financial position, cash flows or operating results.

**4.1.3.** Most of the Company's human, financial and material resources are allocated to developing three drug candidates, Imeglimin, PXL770 and PXL065.

The Company's business and future success depends on its ability to complete clinical development of its lead drug candidate and of PXL770 and PXL065, its two other drug candidates, and obtain regulatory approval for and successfully market these three drug candidates.

The Company is particularly exposed to delays in the development and commercialization of its main drug candidate, Imeglimin. In late 2017, the Company started a phase III trial program in Japan as part of a partnership established in October 2017 with Sumitomo Dainippon Pharma, according to the financial terms described in this agreement. As part of a partnership with Roivant Sciences established in February 2018, it is currently preparing the phase III development program in the United States and Europe. The Company's objective is to initiate phase III in these geographic areas in 2019.

Therefore, the Company aims to meet the requirements of the PMDA, EMA and FDA simultaneously. However, its capacity to meet all the requirements of these regulatory authorities at the same time is uncertain at this stage.

The Company is also exposed to similar risks for its two other main drug candidates, PXL770 and PXL065, which are currently in preparation for a phase IIa study and for the second part of phase Ia, respectively.

All of the Company's drug candidates, including Imeglimin, PXL770 and PXL065, will require additional clinical and non-clinical development, regulatory review and approval in multiple jurisdictions, substantial investment, access to sufficient manufacturing and marketing capacities and significant marketing efforts before it can generate any revenue from product sales.

As specified below, the Company has established partnerships with Sumitomo Dainippon Pharma and Roivant Sciences. In addition to transfer of the Imeglimin license to the partner, these partnerships include the partner's commitment to finance Imeglimin's phase III development program. Any shortfall or delay in financing by the Company's partners could delay or impede completion of phase

III clinical trials of Imeglimin in a given jurisdiction. The collaboration agreement entered into with DeuteRx for purposes of acquiring its new drug candidate, PXL065, includes the principles governing the collaboration between the Company's teams and those of DeuteRx for developing PXL065 (refer to Section 4.2 "Risks Related to the Company's dependence on third parties" of this document de référence) which, if they were not implemented, could delay or impede the performance of clinical trials for PXL065.

If the Company fails to successfully develop or market Imeglimin, PXL770 and PXL065, or causes a delay in their development or marketing, this could have material adverse effects on its business, prospects, financial position, cash flows or operating results.

**4.1.4.** The Company's capacity to continue its acquisition and/or development strategy for new drug candidates will be important for its future prospects.

In August 2018, the Company acquired PXL065 from DeuteRx LLC (initially called DRX-065) as well as other programs (refer to Chapter 6, "Business Overview" of this document de référence).

Although the Company seeks to continue its drug candidate acquisition and development strategy, it cannot guarantee that it will be able to develop or market them successfully. Nor can it guarantee that the future drug candidates will receive the regulatory authorizations necessary for their marketing and commercialization.

The Company could also envisage acquiring companies or technologies, permitting it to have access to new drugs, research projects or new geographic areas, or create synergies with its existing activities. If such acquisitions are envisaged, the Company may not be able to identify interesting targets or conclude these operations at advantageous conditions.

The Company also may be unable to obtain the financing necessary for these acquisitions. The Company could be obliged to finance these operations using the cash flow that could be devoted to other purposes in the context of existing activities.

If the Company were to acquire companies that own important brands or promising technologies, without being able to integrate them in its current activities and business culture, the expected benefits of such acquisitions could be reduced. For example, the Company may encounter difficulties in the development, manufacture and commercialization of new products resulting from a strategic alliance or an acquisition, which would delay or reduce the expected benefits. The Company cannot guarantee that following such acquisitions it will be able to create the expected synergies to justify the operation, which could have a significant negative impact on its activity, financial position, profits and prospects.

Moreover, the successful launch of drug candidates developed by the Company will depend on many factors, and namely its ability to:

- properly identify and anticipate patient needs;
- develop and launch new drug candidates;
- not infringe on third-party intellectual property rights;
- demonstrate, if applicable, the safety and efficacy of new drug candidates, relying on results of scientific studies and preclinical and clinical trials;

- Obtain regulatory authorizations or approval required for the use and commercialization of new drug candidates;
- Access sufficient manufacturing and commercialization capacities;
- Develop a specialized distribution and commercialization network;

Nevertheless, if the Company does not manage to continue its new product acquisition and development strategy in a way to respond to market needs at the appropriate time, or if the demand for these products turns out to be insufficient, its activity, financial position, profits and prospects in the medium and long terms could be affected significantly.

## **4.2. Risks related to the Company's dependence on third parties**

**4.2.1.** The Company established partnership agreements with third parties for the development and commercialization of its main drug candidate. Its prospects will depend in large part on maintenance and/or proper execution of these partnership agreements.

The Company signed a partnership agreement with Sumitomo Dainippon Pharma for co-development and commercialization of Imeglimin in Japan, China and other Asian countries. It also signed a license agreement with Roivant Sciences for development and commercialization of Imeglimin in the United States, Europe and other Asian countries not covered by its agreement with Sumitomo Dainippon Pharma. In addition, the Company signed a license agreement with Enyo Pharma for a new FxR receptor (farnesoid X receptor) agonist.

The Company will have limited control over the amount and timing of resources that its collaborators will dedicate to the development or commercialization of its drug candidates. The Company's ability to generate revenues from these agreements will depend on any future partners' abilities to successfully perform the functions assigned to them in these agreements. In addition, any future partners may have the right to abandon research or development projects and terminate applicable agreements, including funding obligations, prior to or upon expiration of the agreed upon terms.

Collaborations involving the development and commercialization of Imeglimin pose a number of risks, including the following:

- partners have significant discretion in determining the efforts and resources that they will apply to these partnerships;
- partners may not perform their obligations as expected;
- partners may not pursue development and commercialization of the Company's drug candidates or may elect not to continue or renew development or commercialization programs, based on clinical trial results, changes in the collaborators' strategic focus or available funding or external factors that divert resources or create competing priorities;
- partners may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon Imeglimin, repeat or conduct new clinical trials or require a new formulation of Imeglimin for clinical testing;
- partners could independently develop, or develop with third parties, products that compete directly or indirectly with Imeglimin;

- partners with marketing and distribution rights to Imeglimin may not commit sufficient resources to the marketing and distribution of this product;
- disagreements with partners, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays or termination of the research, development or commercialization of Imeglimin, might lead to additional responsibilities for the Company with respect to Imeglimin, or might result in litigation or arbitration, any of which would be time-consuming and expensive;
- partners may not properly maintain or defend the Company's intellectual property rights or may use its proprietary information in such a way as to invite litigation that could jeopardize or invalidate its intellectual property or proprietary information or expose the Company to potential litigation;
- partners may infringe on the intellectual property rights of third parties, which may expose the Company to litigation and potential liability;
- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of Imeglimin; and
- if one of the Company's partners is involved in a business combination, it could decide to delay, diminish or terminate the development or commercialization of Imeglimin licensed to it by the Company. Collaboration agreements might not result in highly performing development or commercialization of Imeglimin, or might simply not give any results at all.

**4.2.2.** The Company relies on third parties to conduct its clinical trials, which may result in costs and delays that prevent it from successfully commercializing its drug-candidates.

The Company relies on third parties, such as contract research organizations, clinical data management organizations, medical institutions and clinical investigators, to conduct its clinical trials and, in particular, for its phase III clinical trials of Imeglimin in Japan, in the context of obligations resulting from the contract signed with Sumitomo Dainippon Pharma. The Company may not be able to locate a suitable partner and may not be able to enter into an agreement on commercially reasonable terms or at all. In the framework of such agreements, the Company's development activities or clinical trials conducted by third parties may be delayed, suspended or terminated if:

- the third parties do not devote a sufficient amount of time or effort to the Company's activities or otherwise fail to successfully carry out their contractual duties or meet regulatory obligations or expected deadlines;
- the quality or accuracy of the data obtained by third parties is compromised due to their failure to adhere to clinical protocols, regulatory requirements or for other reasons; or
- in general, the Company is unable to control the performance by third parties of their obligations relating to completion of development activities.

Third-party performance failures may increase the Company's development costs, delay its ability to obtain regulatory approval, and delay or prevent commercialization of its drug candidates. While the Company believes that there are numerous alternative sources to provide these services, in the event

that the Company seeks such alternative sources, it may not be able to enter into replacement arrangements without incurring delays or additional costs.

Regarding PXL065 more specifically, the Company acquired this program from DeuteRx in August 2018. The first part of phase Ia clinical studies for PXL065 have been conducted by DeuteRx in the past (refer to Section 6.5 “PXL770 and PXL065, two Novel Drug Candidates for Purposes of treating NASH patients” of this document de reference). The Company's current development and clinical trial activities for PXL065 could be delayed, suspended or interrupted if the quality or accuracy of data obtained by DeuteRx in the past is compromised or challenged for any reason, especially if DeuteRx failed to comply with clinical protocols or any regulatory requirements.

The Company's dependence on clinical studies conducted by DeuteRx in the past could lead to expenses and delays impeding successful marketing of PXL065 according to the planned timetable. Furthermore, the failure of DeuteRx to execute certain obligations under the agreement signed with this company may increase the Company's development costs, delay its ability to obtain regulatory approval, and delay or prevent the commercialization of its third drug candidate, PXL065. This could have a material adverse effect on the Company's business, prospects, financial position, cash flows or operating results.

#### **4.2.3. The Company uses a small number of suppliers and external providers.**

Currently, the Company uses, and counts on using, a small number of suppliers and external providers for the supply of raw materials, chemical products and clinical batches necessary for its clinical and preclinical trials and their execution. The Company may be unable to establish any additional agreements with suppliers and external providers or to do so on acceptable terms.

Even if the Company is able to establish such agreements, reliance on suppliers or external providers entails additional risks, including:

- reliance on the supplier or external provider for regulatory compliance and quality assurance;
- the possible breach of the supply agreement by the supplier or external provider;
- the possible termination or non-renewal of the agreement by the supplier or external provider at a time that is costly or inconvenient for the Company; and
- reliance on the supplier or external provider for regulatory compliance, quality assurance and safety.

Third-party manufacturers may not be able to comply with current good manufacturing practices (“Good Manufacturing Practices”), regulations or applicable regulatory requirements. In the event of non-compliance with the applicable regulation by the Company or its suppliers or external providers, it may be subject to sanctions, such as fines; injunctions; civil penalties; postponement, suspension or withdrawal of authorizations; withdrawals of licenses; seizure or recall of drug-candidates; operation restrictions and criminal proceedings. These sanctions could have significant negative effects on the duration, cost or continuation of clinical trials, which would have an impact on the future manufacturing and commercialization of the Company's drugs and would be prejudicial for its business and operational results.

Any performance failure on the part of the Company's existing or future suppliers could delay clinical development or marketing approval. If any one of the Company's current suppliers or providers cannot perform as agreed, the Company may be required to replace that supplier or provider. Although there are several potential alternative suppliers who could supply the various raw materials and chemical products and adequate batches needed for the Company's preclinical studies and clinical trials, it may incur added costs and delays in identifying and qualifying any such replacement.

The Company's current and anticipated future dependence upon third parties for the supply and manufacture of its drug-candidates may adversely affect its future profit margins and its ability to commercialize any drug-candidates that receive marketing approval on a timely and competitive basis.

**4.2.4.** The Company currently has no sales organization. If the Company is unable to enter into sales, marketing and distribution agreements with third parties, it may not be successful in commercializing its drug candidates if and when they are approved.

The Company does not have a sales or marketing infrastructure and has no experience in the sale, marketing or distribution of pharmaceutical products. To achieve commercial success for any drug candidate for which the Company obtains marketing approval, it will need to establish a sales and marketing organization or make arrangements with third parties to perform sales and marketing functions, and it may not be successful in doing so.

The Company has entered into and will rely on partnerships with third parties to advance development and ultimately commercialize its drug candidates. Therefore, the Company's turnover for such products and the profitability of sales of its drugs will be lower, even much lower compared to if the Company had commercialized and sold its drugs itself.

The Company has little control over such third parties, and these partners may fail to devote the necessary resources and attention to sell and market its drugs effectively. For example, the Company's partners' budgeting restrictions or strategy changes could delay or prevent successful clinical development or marketing efforts. Similarly, the Company's partners could decide to give priority to the clinical development or marketing of other drug candidates or develop or seek to develop drug candidates in competition with the Company's drug candidates.

The Company's failure to pursue its partnerships could have a material adverse effect on its business, prospects, financial position, cash flows or operating results.

#### **4.3. Risks related to product development, approval of regulatory authorities and the Company's market.**

**4.3.1.** The Company's drug candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following marketing approval, if any.

Undesirable side effects caused by the Company's drug candidates could cause the Company or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the EMA, FDA, PMDA or other comparable authorities in other jurisdictions. Furthermore, the Company's drug candidates may be found to have interactions with other drugs or treatments that are not acceptable or not mitigated. In such an event,

the Company's trials could be suspended or terminated and the EMA, FDA, PMDA or comparable foreign regulatory authorities could order the Company to cease further development of or deny approval of its drug candidates for any or all targeted indications. Product-related side effects could affect patient enrollment in the Company's clinical trials or the ability of any enrolled patients to complete such trials, or even result in potential product liability claims. Any of these occurrences may significantly harm the Company's business, financial position and prospects.

If one or more of the Company's drug candidates received marketing approval, and the Company or others later identify undesirable side effects caused by such drugs, or negative interactions with other products or treatments (including, for example, as a result of interactions with other products once on the market, as illustrated in the section "Interaction with other products may delay or prohibit marketability of the Company's drug candidates"), a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw approvals of such product;
- regulatory authorities may require additional warnings on the product's label;
- the Company may be required to create a medication guide outlining the risks of such side effects for distribution to patients;
- the Company could be sued and held liable for harm caused to patients; and
- the Company's reputation may suffer.

Any of these events could prevent the Company from achieving or maintaining market acceptance of the particular drug candidate, if approved, and could have a material adverse effect on its business, prospects, financial position, cash flows or operating results.

**4.3.2.** Interaction with other products may delay or prohibit marketability of the Company's drug candidates.

The Company's drug candidates are intended to be used in combination with certain other products. The Company undertakes studies to determine any risks arising from the Company's drug candidates' interaction with other products and treatments when taken in combination. For example, combined use of Imeglimin and metformin may in the future show additive toxicities despite the Company's belief of sufficient mechanistic differences between these drugs. These studies, by their nature, cannot cover every possible combination. In addition, the Company's drug candidates may interact negatively with other products and treatments in certain populations not covered by any of its studies. Furthermore, such negative interactions may only arise once the Company's drugs, if approved, have been released to the market. Any such interactions may have unacceptable or undetected side effects or reduce or negate the efficacy of the Company's drug candidates, which could reduce the marketability of its drug candidates, delay the development of its drug candidates and, in turn, have a material adverse effect on its business, prospects, financial position, cash flows or operating results.

**4.3.3.** Delays, suspensions and terminations in its clinical trials could result in increased costs to the Company and delay or prevent its ability to generate revenues.

Human clinical trials are very expensive, time-consuming, and difficult to design, implement and complete. The completion of trials for Imeglimin or the Company's other drug candidates may be delayed, suspended or terminated due to a number of factors, including:

- lack of effectiveness of drug candidates during clinical trials;



- adverse events, safety issues or side effects relating to the drug candidates or their formulation;
- inability to raise additional capital in sufficient amounts to continue clinical trials or development programs, which are very expensive;
- the need to sequence clinical trials as opposed to conducting them concomitantly in order to conserve resources;
- the Company's inability to conduct clinical trials in accordance with regulatory requirements;
- the Company's inability to manufacture or obtain from third parties materials sufficient for use in preclinical studies and clinical trials;
- governmental or regulatory delays or changes in regulatory requirements, policy and guidelines, including mandated changes in the scope or design of clinical trials or requests for supplemental information with respect to clinical trial results;
- delays in patient enrollment, variability in the number and types of patients available for clinical trials, and lower-than anticipated retention rates for patients in clinical trials;
- difficulty in patient monitoring and data collection due to failure of patients to maintain contact after treatment; and
- varying interpretations of the Company's data and regulatory commitments and requirements by the EMA, FDA, PMDA and other regulatory authorities.

Many of these factors may also ultimately lead to denial of the Company's marketing application for Imeglimin, PXL770, PXL065 or even the Company's other drug candidates. If the Company experiences delays, suspensions or terminations in a clinical trial, the commercial prospects for the related drug candidate will be harmed, and its ability to generate product revenues will be delayed or such revenues could be reduced or fail to materialize.

**4.3.4.** Changes in regulatory requirements, guidance from regulatory authorities or unanticipated events during the clinical trials of the Company's drug candidates could necessitate changes to clinical trial protocols or additional clinical trial requirements, which would result in increased costs for the Company and could delay its development time line.

Changes in regulatory requirements, FDA guidance or guidance from the EMA, PMDA or other regulatory authorities, or unanticipated events during the Company's clinical trials may force the Company to amend clinical trial protocols. The regulatory authorities could also impose additional clinical trial requirements. Amendments to the Company's clinical trial protocols would require resubmission to the EMA, FDA, PMDA, national clinical trial regulators and Institutional Review Board, or IRB, for review and approval, which may adversely impact the cost, timing or successful completion of a clinical trial. These events could lead to increased costs in obtaining and maintaining regulatory authorizations, limit the economic value of the Company's drug candidates, result in clinical trial delays, or force the Company to end or conduct additional clinical trials, which may harm the commercial prospects for its drug candidates, and its ability to generate product revenue will be delayed.

- 4.3.5.** If the Company, or any of its current or future partners, experiences delays or difficulties in the enrollment of patients in clinical trials, the receipt of necessary regulatory approvals could be delayed or prevented.

The Company or its current or future partners may not be able to initiate or continue clinical trials for its drug candidates or any future drug candidates that the Company or its current or future partners would be likely to develop, if the Company or its current or future partners were not able to identify and enroll a sufficient number of eligible patients to participate in clinical trials, especially for NASH treatment, for which a large number of players are present for a limited number of study sites (refer to Section 4.4.5 “There are numerous competitors in the market for therapeutic treatments of metabolic pathologies” of this *document de référence*). Patient enrollment is a significant factor in the timing of clinical trials, and is affected by many factors, including:

- the size and nature of the patient population;
- the severity of the disease under investigation;
- the availability of approved therapeutics for the relevant disease;
- the proximity of patients to clinical sites;
- the eligibility criteria for the trial;
- the design of the clinical trial;
- efforts to facilitate timely enrollment of patients within deadlines;
- competing clinical trials; and
- clinicians’ and patients’ perceptions as to the potential advantages and risks of the drugs being studied in relation to other available therapies, including any new drugs that may be approved for similar indications.

In addition, the Company may have difficulty in retaining patients to participate in clinical trials of its drug candidates. Once recruited, patients enrolled in such trials may suspend or terminate their participation at will, at any time. If too many patients withdraw from a trial, the analysis of the results of such trial may not have a statistically significant scope.

The Company's inability, or the inability of any of its current or future partners, to recruit and retain a sufficient number of patients for its clinical trials or those of its partners could result in significant delays or may require the Company or its partners to abandon one or more clinical trials altogether, particularly for NASH treatment (refer to Section 4.4.5 “There are numerous competitors in the market for therapeutic treatments of metabolic pathologies” of this *document de référence*). Enrollment delays in the Company's or its partners’ clinical trials may result in increased development costs for its drug candidates, delay or halt the development of and approval processes for its drug candidates and jeopardize the Company's, or any current or future partners’, ability to commence sales of and generate revenues from its drug candidates, which could cause the value of the Company to decline and limit its ability to obtain financing.

- 4.3.6.** Clinical failure can occur at any stage of clinical development. The results of earlier clinical trials are not necessarily predictive of future results and any drug candidate the Company advances through clinical trials may not have favorable results in later clinical trials or receive regulatory approval.

Clinical failure can occur at any stage of the Company's clinical development. Clinical trials may produce negative or inconclusive results, and the Company may decide, or regulators may require it

to conduct additional clinical trials or preclinical studies. Moreover, success in preclinical studies and early clinical trials does not ensure that subsequent clinical trials will generate the same or similar results or otherwise provide adequate data to demonstrate the efficacy and safety of a drug candidate. A number of companies in the pharmaceuticals industry, including those with greater resources and experience than the Company, have suffered significant setbacks in phase III clinical trials, even after seeing promising results in earlier clinical trials, and the Company could face similar setbacks. The design of a clinical trial can determine whether its results will support approval of a product, and flaws in the design of a clinical trial may not become apparent until the clinical trial is well-advanced. In addition, data obtained from clinical trials and preclinical studies are susceptible to varying interpretations and analyses. Many companies that believed their drug candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval for the drug candidates. Even if the Company, or any current or future partners, believes that the results of clinical trials for its drug candidates warrant marketing approval, the EMA, FDA, PMDA or other regulatory authorities may disagree and may not grant marketing approval of the Company's drug candidates.

In some instances, there can be significant variation in safety or efficacy results between different clinical trials of the same drug candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, changes in and adherence to the dosing regimen and other clinical trial protocols, and the rate of dropout among clinical trial participants. If the Company fails to receive positive results in the clinical trials of its drug candidates, the development time line and regulatory approval and commercialization prospects for its most advanced drug candidates, and, correspondingly, its business and financial prospects will be negatively impacted.

If the Company's drug candidates are not approved for marketing by applicable government authorities, it will be unable to commercialize them. The European Commission (following review by the EMA) in Europe, the FDA in the United States, the PMDA in Japan and comparable regulatory authorities in other jurisdictions must approve new drug or biologic candidates before they can be commercialized, marketed, promoted or sold in those territories. The Company must provide these regulatory authorities with data from preclinical studies and clinical trials that demonstrate that its drug candidates are safe and effective for a defined indication before they can be approved for commercial distribution. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is inherently uncertain as to outcome. The Company must provide data to ensure the identity, strength, quality and purity of the drug substance and drug product. Also, the Company must assure the regulatory authorities that the characteristics and performance of the clinical batches will be replicated consistently in the commercial batches. The Company has focused its development and planned commercialization efforts in Europe, the United States and Japan. However, the processes by which regulatory approvals are obtained from the EMA, FDA and PMDA to market and sell a new product are complex, require a number of years and involve the expenditure of substantial resources. The Company cannot guarantee that any of its drug candidates will receive EMA, FDA or PMDA approval. Even if the Company obtains marketing approval of any of its drug candidates in a major pharmaceutical market, such as the United States, Europe or Japan, it may never obtain approval or commercialize its drug candidates in other major markets, due to varying approval procedures or otherwise, which will limit its ability to realize their full market potential.

Delays in obtaining, or a failure to secure such approvals for any or all of the Company's markets for a given drug candidate may result in a loss of development costs, loss in market value of the drug candidate and its associated intellectual property and an inability to widely market the product to the

public, which, in turn, could have a material adverse effect on the Company's business, prospects, financial position, cash flows or operating results.

**4.3.7.** The regulatory environment for the Company's drugs may change.

The Company operates in a heavily regulated industry, and regulations in some of its key markets, including in the United States, Europe and Japan, is subject to change. Any such changes could result in a limitation of the indications for which the Company may market its drugs or prevent such marketing at all. The cost of compliance with applicable regulations is significant and increasing. If this trend continues, it could reduce the economic value of any of the Company's new drugs.

For example, certain regulatory authorities, particularly the FDA, have imposed increasingly burdensome data provision requirements in order to prove the efficacy and safety of a drug candidate. These requirements have reduced the number of drug candidates meeting the criteria for approval of a New Drug Application (NDA) or for marketing approval and, accordingly, the number of products authorized. Marketed products are also subject to regular re-evaluation of the benefit-to-risk ratio after the granting of marketing approval. The discovery of problems not identified during the research stage can lead to marketing restrictions, product suspension or withdrawal and a heightened risk of legal action.

Given the progress of Imeglimin development and how close it is to being marketed in Japan, a change in regulation by the PMDA could also lead to a significant delay in the final steps of Imeglimin development and its marketing, which would have a significant impact on the Company's business, prospects, financial position, cash flows or operating results.

If the Company fails to comply with such regulations and changes in regulations, it could become subject to substantial penalties, including fines, product recalls, restrictions on sale, temporary or permanent suspension of operations and civil or criminal proceedings. Such a situation could have a material adverse effect on the Company's business, prospects, financial position, cash flows or operating results.

Moreover, given the current unfavorable context in the United States due to the government shutdown, especially of the FDA, that occurred in early 2019 and which could be repeated, the Company cannot rule out that there might be delays in the processing by the FDA of registration dossiers filed by the Company to continue clinical studies of its drug candidates. Indeed, the government shutdown, particular that of the FDA, could have a significant impact on the FDA's ability to respond to the Company within the expected time frames regarding the registration dossiers filed by the Company for the pursuit of clinical trials for the Company's drug candidates. Such a situation could have a material adverse effect on the Company's business, prospects, financial position, cash flows or operating results.

Finally, regarding the Company's drug candidate PXL065, the Company intends to undertake an accelerated procedure for submitting an NDA, under Article 505(b)(2) of the U.S. Federal Food, Drug, and Cosmetic Act (FDCA). This is a regulatory process particularly applicable to new drug candidates modifying a pharmaceutical product already approved by the FDA. This approach would allow the Company, under certain conditions, to do fewer preclinical and/or clinical studies necessary for marketing approval for PXL065, thereby accelerating the regulatory and clinical process and reducing development costs. However, the Company cannot rule out that the FDA will reject the application for accelerated process under Article 505(b)(2) of the FDCA, which would imply a return to the FDA's

conventional NDA procedure and, consequently, a shift in the original schedule. This could have a significant negative impact on the Company's business, prospects, financial position, cash flows or operating results.

- 4.3.8.** The Company is subject to health care laws and regulations which may require substantial compliance efforts and could expose it to criminal sanctions, civil penalties, contractual damages, damage to its professional reputation and diminished profits and future earnings, among other penalties.

Health care providers, in particular physicians, will play a primary role in the recommendation and prescription of the Company's products, if approved. Given the Company's operations with these providers and third-party payers, as well as its various commercial activities, the Company will be subject to applicable health legislation and regulations, including related to fraud and abuse. These texts could limit the relationships and financial or commercial agreements under which the Company conducts research, marketing and sales operations and distributes its drugs, as long as marketing approval is obtained. The limitations resulting from the applicable health legislation and regulations in the United States, on federal and state levels, and in other countries, are as follows:

- the US federal Anti-Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving or providing remuneration, including any kickback, bribe or rebate, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase or lease, order or recommendation of, any item, good, facility or service, for which payment may be made under federal healthcare programs;
- US federal civil and criminal false claims laws and civil monetary penalties laws, including the civil False Claims Act, which impose criminal and civil penalties, including those from civil whistleblower or qui tam actions, on individuals or entities for, among other things, knowingly presenting, or causing to be presented, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;
- the US federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created additional federal criminal statutes that impose criminal and civil liability for, among other things, executing or attempting to execute a scheme to defraud any health care benefit program or knowingly and willingly falsifying, concealing or covering up a material fact or making false statements relating to health care matters;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health (HITECH) Act, and its implementing regulations, which impose certain requirements on covered entities and their business associates, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information; and
- similar laws and regulations of any American state or other country, such as state anti-kickback and false claims laws, which may apply to items or services reimbursed by any third-party payer, including commercial insurers, American state marketing and/or transparency laws applicable to manufacturers that may be broader in scope than the federal requirements, American state laws that require biopharmaceutical companies to comply with the biopharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, and American state laws governing the

privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect as HIPAA, thus complicating compliance efforts.

Ensuring that the Company's business arrangements with third parties comply with applicable health care laws and regulations will likely be costly. It is possible that governmental authorities will conclude that the Company's business practices do not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other health care laws and regulations. If the Company were found to be in violation of any of these laws or any other governmental regulations that may apply to it, it may be subject to significant civil, criminal and administrative penalties, such as payment of damages, fines, exclusion from government-funded health care programs, contractual damages, reputational harm and curtailment of its operations, any of which could substantially disrupt its operations. If the physicians or other providers or entities with whom the Company expects to do business are found not to be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government-funded health care programs.

#### **4.4. Risks related to commercialization of drug candidates and the Company's market**

- 4.4.1.** Even if the Company obtains marketing approvals for its drug candidates, the terms of approvals and ongoing regulation of its drugs may limit how the Company markets its drugs, which could materially impair its ability to generate revenue.

Even if the Company receives regulatory approval for a drug candidate, this approval may carry conditions that limit the market for the drug or put the drug at a competitive disadvantage relative to alternative therapies. For instance, a regulatory approval may limit the indicated uses for which the Company can market a drug, or the patient population that may utilize the drug, or the Company may be required to add a warning to its labeling and on its packaging. Drugs with boxed warnings are subject to more restrictive advertising regulations than drugs without such warnings. These restrictions could make it more difficult to market any drug candidate. Accordingly, assuming the Company receives marketing approval for one or more of its drug candidates, it will continue to devote resources to the areas of regulatory compliance.

- 4.4.2.** Any of the Company's drug candidates for which it obtains marketing approval could be subject to post-marketing restrictions or withdrawal from the market, and the Company may be subject to substantial penalties if it fails to comply with regulatory requirements or experiences unanticipated problems with its drugs following approval.

For any of the Company's drug candidates that receive marketing approval, the manufacturing processes, post-approval studies, measures, labeling, advertising and promotional activities will be subject to continual requirements of and review by the EMA, FDA, PMDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and record keeping. Even if marketing approval of a drug candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to the conditions of approval, including the FDA requirement to

implement a Risk Evaluation and Mitigation Strategy, or REMS, to ensure that the benefits of a drug or biological product outweigh its risks.

The EMA, FDA and PMDA may also impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of a product, such as long-term observational studies on natural exposure. The FDA and other agencies, including the Department of Justice, closely regulate and monitor the post-approval marketing and promotion of products to ensure that they are manufactured, marketed and distributed only for the approved indications and in accordance with the provisions of the approved labeling. Any violation of the US FDCA and other statutes, including the False Claims Act, relating to the promotion and advertising of prescription drugs may lead to investigations or allegations of violations of US federal and state health care fraud and abuse laws and state consumer protection laws.

**4.4.3.** Even if the Company successfully completes clinical trials of its drug candidates, those candidates may not be commercialized successfully for other reasons.

Even if the Company successfully completes clinical trials for one or more of its drug candidates, those candidates may not be successfully commercialized for other reasons, including:

- failing to receive regulatory clearances required to market them as drugs;
- being subject to proprietary rights held by others;
- failing to obtain clearance from regulatory authorities on the manufacturing of its drugs;
- being difficult or expensive to manufacture on a commercial scale;
- having negative adverse effects reducing their use;
- having negative interactions with other products or treatments;
- failing to compete effectively with products or treatments commercialized by competitors; or
- failing to show that the long-term benefits of the drugs exceed their risks.

**4.4.4.** Even if any of the Company's drug candidates are commercialized, they may fail to achieve the degree of market acceptance by physicians, patients, healthcare prescribers, third-party payers or the medical community in general that is necessary for commercial success.

To date, the Company has never commercialized a product, and even if one of its drug candidates is approved by the appropriate regulatory authorities for marketing and sale, it may nevertheless fail to gain sufficient market acceptance by physicians, patients, healthcare prescribers, third-party payers and others in the medical community.

Even if the medical community accepts a product as safe and effective for its indicated use, physicians may choose to restrict the use of the product if the Company is unable to demonstrate that, based on experience, clinical data, side-effect profiles and other factors, the Company's product is preferable to any existing products or treatments. The Company cannot predict the degree of market acceptance of any drug candidate that receives marketing approval, which will depend on a number of factors, including, but not limited to:

- the demonstration of the clinical efficacy and safety of the product; and the perception of its therapeutic benefit by prescribers and patients;
- the approved labeling for the product and any required warnings;

- the potential occurrence of unfavorable side-effects and interactions;
- the product's ease of use, in particular in respect of its method of administration;
- the advantages and disadvantages of the product compared to alternative treatments;
- the Company's ability to educate the medical community about the safety and effectiveness of the product;
- the market price of the Company's product relative to competing treatments;
- the availability of coverage and adequate reimbursement from governments and other third-party payers, and patients' willingness to pay out-of-pocket for copayments or the product itself if third-party payer reimbursement is limited or not available;
- the effective implementation of a scientific publication strategy;
- the support of opinion leaders in the field of metabolic pathologies; and
- the development of one or more competing products for the same indication.

If one or more of the Company's drugs fails to be accepted by the market for any of the reasons set forth above or for any other reason in one or more jurisdictions, this could negatively affect the profitability and marketability of such drugs, which could, in turn, have a material adverse effect on the Company's business, prospects, financial position, cash flows or operating results.

**4.4.5.** There are numerous competitors in the market for therapeutic treatments of metabolic pathologies.

The biotechnology and pharmaceutical industries are highly competitive and subject to significant and rapid technological change as researchers learn more about diseases and develop new technologies and associated treatments. Numerous biopharmaceutical laboratories, biotechnology companies, institutions, universities and other research entities are actively engaged in the discovery, research, development and marketing of therapeutic solutions to treat metabolic pathologies, making it a highly competitive field. Significant competitive factors in the Company's industry include product efficacy and safety; quality and breadth of an organization's technology; skill of an organization's employees and its ability to recruit and retain key employees; timing and scope of regulatory approvals; government reimbursement rates for, and the average selling price of, products; the availability of raw materials and qualified manufacturing capacity; manufacturing costs; intellectual property and patent rights and their protection; and sales and marketing capabilities. Inasmuch as competition is intense in the Company's business sector, the Company cannot guarantee that the products it will develop will be clinically superior or scientifically preferable to products developed or presented by its competitors, and particularly regarding NASH treatment, for which many products competing with the Company's products are being developed and could reach the market before its products (refer to Chapter 6 "Business Overview" of this *document de référence*).

In addition, significant delays in the development of the Company's drug candidates could allow its competitors to succeed in obtaining EMA, FDA, PMDA or other regulatory approvals for their drug candidates faster than the Company, which could place it at a significant competitive disadvantage or deny it marketing exclusivity rights.

Furthermore, the Company's competitors may be more effective at using their technologies to develop competing products. Many of the competitors competing with the Company have significantly greater financial resources and expertise in research and development, manufacturing, preclinical studies, obtaining regulatory approvals and marketing, especially regarding NASH treatment. Mergers



and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of the Company's competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through partnership arrangements with large and established companies. These companies also compete with the Company in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, its programs.

In addition, a number of surgical and other alternative therapies to combat metabolic pathologies are being researched and are in various stages of development. Should these therapies prove effective, this could reduce the potential size of the market for the Company's drugs. In addition, there can be no assurance that the Company's competitors will not deploy their superior resources to damage the Company and its drug candidates' prospects.

The occurrence of any of the foregoing could have a significant impact on the Company's ability to generate profits from its drugs, which could, in turn, have a material adverse effect on its business, prospects, financial position, cash flows or operating results.

**4.4.6.** The Company's future growth depends, in part, on its ability to penetrate certain markets, where it would be subject to additional regulatory burdens and other risks and uncertainties.

The Company's future success will depend, in part, on its ability to commercialize its drug candidates in the United States, in Japan and in Europe and outside those markets. If the Company commercializes its drug candidates on other markets, it will be subject to additional risks and uncertainties, including:

- economic weakness, including inflation, or political instability in particular economies and markets;
- the burden of complex and changing foreign regulatory, tax, accounting and legal requirements, many of which vary between countries;
- different medical practices and customs in these countries affecting product acceptance;
- tariffs and trade barriers;
- other trade protection measures, import or export licensing requirements or other restrictive actions by governments of these countries;
- longer accounts receivable collection times;
- longer lead times for shipping;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- workforce uncertainty in countries where labor unrest is common;
- language barriers for technical training;
- reduced protection for intellectual property rights in some countries, and related prevalence of generic alternatives to therapeutics;
- foreign currency exchange rate fluctuations and currency controls;
- uncertain, differing and potentially inadequate reimbursement of the Company's drugs; and

- the interpretation of contractual provisions governed by foreign laws in the event of a contract dispute.

Sales of the Company's drugs on certain markets could also be adversely affected by the imposition of governmental controls, political and economic instability, trade restrictions and changes in tariffs.

- 4.4.7.** If marketing authorization is obtained for the third drug candidate, PXL065, the Company will have to pay a portion of the revenues related to the sales of PXL065 to DeuteRx.

The Company has entered into a collaboration agreement with DeuteRx for acquiring PXL065 (initially under the name DRX-065), and under the terms thereof, it agrees to honor certain commitments described in Section 22.4 "Contract with DeuteRx" of this *document de référence*. In particular, the Company agrees to pay DeuteRx a portion of the revenues that will arise from the sales of PXL065.

Therefore, supposing that the Company obtains a marketing authorization for PXL065 and, consequently, that it is able to market PXL065, it would be obligated to pay fees to DeuteRx based on the revenues from sales of PXL065, which would limit its ability to generate profits from PXL065.

## **4.5. Risks related to the Company's operations**

- 4.5.1.** The Company expects to expand its organization, and as a result, it may encounter difficulties in managing its growth, which could disrupt its operations.

As of February 28, 2019 the Company had 41 employees. The Company expects a significant increase in the number of employees and strong growth in its activities, in particular in the domains of product development, regulatory affairs, clinical affairs and manufacturing.

In order to manage the Company's anticipated growth and expansion, including the potential commercialization of its drug candidates in Europe, the United States and Japan, it must continue to implement and improve its managerial, operational and financial systems, expand its facilities and continue to recruit and train qualified personnel. Due to the Company's limited financial resources and the limited experience of its management team in managing a company with such expected growth, it may not be able to effectively manage the expansion of its operations or recruit and train additional qualified personnel. The expansion of the Company's operations may lead to significant costs and may divert its management and business development resources. Any inability to manage growth could delay the execution of the Company's business plans or disrupt its operations. If the Company's management is unable to effectively manage its expected development and expansion, its expenses may increase more than expected, its ability to generate or increase its revenue could be reduced and the Company may not be able to implement its business strategy. The Company's future financial performance and ability to commercialize its drug-candidates, if approved, and compete effectively will depend, in part, on its ability to effectively manage the Company's future development and expansion.

- 4.5.2.** The Company's future success depends on its ability to retain its key executives and to attract, retain and motivate qualified personnel.

The Company's success depends to a significant degree upon the work, expertise and technical and management skills of its senior management team, including, in particular, those of Thomas Kuhn, its

Chief Executive Officer. Any temporary or permanent loss of the services of any of these key individuals would have a material adverse effect on the Company.

Recruiting and retaining additional qualified management and scientific, clinical, manufacturing and sales and marketing personnel will also be critical to the Company's success, particularly as it expands, in order to acquire additional skills, such as manufacturing, quality assurance and regulatory and medical affairs. The loss of the services of the Company's senior management team or other key employees could impede the achievement of its research, development and commercialization objectives and seriously harm its ability to successfully implement its business strategy. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in the Company's industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize drug candidates. The Company may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel.

The Company is also experiencing intense competition for the hiring of scientific and clinical personnel from other companies, universities and research institutions. In addition, the Company relies on consultants and advisors, including scientific and clinical advisors, to assist it in formulating its research and development and commercialization strategy. The Company's consultants and advisors may be employed by employers other than the Company and may have commitments under consulting or advisory contracts with other entities that may limit their availability to the Company.

If the Company is unable to continue to attract and retain high quality personnel, the marketing and production of its drugs could be delayed or prevented, which could, in turn, have a material adverse effect on its business, prospects, financial position, cash flows or operating results.

**4.5.3.** The Company's employees may engage in misconduct or other improper activities, including violating applicable regulatory standards and requirements or engaging in insider trading, which could significantly harm its business.

The Company is exposed to the risk of employee fraud or other misconduct. Misconduct by employees may include the following deliberate acts:

- non-compliance with legal requirements or the regulations of the EMA, FDA, PMDA and control authorities of other States;
- providing inaccurate information to the EMA, FDA, PMDA and supervisory authorities of other States;
- non-compliance with legal requirements or regulations regarding fraud and abuse and other health care laws and regulations in Europe, the United States, Japan and elsewhere;
- non-reporting of accurate financial information or data; or
- non-disclosure of unauthorized activities to the Company.

In particular, sales, marketing and business agreements in the health care industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations restrict or prohibit a wide range of agreements related to pricing, discounting, marketing and promotion, sales commissions, customer incentive programs, etc. Employee misconduct could also involve the improper use of, including trading on,

information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to the Company's reputation. It is not always possible to identify and deter employee misconduct. The precautions the Company takes to detect and prevent this activity may be ineffective in controlling unknown or unmanaged risks or losses or in protecting it from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against the Company, and it is not successful in defending itself or asserting its rights, those actions could have a significant impact on its business, including the imposition of significant fines or other sanctions.

**4.5.4.** Product liability and other lawsuits could divert the Company's resources, result in substantial liabilities and reduce the commercial potential of its drug candidates.

The risk that the Company may be sued on product liability claims is inherent in the development and commercialization of its drug candidates. Side effects of, or manufacturing defects in, the drug candidates the Company develops could result in the deterioration of a patient's condition, serious injury or even death. For example, patients participating in the clinical trials as part of the development of tested therapeutic products may hold the Company liable for unexpected side effects resulting from the administration of these drugs. In addition, the Company could face liability due to undetected side-effects caused by the interaction of its drugs with other drugs following release of the drug candidate to the market. Once a product is approved for sale and commercialized, the likelihood of product liability lawsuits increases. Criminal or civil proceedings might be filed against the Company by patients, regulatory authorities, biopharmaceutical companies and any other third party using or marketing its drugs. These actions could include claims resulting from actions by the Company's partners, licensees and subcontractors, over which the Company has little or no control. These lawsuits may divert the Company's management from pursuing its business strategy and may be costly to defend. In addition, if the Company is held liable in any of these lawsuits, it may incur substantial liabilities and may be forced to limit or forgo further commercialization of the affected products.

The Company maintains product liability insurance coverage for its clinical trials at levels which it believes are appropriate for its clinical trials. Nevertheless, the Company's insurance coverage may be insufficient to reimburse it for any expenses or losses it may suffer. In addition, in the future, the Company may not be able to obtain or maintain sufficient insurance coverage at an acceptable cost or to otherwise protect against potential product or other legal or administrative liability claims on it or its partners, licensees or subcontractors. This could prevent or inhibit the commercial production and sale of any of the Company's drug-candidates that receive regulatory approval. Product liability claims could also harm the Company's reputation and the marketability of its drugs, which may adversely affect its ability to commercialize its drugs successfully.

**4.5.5.** The Company is exposed to liability through its suppliers, contractors and subcontractors.

The Company relies and will continue to rely on suppliers, contractors and subcontractors in every aspect of its business. Such reliance exposes the Company to potential claims relating to the performance and activities of such suppliers, contractors and subcontractors, over which the Company can exert limited, if any, control. For example, contractors and subcontractors use certain regulated materials in the activities they conduct under contracts signed with the Company. If the Company's contractors and subcontractors do not properly and safely handle such regulated materials, the Company may be held liable for their actions.

Additionally, although the Company maintains insurance to cover it for costs and expenses it may incur due to any accidents involving its suppliers, contractors and subcontractors resulting in damage, injury or death, this insurance may not provide adequate coverage against potential liabilities. Any such liability, whether or not adequately covered by the Company's insurance policies, could have a material adverse effect on its business, prospects, financial position, cash flows or operating results.

**4.5.6.** The Company's inability to maintain certain tax benefits applicable to French biopharmaceutical companies may adversely affect its operating results.

As a French biopharmaceutical company, the Company has benefited from certain tax advantages, including, for example, the Research Tax Credit (*crédit impôt recherche*), which is a French tax credit aimed at stimulating research and development. The Research Tax Credit can be offset against French corporate income tax due, and the portion in excess, if any, may be refunded. The Research Tax Credit is calculated based on the Company's claimed amount of eligible research and development expenditures in France and represented, respectively, €3,122k and €3,552k for financial years 2017 and 2018. The French tax authorities, with the assistance of the Higher Education and Research Ministry, may audit each research and development program in respect of which a Research Tax Credit benefit has been claimed and assess whether such program qualifies in its view for the Research Tax Credit benefit. The French tax authorities may challenge the Company's eligibility for, or its calculation of, certain tax reductions or deductions in respect of its research and development activities. Furthermore, the French Parliament may decide to eliminate, or to reduce the scope or the rate of, the Research Tax Credit benefit, either of which it could decide to do at any time. If the Company fails to receive future Research Tax Credit amounts, its business, prospects, financial position, cash flows or operating results could be adversely affected.

**4.5.7.** The Company may be unable to carry forward existing tax losses.

The Company has received several conditional advances of a total amount of €1,086k on the part of BPI France Innovation for innovation. To date, the Company has repaid €471k, including €188k during financial year 2018 (refer to note 14.2 of the appendices to the IFRS financial statements presented in Section 20.1 "*IFRS accounts established for the financial year ended December 31, 2018*" of this *document de référence*). If the Company does not comply with the repayment schedule stipulated in the relevant agreements, the early repayment of all sums could be required. Such early repayment could have a negative impact on the ability of the Company to finance its research and development projects. The Company cannot ensure that it will then have the additional financial means, the time or the ability to replace these financial resources. This could, in turn, have a material adverse effect on the Company's business, prospects, financial position, cash flows or operating results.

**4.5.8.** The Company may be exposed to significant foreign exchange risk. Exchange rate fluctuations may adversely affect the foreign currency value of the Company's ordinary shares.

The Company incurs some of its expenses, and may in the future derive revenues, in currencies other than the euro. As the Company expands into new markets and its drug candidates approach advanced clinical trials and marketability, it is likely that non-euro-denominated arrangements will increase in number and value. The Company is expanding its operations and currently conducting clinical trials in the United States, Europe and Japan. The Company therefore necessarily incurs expenses in US dollars, Japanese yen and other foreign currency. As a result, the Company is exposed to foreign exchange

risk, as its operating results and cash flows are subject to fluctuations in foreign currency exchange rates (refer to Note 26 of the appendices to IFRS financial statements presented in Section 20.1 “IFRS financial statements established for the year ended December 31, 2018” of this *document de référence*). The Company took out hedging instruments, where it believed it necessary, to protect against foreign currency fluctuations between the euro, dollar and yen. Therefore, for example, an increase in the value of the yen and/or dollar against the euro could adversely affect the Company's operating expenses and net profit in the event that operating expenses incurred in yen and/or dollars are translated into euros at a higher value. The Company cannot predict the impact of foreign currency fluctuations, and foreign currency fluctuations in the future may adversely affect its financial position, operating results and cash flows.

**4.5.9.** The Company's internal computer systems, or those of its collaborators or other contractors or consultants, may suffer security breaches.

The Company's internal computer systems and those of its collaborators and contractors or consultants may suffer security breaches. While the Company does not believe that it has experienced any such security breach to date, if such an event were to occur and cause interruptions in its operations, it could result in a material disruption of its development programs and its business operations, whether due to a loss of its trade secrets or other proprietary information. For example, the pirating of clinical trial data for the Company's drug candidates from completed or future clinical trials could result in delays in the Company's regulatory approval efforts. If a disruption or act of pirating should cause the Company's data or applications to be corrupted, or other data or applications related to its technology or drug candidates to be corrupted, or lead to the unauthorized distribution of confidential or proprietary information, the Company would be exposed to sanctions, its competitive position could be affected and the development and marketing of its drug-candidates could be delayed.

**4.5.10.** The Company's capital could be diluted.

Since the Company was created, it has issued stock subscription warrants (“**Subscription Warrants**” or “**BSA**”), Founder warrants (“**Founder Warrants**” or “**BSPCE**”), stock options (“**Stock Options**”, or “**SO**”) and free performance shares (“**Free performance shares**” or “**AGA**”). As of the date of this *document de référence*, the exercise of all issued equity and equity-linked securities would allow for the issuance and subscription of 2,463,290 new ordinary shares of the Company, resulting in potential total dilution representing 8.69 % of the Company's share capital (on a fully diluted capital basis).

As part of the Company's policy to motivate its management and employees so as to attract new skills, it may, in the future, undertake other issuances or allocations of shares or equity securities.

Moreover, the Company may need to raise additional funding and use additional financing through the issue of shares or securities giving access to capital in order to pursue its development (refer to Section 4.5.11 “The Company may need to raise additional funding, which may not be available on acceptable terms or at all, and failure to obtain this necessary capital when needed may force it to delay, limit or terminate its product development efforts or other operations” below).

In addition, this agreement specifies the issue of up to 4 million shares in the Company in favor of DeuteRx, and milestone payments linked to the attainment of development, regulatory and sales targets, amounting to a maximum of \$545 million, part of which may be paid through the issue of shares in the Company (refer to Sections 10.1 “Information on the capital, liquidity and funding

sources" and 20.1 "Financial statements established using IFRS standards for the financial years ended December 31, 2017 and December 31, 2018").

These new issuances of shares or equity securities could result in additional potential dilution for the Company's current and future shareholders. Dilution of the equity ownership of shareholders may cause the market price of the Company's shares to decline.

**4.5.11.** The Company may need to raise additional funding, which may not be available on acceptable terms or at all, and failure to obtain this necessary capital when needed may force it to delay, limit or terminate its product development efforts or other operations.

The Company is currently improving its drug candidates through clinical development and leading preclinical studies of other programs. Developing drug candidates is expensive, time-consuming and risky, and the Company expects its research and development expenses to increase substantially in connection with its ongoing activities, particularly as the Company seeks to advance its drug candidates toward commercialization.

The Group undertook a specific review of its liquidity risk and considers that the Company is in a position to fund its current operations for the next 12 months, in light of its cash and cash equivalents as of December 31, 2018, namely €66.7 million, mainly consisting of fixed-term deposits that may be drawn on immediately and without penalties, in the event of cash needs.

However, the Company's operating plans may change as a result of a variety of factors, and it may need to seek additional funds sooner than planned, through public or private equity or debt financings, government or other third-party funding, marketing and distribution arrangements and other forms of collaboration, strategic alliances and licensing arrangements or a combination of these sources.

In any event, the Company will require additional capital to pursue preclinical and clinical activities, obtain regulatory approval for and commercialize its drug candidates. Furthermore, the Company may seek additional capital if market conditions are favorable or if it has specific strategic considerations. In relation to all of the above, the Company may seek additional financing in the form of public or private equity or debt financings, government or other third-party funding, marketing and distribution arrangements and other forms of collaboration, strategic alliances and licensing or other arrangements or a combination of these sources.

Any additional fundraising efforts may divert the Company's management from their day-to-day activities, which may adversely affect its ability to develop and commercialize its drug candidates. In addition, the Company cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to it. Moreover, the terms of any financing may adversely affect the holdings or the rights of the Company's shareholders, and the issuance of additional securities, whether equity or debt, by it, or the possibility of such issuance, may cause a drop of the market price of its shares. The sale of additional equity or convertible securities would be dilutive to the Company's shareholders. The incurring of indebtedness would result in increased fixed payment obligations and the Company may be required to agree to certain restrictive covenants, such as limitations on its ability to incur additional debt, limitations on its ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact its ability to conduct its business.

The Company's financial risks are described in more detail in note 26 to the IFRS financial statements set out in Section 20.1 "IFRS financial statements for the financial year ended December 31, 2018 of this *document de référence*.

#### 4.6. Risks related to the intellectual property of the Company

- 4.6.1. The Company's capacity to remain competitive may be weakened if it does not manage to protect its intellectual property rights or if it does so inadequately, or if its intellectual property rights are not adapted to exploitation of its technology and drug candidates.

The commercial success and viability of the Company depends on its capacity to obtain and maintain the protection of patents associated with its drug candidates, in the United States, in Europe, in Japan and in other countries, regarding drug candidates the Company owns or holds license to, as well as its capacity to defend these rights if they are contested by third parties in all of the territories. The strategy and the Company's future prospects depend more specifically on its portfolio of patents, namely the patents concerning Imeglimin and PXL770.

Moreover, the Company will be able to protect its drug candidates from unauthorized use by third parties only if they are covered by valid and enforceable patents, or by effectively protected manufacturing secrets. Moreover, intellectual property rights have limitations and do not necessarily protect the Company from all possible threats from competition. The Company's ability to obtain patent protection for its drug candidates is uncertain, and the degree of future protection afforded by its intellectual property rights is uncertain due to a number of factors, including, but not limited to:

- the Company or its licensor may not have been the first to produce and/or disclose or publish the inventions covered by patent applications currently undergoing examination or by granted patents;
- the Company or its licensor may not have been the first to file patent applications for its drug candidates or the compositions it developed or for their uses;
- others may independently develop identical, similar or alternative products or compositions and uses thereof;
- the Company's or its licensors' disclosures in patent applications may not be sufficient to meet the applicable statutory requirements for patentability;
- any or all of the Company's or its licensors' patent applications currently undergoing examination may not result in issued patents;
- the Company or its licensor may not obtain patent protection in countries that may eventually provide it with a significant business opportunity;
- the Company's partners could make decisions in one jurisdiction having an impact on its patents in another jurisdiction;
- any patents issued to the Company or its licensor may not provide a basis for commercially viable products, may not provide any competitive advantages or may be successfully challenged by third parties;
- the Company's or its licensors' compositions and methods may not be patentable;



- third parties may draw inspiration from the Company's patent claims or those of its licensor to design competitive products that would circumvent those claims so as not to infringe on its patents;
- others may identify prior know-how or other prior art which could invalidate the Company's or its licensors patents;
- due to third-party requests, the Company's partners could request modifications in its patent claims or patent applications;
- partnership agreements contain certain stipulations relative to protection, exploitation and transfer of intellectual property, which, if not respected, could adversely affect the Company's intellectual property rights or those of its licensor;
- the Company's competitors might conduct research and development activities in the United States and other countries that are insecure areas in relation to patent infringement claims for certain research and development activities, as well as in countries where it does not have patent rights, and then use the information learned from such activities to develop competitive products for sale in its major commercial markets; or
- the Company may not develop existing or new patentable technologies.

Even if the Company has or obtains patents covering its drug candidates or compositions, it may still be barred from making, using and selling the Company's drug candidates or technologies because of the patent rights of others. Others may have filed, and in the future may file, patent applications covering compositions or products that are similar or identical to ours. There are many issued US and foreign patents relating to therapeutic drugs, and some of these relate to compounds the Company intends to commercialize. In the field of metabolic pathologies, there are numerous US- and foreign-issued patents owned by third parties, and numerous patent applications currently undergoing examination have been filed by third parties. These could materially affect the Company's ability to develop its drug candidates or sell its drugs, if approved. Because patent examination can take many years to process, there may be unpublished applications currently undergoing examination unknown to the Company that may later result in issued patents that its drug candidates or compositions may violate. These patent applications may have priority over patent applications filed by the Company.

Obtaining and maintaining a patent portfolio entails significant expense and resources. The Company may be forced to cease to extend or maintain the protection of specific inventions. Furthermore, failure to make payments or noncompliance with certain requirements in the patent process can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. If the Company chooses to forgo patent protection or allow a patent application or patent to lapse purposefully or inadvertently, its competitive position could suffer.

Legal actions to defend or enforce the Company's patent rights can be expensive and may involve the diversion of significant management time. In addition, these legal actions could be unsuccessful and could also result in complete or partial invalidation of the Company's patents or find that they are unenforceable. If the Company fails to protect, maintain, defend or enforce its intellectual property rights, its competitive position could suffer, which could harm its operating results.

#### 4.6.2. Biopharmaceutical patents and patent applications involve highly complex legal and factual questions.

The patent positions of biopharmaceutical companies can be uncertain and involve complex legal and factual questions. The interpretation and breadth of claims granted in some patents covering biopharmaceutical compositions may be uncertain and difficult to determine, and are often affected materially by the facts and circumstances that pertain to the patented compositions and the related patent claims. The standards of national or regional patent offices, particularly the U.S. Patent and Trademark Office (USPTO) or the European and Japanese offices, may change. Consequently, the Company cannot predict the publication, grant and scope of patents with certainty. Patents, if issued, may be completely or partially challenged, invalidated or circumvented. For example, US patents and patent applications may also be subject to interference proceedings, and US patents may be subject to reexamination proceedings, post-grant review and/or inter partes review in the USPTO. The publication and grant of a patent is not conclusive as to its inventorship, scope, extent of protection, validity or enforceability, and the Company's patents or patent applications currently undergoing examination may be challenged in the courts or national or regional patent offices. There is no guarantee that all prior art documents and prior know-how related to the Company's patents and patent filings have been disclosed. For example, reporting of discoveries in scientific publications is often made long after the discovery date, and patent filings are generally not published until 18 months after the filing, and in some cases are simply not published at all.

The Company cannot know with certainty if it was the first to invent what is described in its patents or patent applications, nor that its licensor was the first to invent what it claims to be its invention in its patents licensed to the Company, or whether it was the first to file an application for patent protection of these inventions. If such prior art or know-how exists, it may be used to invalidate a granted patent, or may prevent the grant of a patent from a patent application currently undergoing examination. The Company's patent applications currently undergoing examination and future patent applications may therefore not result in patents being granted that protect its technology and/or products, in whole or in part, or may not effectively prevent others from commercializing competitive technologies and products. Furthermore, the Company may become involved in post-grant review procedures, oppositions, derivations, proceedings, re-examinations, inter partes review or interference proceedings which would call into question its patents or patent applications, including the patents by which the Company intends to protect its technology and/or products and/or business. The outcome of these challenges could result in a loss of exclusivity or the limitation of patent claims and therefore the extent of protection or the invalidation or total or partial nullity of the patent, which could restrict the Company's capacity to prevent third parties from using or marketing similar or identical products or technologies, or reduce the duration of patent protection of its technology and products. Patents may be subject to opposition proceedings before national or regional patent offices, especially in the United States or Europe, which could lead either to loss of the granted patent or a refusal to grant the patent application, or even a limitation of the claims of the patent or patent application. In addition, such interference, reexamination, post-grant review, inter partes review and opposition proceedings may be costly. Also, given the amount of time required for the development, testing and regulatory review of new drug candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. Accordingly, rights under any granted patents may not provide the Company with sufficient protection against competitive products or processes.

Moreover, changes made to legal and regulatory provisions regarding patents in the countries in which the Company operates, or different applications and interpretations that may be made of these

provisions, may decrease the value of the patents and patent licenses or reduce the scope of the Company's patent protection. Legislation to reform patents could increase uncertainty and make it more expensive to continue to review the Company's patent applications and to enforce or defend the patents it has obtained. For example, changes in or different applications or interpretations of patent laws may result in third parties using the Company's or its licensor's technology, or developing and commercializing its technology or another technology and its products or other products, without paying or compensating the Company in any way, or may limit the number of patents the Company may obtain or the number of patent applications it may file. The laws of some countries may not protect intellectual property rights sufficiently, and those countries may lack adequate rules and procedures for defending the Company's intellectual property rights, or vice versa.

If the Company fails to obtain and maintain patent protection and trade secret protection for its drug candidates, the Company could lose its competitive advantage, and the competition it faces would increase, reducing any potential revenues and adversely affecting its ability to attain or maintain profitability.

**4.6.3.** If the Company is unable to protect the confidentiality of its trade secrets and know-how, its business and competitive position would be harmed.

In addition to seeking patent protection for the Company's drug candidates, the Company also relies on trade secrets, including unpatented know-how, technology and other confidential proprietary information, to maintain its competitive position. The Company seeks to protect its trade secrets and confidential information, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to these trade secrets and confidential information, such as its employees, collaborators, consultants, advisers, university and/or institutional researchers and other third parties. The Company has also entered or seeks to enter into confidentiality and invention or patent assignment agreements with its employees, associates, advisers and consultants. Despite these efforts, any of these parties may breach the agreements and disclose the Company's confidential information, including its trade secrets, and it may not be able to obtain adequate remedies for such breaches. The Company's trade secrets may also be obtained by third parties by other means, such as breaches of its physical or computer security systems. Proving that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. Moreover, if any of the Company's trade secrets were to be lawfully or legitimately obtained or independently developed by a competitor, it would have no right to prevent them, or those to whom they communicate it, from using that technology or information. If any of the Company's trade secrets were to be disclosed to, or independently developed by, a competitor, its competitive position would be harmed.

**4.6.4.** The Company will not seek to protect its intellectual property rights in all jurisdictions throughout the world and it may not be able to adequately enforce its intellectual property rights even in the jurisdictions where it seeks protection.

Filing, maintaining and defending patents on the Company's drug candidates in all countries and jurisdictions throughout the world would be prohibitively expensive, and its intellectual property rights in some countries outside the United States could be less extensive than those in the United States, assuming that rights are obtained in the United States. Competitors may use the Company's technologies in jurisdictions where it does not pursue and obtain patent protection, particularly by reproducing the inventions covered by its patents, to develop their own products, and may then

export these products (which would violate the Company's rights under other circumstances) to territories where the Company has patent protection, and where enforcement is not as simple as in France, Europe or the United States. These products may compete with the Company's drugs, and the Company's patents or other intellectual property rights may not be effective or sufficient to prevent them from competing. Even if the Company files and obtains issued patents in particular jurisdictions, the application of its patent rights or other intellectual property rights may not be effective or sufficient to prevent third parties from so competing.

In addition, the laws of some countries do not protect intellectual property rights to the same extent as the federal and state laws in the United States. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. The legal systems of some countries, particularly developing countries, do not favor the enforcement of patents and other intellectual property protection, especially those relating to biopharmaceuticals or biotechnologies. This could make it difficult for the Company to stop the infringement of its patents, if obtained, or the misappropriation of its other intellectual property rights. For example, many countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. In addition, many countries limit the enforceability of patent rights against third parties, in particular government agencies or government contractors. In these countries, patents may provide limited or no benefit. Patent protection must ultimately be sought on a country-by-country basis, which is an expensive and time-consuming process with uncertain outcomes. Consequently, the Company may decide not to file patent applications, or to maintain, defend or enforce its patents in certain countries, and therefore would not benefit from patent protection in these countries. Moreover, the Company may also have difficulties obtaining protection for PXL065 in some jurisdictions, especially given what DeuteRx has been able to do in the past in terms of applications for patent protection in these jurisdictions (especially in jurisdictions where the patent covering PXL065 has not been filed).

The procedures for enforcing and defending the Company's patents in certain jurisdictions could result in considerable costs and divert the efforts and the attention of the Company from other aspects of its activity. They may result in a risk to the Company that its patents are invalidated, limited or interpreted narrowly, that its patent applications are rejected and that third parties may file complaints against it. The Company may not be successful in the actions it undertakes, and the indemnities or other damages awarded to it, if applicable, may not be very relevant on the commercial level. Moreover, the modifications made to legal and regulatory provisions and judicial and administrative jurisprudence of the countries where the Company operates may affect the Company's capacity to obtain adequate protection of its technology and enforce intellectual property. Consequently, the Company's efforts to enforce its intellectual property rights internationally may be inadequate to obtain significant commercial advantage based on the intellectual property it develops and holds itself or via a license.

**4.6.5.** The patent duration may be inadequate for the protection of the competitive position of the Company's drugs over an adequate period of time.

Given the duration of development, testing and regulatory review of new drug candidates, patents protecting such drug candidates might expire before or shortly after they are commercialized. The Company expects to seek extensions of patent terms in the United States and in other countries where it considers this appropriate. In the United States, the Drug Price Competition and Patent Term Restoration Act of 1984 permits a patent term extension of up to five years beyond the normal expiration of the patent, which is limited to the approved indication (or any additional indications

approved during the period of extension). However, the applicable authorities, including the FDA and the USPTO in the United States, and any equivalent regulatory authority in other countries, may refuse to grant such extensions, or may grant more limited extensions. In this case, the Company might not benefit from the expected patent protection, which could have a non-negligible negative impact on its business, prospects, financial position, cash flows or operating results.

- 4.6.6.** Third parties may contest the Company's patent applications and other intellectual property by declaring that it is not the inventor, or may assert ownership to inventions developed by the Company, as well as, in particular, commercial rights relating thereto.

Third parties may make claims challenging the inventorship or ownership of the Company's intellectual property. The Company or its licensor have written agreements with partners that relate to potential intellectual property rights arising from these partnerships. These agreements provide that the Company or its licensor must negotiate certain commercial rights, in particular exploitation rights, with these partners with respect to joint inventions or creations or inventions made by the Company's or its licensor's partners that arise from the results of this collaboration. In some instances, there may not be adequate written provisions to clearly address the resolution of intellectual property rights that may arise from collaboration. If the Company or its licensor are not able to negotiate property rights and/or commercial rights including sufficient exploitation rights over the results of a collaboration, or if disputes arise over the results and intellectual property developed through the use of elements to one of the parties in collaboration, the Company may be limited in its ability to capitalize on the commercial potential of these inventions. In addition, the Company may face claims by third parties that its agreements with employees, contractors or consultants obligating them to assign intellectual property to it are ineffective, or in conflict with prior or competing contractual obligations of assignment, which could result in ownership disputes regarding intellectual property the Company has developed or will develop and interfere with its ability to capture the commercial value of such inventions. Litigation may be necessary to resolve an ownership dispute, and if the Company is not successful, it may be precluded from using certain intellectual property, or may lose its exclusive rights in regard to that intellectual property. Either outcome could have an adverse impact on the Company's business.

- 4.6.7.** Third parties may assert that the Company's licensors, employees or consultants or the Company has wrongfully used or disclosed confidential information or misappropriated trade secrets, or may claim ownership of what the Company regards as its own intellectual property.

The Company and its licensor employ individuals who were previously employed at universities or other biotechnology or pharmaceutical companies, including the Company's competitors or potential competitors. Although the Company tries to ensure that its employees and consultants do not use the proprietary information or know-how of others in their work for the Company, and no such claims against it are currently pending, it may be subject to claims that the Company or its licensors, employees, consultants or independent contractors have used or disclosed confidential information, including trade secrets, know-how or other proprietary information belonging to a former employer or other third parties. Litigation may be necessary to defend against these claims. If the Company fails in defending any such claims, in addition to paying monetary damages, it may lose valuable intellectual property rights or personnel. Even if the Company is successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

- 4.6.8.** The Company may become involved in lawsuits to defend or enforce its patents or other intellectual property, which could be expensive, time-consuming and unsuccessful and have a material adverse effect on the success of its business.

Competitors may copy or use the Company's patents, trademarks, copyrights or other intellectual property without its authorization. In order to prevent or terminate these violations or unauthorized use, the Company may have to file a complaint or take legal action for infringement of these intellectual property rights, which can be expensive and time-consuming and divert the time and attention of its management and scientific personnel who have to deal with it. Any claims the Company asserts against alleged infringing parties could provoke these parties to assert counterclaims against it alleging that the Company violates their patent rights, in addition to counterclaims asserting that the Company's patents are completely or partially invalid or unenforceable, or both. In any patent violation or infringement proceeding, there is a risk that a court will decide that a patent belonging to the Company is invalid or unenforceable, in whole or in part, and that the Company does not have the right to stop the other party from using the invention covered by the patent at issue. There is also a risk that, even if the validity of such patents is confirmed, the court will construe the patent's claims narrowly or decide that the Company does not have the right to stop the other party from using its product on the grounds that its patent claims do not cover its product. An adverse outcome in a litigation or proceeding involving one or more of the Company's patents could limit its ability to oppose those patents against those parties or other competitors, and may curtail or preclude its ability to prevent third parties from making and selling similar or competitive products. Similarly, if the Company asserts trademark infringement claims, a court may rule that the trademarks it has asserted are null or void, or that the party against whom the Company has asserted trademark infringement has prior rights to the trademarks at issue. In this case, the Company could ultimately be forced to cease use of such trademarks.

Even if the Company establishes violation or infringement, the court may decide not to grant an injunction against further violating or infringing activity and instead award only monetary damages. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of the Company's confidential information could be compromised by disclosure during litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could adversely affect the market price of the company's ordinary shares. Moreover, there can be no assurance that the Company will have sufficient financial or other resources to file and pursue such infringement claims, which typically last for years before they are concluded. Even if the Company ultimately prevails in such claims, the monetary cost of such litigation and the diversion of the attention of its management and scientific personnel could outweigh any benefit it receives as a result of the proceedings.

- 4.6.9.** The Company may be sued for violating intellectual property rights of third parties, and in this case, such litigation could be costly and time-consuming and could prevent or delay the Company from developing or commercializing its drug candidates.

The Company's commercial success depends, in part, on its ability to develop, manufacture, market and sell its drug candidates without violating the intellectual property and/or other proprietary rights of third parties. Third parties may have US and non-US issued patents and patent applications undergoing examination relating to compounds and methods of use for the treatment of the disease indications for which the Company is developing its drug candidates. If any third-party patents or patent applications are found to cover the Company's drug candidates or their methods of use, it may

not be free to manufacture or market its drug candidates as planned without obtaining a license, which may not be available on commercially reasonable terms, or at all.

There is a substantial amount of intellectual property litigation in the biopharmaceutical industry, and the Company may become party to, or threatened with, litigation or other adversarial proceedings regarding intellectual property rights with respect to its drug candidates, including interference proceedings before the USPTO. There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of the Company's drug candidates. Because patent applications can take many years before being granted, there may currently be patent applications under examination which may later result in the publication and grant of patents that the Company's drug candidates may be accused of violating. In addition, third parties may obtain patents in the future and claim that use of the Company's technologies violates these patents. Accordingly, third parties may take action against the Company for infringement of existing or future intellectual property rights. The outcome of intellectual property litigation is subject to uncertainties that cannot be adequately quantified in advance. The biopharmaceutical industry has produced a significant number of patents, and it may not always be clear to industry participants, including the Company, which patents cover various types of products or methods of use. The coverage of patents is subject to interpretation by the courts, and the interpretation is not always uniform. If the Company were sued for patent infringement, it would need to demonstrate that its drug candidates, products or methods either do not violate the patent claims of the relevant patent or that the claims of this patent are invalid or unenforceable, and it may not be able to do so. Proving invalidity is difficult. For example, in the United States, proving invalidity requires a showing of clear and convincing evidence to overcome the presumption of validity enjoyed by issued patents. Even if the Company is successful in these proceedings, it may incur substantial costs, and the time and attention of its management and scientific personnel could be diverted in pursuing these proceedings, which could significantly harm its business and operating results. In addition, the Company may not have sufficient resources to bring these actions to a successful conclusion.

If the Company is found to violate a third party's intellectual property rights, it could be forced, including by judicial means, to cease developing, manufacturing or commercializing the infringing drug candidate or product in one or more jurisdictions. Alternatively, the Company may be required to obtain a license from such a third party to use the infringing technology and continue developing, manufacturing or marketing the infringing drug candidate or product. However, the Company may not be able to obtain the required license on commercially reasonable terms, or at all. Even if the Company is able to obtain a license, it could be non-exclusive, thereby giving its competitors access to the same technologies licensed to it. Alternatively, or additionally, it could include terms that impede or destroy the Company's ability to compete successfully in the commercial marketplace. In addition, the Company could be found liable for monetary damages, including treble damages and attorneys' fees if it is found to have willfully infringed a patent. The Company may also be required to develop or obtain alternative technologies, review product design or, in the case of claims concerning registered trademarks, rename its drugs. A decision that there has been patent infringement could prevent the Company from commercializing its drug candidates or force it to cease some of its business operations, which could harm its business. Claims that the Company has misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on its business.

- 4.6.10.** If the Company's trademarks and trade names are not adequately protected, then it may not be able to build name recognition in its markets of interest, and its business may be adversely affected.

The Company's filed or unfiled trademarks, registered or unregistered trademarks and trade names may be contested, violated, circumvented, declared generic or descriptive, or found to be infringing. The Company may not be able to protect its rights to these trademarks and trade names, which it needs to build name recognition among potential partners or customers in its markets of interest. At times, competitors may adopt trademarks and trade names similar to the Company's, thereby impeding its ability to build brand identity and possibly leading to market confusion. Owners of other filed or unfiled trademarks, registered or unregistered trademarks, or trademarks with variations of the Company's filed or unfiled trademarks or registered or unregistered trademarks could also file a trademark infringement claim. Over the long term, if the Company is unable to establish name recognition based on its trademarks, then it may not be able to compete effectively, and its business may be adversely affected.

- 4.6.11.** Obtaining and maintaining patent protection depends on compliance with various procedural rules, document submission, fee payment and other requirements imposed by national patent offices, and the Company's patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance fees, renewal fees, annuities and various other fees and taxes levied by various governments on patents and patent applications shall be paid to various national or regional patent offices, including USPTO, the European Patent Office or the National Institute of Intellectual Property in France, at several stages during the lifetime of patents and patent applications. National and regional patent offices require compliance with a number of procedural rules, the submission of certain documents, the payment of fees and taxes, and other similar provisions during the patent application examination procedure and even after the publication and grant of a patent. There are situations in which non-compliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction.

- 4.6.12.** If the Company fails to comply with its obligations under its existing and any future intellectual property licenses with third parties, it could lose license rights that are important to its business.

The Company's business depends, in part, on an assignment and licensing agreement entered into with Merck Serono, called the MS Agreement, under which it was transferred certain patents and granted a license in relation to certain other patents and know-how for the research, development and marketing of pharmaceutical products. Merck Serono may terminate the MS Agreement if the Company breaches any of its major provisions. If Merck Serono terminates the MS Agreement, the Company's inability to use the intellectual property under the patents pursuant to the MS Agreement could adversely affect its business, prospects, financial position, cash flows or operating results.

The Company may enter into additional license agreements in the future. The Company's existing license agreements impose, and the Company expects that future license agreements will impose, various diligence, milestone payment, royalty, insurance and other obligations on it. If the Company fails to comply with its obligations under these licenses, its licensors may have the right to terminate these license agreements, in which event the Company might not be able to market any product that is covered by these agreements, or its licensors may convert the license to a non-exclusive license,



which could adversely affect the value of the drug candidate being developed under the license agreement. Termination of these license agreements or a reduction or elimination of the Company's licensed rights may also result in the Company having to negotiate new or reinstated licenses with less favorable terms.

The strategic agreement the Company signed with DeuteRx in August 2018 provides, for the entire product portfolio, the maximum issue of the Company's securities for the benefit of DeuteRx, and payments related to the achievement of development, regulatory and sales objectives, some of which may be realized by issuing its securities. It also provides for the payment of royalties at a low-range figure on sales. If the Company fails to comply with its contractual obligations, DeuteRx may have the right to terminate this license agreement, in which event the Company might not be able to market the products covered by this agreement, including PXL065, or its licensors may convert the license to a non-exclusive license, which could adversely affect the value of the drug candidate or candidates being developed under this agreement.

#### 4.7. Risks related to litigation

As of the date of this *document de référence*, there is no governmental, judicial or arbitration procedure, including any procedure of which the Company has knowledge, which is outstanding or with which it is threatened, likely to have or have had in the past 12 months, significant effects on the financial position or the profitability of the Company or Group.

In connection with the application of the assignment and license agreement concluded with Merck Serono on March 19, 2009 (as amended by amendments on July 30, 2009, on June 22, 2010, on May 23, 2014 and November 28, 2014) (referred to in Section 22.1 "Merck Serono Agreement") to the partnership agreement signed with Roivant Sciences in February, 2018, the Company and Merck Serono have a different interpretation of the basis for calculating the Company's income to be subject to royalties (refer to Note 25.2 "Commitment under the Merck Serono Agreements at the creation of the Company" in Section 20.1.7 "Notes to the IFRS financial statements"). If the Company was unable to reach an agreement with Merck Serono, the assignment and licensing agreement with Merck Serono includes the faculty to recourse to arbitration, the implementation of such proceedings could have a material adverse effect on the Company's business, prospects, financial position, cash position or operating results.

#### 4.8. Financial risks related to the effects of climate change

The Company has not identified significant financial risk to its business related to climate change.

#### 4.9. Insurance

The Company is exposed to a risk of high responsibility in the framework of the development, manufacture and possible commercialization of its products. Among the other potential risks, the occurrence of side effects and unexpected interactions and disputes relating to its intellectual property could lead to invoking its liability for damages not covered or exceeding the amounts of guarantee provided by its insurance policies. The Company cannot guarantee that it will always be able to keep, and where appropriate to obtain, at any time, insurance coverage at an acceptable cost. If the Company were not able to maintain such coverage, this could have a significant adverse effect

on its business, prospects, ability to achieve its objectives, financial position, cash flow or operating results.

In addition, all the losses that the Company could suffer as a result of the unavailability of its leaders may not be sufficiently covered by its current “key man” insurance policies.

## 5. INFORMATION ABOUT THE ISSUER

### 5.1. History and evolution of the Company

#### 5.1.1. Company name:

The Company name is: Poxel.

#### 5.1.2. Place of registration and registration number of the Company

The Company is registered with the Lyon Trade and Company Registry (RCS) under the number 510 970 817.

The Company's NAF (business activity) code is 7219Z.

#### 5.1.3. Date of incorporation and term

The Company was incorporated on March 11, 2009 for a term of 99 years expiring on March 11, 2108, save in the event of early dissolution or an extension.

#### 5.1.4. Registered office of the Company, legal form and applicable law

The Company's registered office is:

259/261 Avenue Jean Jaurès – Immeuble le Sunway – 69007 Lyon

Phone: 4 37 37 20 10

Fax: 04 37 70 88 15

Email: [investors@poxelpharma.com](mailto:investors@poxelpharma.com)

Website: [www.poxel.com](http://www.poxel.com)

The Company is a French société anonyme à Conseil d'administration (public limited company with a Board of Directors).

The Company, governed by French law, is primarily subject to Article L. 225-1 et seq. of the French Commercial Code.

#### 5.1.5. History of the Company

2009

- March, creation of the Company as part of a spin-off of the research and development activities of Merck Serono in the cardiometabolic field. As part of this spin-off, Merck Serono transferred a certain number of preclinical and clinical research programs to Poxel (including the drug candidate Imeglemin for which Merck Serono had conducted all the preclinical prerequisites to its standards, phase-I and two phase-II studies, and industrialization of the manufacturing process), as well as the related intellectual property rights. To contribute to its research and development activities and regarding Merck Serono's economic interest in Poxel's development, Merck Serono paid Poxel a total non-refundable amount of €7.2 million (see Sections 22 "Material agreements" and 10.1.5 "Off balance-sheet commitments" of this *document de référence*).

## 2010

- July, raised funds totaling €16 million, released in several stages (€10.8 million in 2010 and €5.2 million in 2011) from funds managed by Edmond de Rothschild Investment Partners, OMNES CAPITAL (formerly Crédit Agricole Private Equity) and Bpifrance Investissement (formerly CDC Enterprises).

## 2011

- October, positive results announced in relation to the phase-II clinical study on the combination of Imeglimin with metformin.
- October, obtained government aid of €1.45 million, in the form of subsidies and repayable advances.

## 2012

- October, signed a convertible bond issuance agreement on a pro-rata basis with historical shareholders, for a total of €13 million, of which €3.3 million was subscribed in 2012 and €9.7 million was subscribed in 2013;
- November, positive results announced in relation to the phase-II study on the combination of Imeglemin and sitagliptin.

## 2013

- October, favorable results announced in relation to the phase-2 clinical study on Imeglimin demonstrating the activity of the drug-candidate on insulin secretion in response to glucose.

## 2014

- July, capital increase subscribed by Bpifrance Participations totaling €5 million and concomitant conversion of all convertible bonds issued in 2012 and 2013;
- A venture loan set up with Kreos Capital IV (Expert Fund), up to a maximum of €8 million, in two tranches. The first tranche, released in July 2014, totaled €5 million;
- December, first positive results announced in relation to the new oral antidiabetic drug (Imeglimin) in a phase-IIb study.

## 2015

- February, IPO launched on the Euronext Paris, Compartment C regulated market. The gross amount raised was €26.8 million. Concomitantly, the Company recorded Merck Serono's exercise of its 1,088,531 MS BSA share warrants for the same number of new shares at an exercise price of €4,354,000;
- May, positive results announced in relation to the Imeglimin phase-I study on Japanese subjects;

- May, Poxel and ENYO Pharma entered into a first license agreement for Poxel's FXR agonist program;
- June, positive results announced in relation to the new phase-II study for Imeglimin;
- July, Poxel raised €20 million as part of a private placement conducted by US investors (91%) and European investors.

## 2016

- March, Jonae R. Barnes appointed as Senior Vice-President, Investor Relations and Public Relations, based in Boston;
- March, US approval of the patent covering PXL770, a direct activator of AMP Kinase for the treatment of type-2 diabetes and related pathologies;
- June, Poxel announced the positive results of the first part of the phase-I study concerning PXL 770. The results indicate that, at this stage, PXL 770 presents a favorable safety and tolerance profile in humans;
- July, Poxel raised €26.5 million through a private placement conducted by prominent institutional investors in the United States and in Europe.

## 2017

- March, the Company announced that Christophe Arbet-Engels, MD, PhD, MBA, had joined Poxel and would serve as Chief Medical Officer and Executive Vice President for Phase-III Clinical Development & Medical Affairs, based in Boston;
- April, Poxel announced the appointment of Anne Renevot as Chief Financial Officer;
- June, announced the additional positive results of the phase-IIb study on Imeglimin conducted in Japan for the treatment of type-2 diabetes;
- October, signing of a contract for a strategic partnership with Sumitomo Dainippon Pharma to develop and market Imeglimin, a drug-candidate for the treatment of type-2 diabetes, for Japan, China and eleven other Asian countries.

## 2018

- February, Poxel announced the signing of a strategic development and licensing agreement with Roivant Sciences for Imeglimin, in the U.S., Europe and other countries not covered by the existing partnership with Sumitomo Dainippon Pharma;
- February, Poxel presented preclinical proof of concept data for PXL770 in non-alcoholic steatohepatitis (NASH) at the 2018 Global NASH Congress;
- March, launch of the TIMES 2 and TIMES 3 studies as part of the program for the phase-III development of Imeglimin, drug-candidate for the treatment of type 2 diabetes, in Japan;

- June, at the 78th scientific session of the American Diabetes Association, Poxel presented new data demonstrating the protective effect of Imeglimin on pancreatic beta cells;
- July, Poxel announced the finalization of the selection of patients for the TIMES 1 phase-III study of Imeglimin, for the treatment of type-2 diabetes, in Japan;
- July, Poxel announced positive results of the phase-Ib study on PXL770 following the administration of multiple and increasing doses and the analysis of potential drug interactions;
- August, Poxel announced the signing of a strategic agreement with DeuteRx for the acquisition of DRX-065, an innovative drug candidate in clinical development for the treatment of NASH, in addition to other programs;
- September, Poxel set up a wholly-owned subsidiary in Japan and appointed Dr. Takashi as Medical Vice President and Chairman of Poxel Japan KK;
- October, Poxel presented the full results of the phase-I study on PXL770, in addition to the cardiac safety profile and the preclinical data on efficacy in NASH, at the AMPK scientific congress;
- October, Poxel announced the finalization of patient selection for the TIMES 2 phase-III study of Imeglimin, for the treatment of type-2 diabetes, in Japan;
- November, Poxel presented promising data on PXL770 and PXL065 in the treatment of NASH, at the AASLD congress;
- November, Poxel announced the launch of the second part of the phase-Ia study on PXL065 in the treatment of NASH.

2019

- January, Poxel presented new data on PXL065 at the 2019 NASH-TAG Conference;

## 5.2. Investments

### 5.2.1. Principal investments made over the last two financial years

The Group's most significant investment was undertaken in August 2018 and involved the acquisition, from DeuteRx, of DRX-065, an innovative drug-candidate in clinical development for the treatment of NASH, in addition to other programs for the treatment of metabolic diseases, for a total of €16,572,000 (refer to Note 4.1 of the notes to the IFRS financial statements set out in Section 20.1 "Financial statements prepared in accordance with IFRS for the financial year ended December 31, 2018" of this document de référence).

The other investments made since the Company's incorporation essentially concern the acquisition of laboratory, IT and office equipment.

### **5.2.2. Principal investments in progress**

No significant investment has been made since January 1, 2019.

### **5.2.3. Principal planned investments**

The Company does not currently intend to make significant investments in the coming years, for which the management bodies of the Company have made firm commitments.

However, for intangible investments, the Company has a projected commitment corresponding to the ongoing clinical studies. This short-term commitment is estimated at a total of €21 million.

## 6. BUSINESS OVERVIEW

### 6.1. General presentation

Poxel is a French biopharmaceutical company specialized in the development of innovative treatments for metabolic diseases, including type 2 diabetes (T2D) and liver diseases such as nonalcoholic steatohepatitis “NASH”. With its expertise and know-how in the development of drug candidates, the Company has been able to develop a portfolio of several drug candidates, including three clinical stage candidates for the treatment of T2D and NASH.

The Company’s most advanced drug candidate, Imeglimin, is intended to complement and augment existing type 2 diabetes therapies, including in patients who no longer fully respond to such therapies, with the goal of helping patients better control their type 2 diabetes and reduce potentially disabling or fatal complications.




















The Company’s second drug-candidate, PXL770, is a direct activator of adenosine monophosphate-activated protein kinase (AMPK). AMPK offers the opportunity to address a wide range of potential indications for treating chronic metabolic diseases, including diseases affecting the liver, such as NASH.

PXL065, the Company's third drug-candidate, offers a new approach to treating NASH. PXL065 is the R stereoisomer (single R-isomer) of pioglitazone, its parent molecule marketed since 1999 for the treatment of T2D. Pioglitazone has been the subject of a large number of studies in the treatment of NASH which have demonstrated its ability to target the resolution of NASH without aggravating fibrosis in phase II, III and IV trials.

#### ***The Company’s Principal Drug Candidates***

*Table 1 - Portfolio of the Company’s drug candidates in development in type 2 diabetes and metabolic diseases*



	Indication	MOA	Preclinical	Phase 1	Phase 2	Phase 3	Partner/ Rights	Next Steps
Imeglimin Japan/ Asia*	Type 2 Diabetes	Mitochondrial Bioenergetics				Ph 3		<ul style="list-style-type: none"> <li>Phase 3 TIMES completion</li> <li>Target JNDA submission 2020</li> </ul>
Imeglimin US/ EU/ Other**	Type 2 Diabetes	Mitochondrial Bioenergetics				Ph 3		<ul style="list-style-type: none"> <li>Manufacturing drug for Phase 3</li> <li>Differentiation studies in CKD patients w/ T2D</li> </ul>
PXL770	NASH/ metabolic diseases	Direct AMPK activator			Ph 2			<ul style="list-style-type: none"> <li>Initiate Phase 2a program in NASH</li> </ul>
PXL007 (EYP001)	Hepatitis B NASH	FXR agonist			Ph 2			<ul style="list-style-type: none"> <li>Complete Phase 1 program by Enyo Pharma</li> </ul>
PXL065 (formerly DRX-065)	NASH	MPC Inhibitor			Ph 2			<ul style="list-style-type: none"> <li>Complete Phase 1, tox, CMC</li> <li>Initiate Pivotal Phase 2 study</li> </ul>
Poxel/ DeuteRx programs	Metabolic (AMN/ALD, NASH,	Direct AMPK activator/ MPC Inhibitor		Ph 1				<ul style="list-style-type: none"> <li>Complete preclinical studies</li> </ul>

The arrows indicate the expected level of development in 2019

\*included: China, South Korea, Taiwan, Indonesia, Vietnam, Thailand, Malaysia, Philippines, Singapore, Myanmar, Cambodia and Laos.

\*\*countries not covered by the Sumitomo Dainippon Pharma agreement

Imeglimin is a first-in-class oral drug candidate that targets the two main metabolic defects at the root of type 2 diabetes—low insulin secretion and elevated insulin resistance. The Food and Drug Administration (FDA) uses the term ‘first-in-class’ to refer to drugs that use an innovative and unique mechanism of action. The Company believes that its drug candidates have a unique mechanism of action, and Imeglimin was granted the first “Glimin” therapeutic agent status by the World Health Organization. The Company believes that it is the most advanced drug candidate targeting mitochondrial dysfunction. The mitochondrion is the power center of the cell, and its dysfunction, which has been examined in over 200 scientific publications per year in each of the last five years, is implicated in the pathophysiology of type 2 diabetes. By targeting the mitochondria, Imeglimin can simultaneously trigger metabolic effects for the treatment of diabetes in the three key organs involved in type 2 diabetes pathophysiology—the liver, muscles and pancreas. Imeglimin has been investigated in 24 completed clinical trials in United States, in Europe and in Japan, which included an aggregate of approximately 1,200 subjects. These tests have obtained statistically significant results for the primary and secondary endpoints, including a reduction of HbA1c and fasting glycemia versus placebo, associated with a favorable profile in terms of safety of use. In October 2017, the Company signed a partnership agreement with Sumitomo Dainippon Pharma for the development and commercialization of Imeglimin in Japan and in certain Asian countries. As a result of this, a phase III “TIMES” (*Trials of Imeglimin for Efficacy and Safety*) clinical program was launched in Japan in December 2017. This program includes three pivotal studies to evaluate the efficacy and safety of Imeglimin in approximately 1,100 patients, for which the Company completed recruitment in these three studies in October 2018. In February 2018, the Company also signed a partnership agreement with Roivant Sciences for development and commercialization of Imeglimin in the United States, Europe and other countries not covered by the agreement with Sumitomo Dainippon Pharma. The clinical development of Imeglimin by Roivant Sciences will initially target type 2 diabetic patients with

moderate to severe chronic renal insufficiency (stages 3b/4), for which a specific clinical study is currently underway.

Poxel's second drug candidate, PXL770, is a first-in-class drug candidate, a direct activator of adenosine monophosphate-activated protein kinase (AMPK). AMPK is a key regulator of cellular energy, which activates the pathways that enable energy to be generated, and inhibits pathways which consume energy, at the level of the cell, thus enabling regulation of lipid metabolism, homeostasis of glucose and inflammation. AMPK was qualified as "enzyme of physical exercise", and the Company believes that PXL770 is currently the most advanced drug candidate mimicking physical exercise. In preclinical studies, PXL770 has shown positive effects on the main symptoms of nonalcoholic fatty liver disease (NAFLD). With its unique mechanism of action, PXL770 acts on a key biological target in the potential treatment of many chronic metabolic diseases, including some liver diseases such as NASH. This mechanism of action could yield benefits in the three key pathophysiologic processes involved in the development of the disease, namely: (i) liver steatosis, (ii) inflammation and (iii) fibrosis. Following a favorable evaluation of the safety and pharmacokinetic profile of PXL770 in the phase Ia clinical trial, the Company conducted a phase Ib study with multiple ascending doses (MAD), the positive results of which were announced in July 2018. In the first half of 2019, the Company also plans to begin a phase IIa program to evaluate the safety and efficacy of PXL770 in patients with NASH.

The Company's third drug-candidate, PXL065, from a strategic agreement with DeuteRx, offers a new approach to NASH treatment. PXL065 is the R-stereoisomer of pioglitazone, its parent molecule that has been marketed since 1999 for the treatment of T2D. Pioglitazone is a mixture, in equal proportions, of two mirror molecules (R and S stereoisomers) that interconvert *in vivo*. Like all other products in its class, pioglitazone targets both inhibition of the mitochondrial pyruvate carrier (MPC) and activation of peroxisome proliferator-activated gamma receptors. Pioglitazone has been the subject of a large number of studies in the treatment of NASH which have demonstrated its ability to target disease resolution without aggravating fibrosis in phase II, III and IV clinical trials. Pioglitazone is the only drug recommended by the American Association for the Study of Liver Diseases (AASLD) and the European Association for the Study of the Liver (EASL) in protocols for the treatment of biopsy-proven cases of NASH. However, its use is restricted due to the adverse effects associated with the activation of PPAR $\gamma$  receptors, such as weight gain, bone fractures and fluid retention.

PXL065, the R stereoisomer, is an inhibitor that targets the MPC with little or no PPAR $\gamma$  agonist effects and associated adverse effects that appear to be related to the S stereoisomer of pioglitazone. Preclinical models have demonstrated its efficacy in NASH with little or no weight gain or fluid retention.

Following the first part of the phase Ia trial conducted by DeuteRx, the Company has observed good safety and tolerance of PXL065, without adverse events. Poxel announced the launch of the second part of the phase Ia trial, the results of which it expects to publish in the first half of 2019.

### **Diabetes Market Overview**

According to the International Diabetes Federation, or IDF, in 2017 an estimated 425 million people between the ages of 20 and 79 were affected by diabetes globally, with more than 90% of those affected having type 2 diabetes. The IDF also estimated that as of 2017, in the United States alone, 30.2 million individuals, or 9.3% of the population, had diabetes. According to the estimates of *Decision Resources*, 75 million people over the age of 20 in the United States, Japan, Germany, Italy, the United Kingdom, France and Spain suffered from type 2 diabetes in 2017.

## **NASH Market Overview**

According to the analyses of the National Institute of Diabetes and Digestive and Kidney Diseases, Nonalcoholic Fatty Liver Disease (“NAFLD”), which results in an accumulation of fat in the liver, is one of the most common liver diseases in the United States. It affects approximately 20% of the world's population<sup>1</sup> and up to 70% of type 2 diabetes patients.

These liver diseases aggravate cases of cirrhosis and hepatocellular carcinoma. NASH is a severe form of NAFLD. According to expert estimations, about 10% to 30% of NAFLD patients also suffer from NASH<sup>2</sup>. In the United States, between 30% and 40% of adults suffer from NAFLD and between 3% and 12% of adults suffer from NASH. The Company estimates that the NASH market is expected to grow from \$135 million to more than \$9 billion by 2025.

## **6.2. The Company's Strategy**

The Company's goal is to develop and commercialize innovative therapies for the treatment of metabolic diseases, including type 2 diabetes and NASH. The Company intends to pursue the following strategies:

- **Continue the development of Imeglimin worldwide with two pharmaceutical partners, Sumitomo Dainippon Pharma and Roivant Sciences.** In October 2017 and February 2018, the Company concluded two agreements on strategic partnerships for the development and commercialization of Imeglimin. After the signing of these partnerships, the Company received an initial cumulative amount of approximately €76 million (including the payment of approximately €12 million as a result of the capital participation of Roivant Sciences). The Company could receive up to €705 million in payments related to the attaining of clinical development, regulatory and sales objectives.

As a result of the signing of the partnership agreement with Sumitomo Dainippon for the development and commercialization of Imeglimin in Japan and some Asian countries, the drug-candidate is currently being evaluated in Japan, in the framework of a phase III “TIMES” clinical program. The Company anticipates submitting a registration dossier (JNDA, “Japanese New Drug Application”) over the course of the year 2020. Following the strategic agreement with Roivant Sciences, the objective is to initiate in 2019 the phase III program in the United States and Europe for the treatment of type 2 diabetic patients suffering from moderate and severe renal insufficiency. This development program will be conducted by Roivant Sciences.

- **Advance the clinical development of PXL770 and PXL065 in NASH.** In preclinical studies, PXL770 was observed to have positive effects on various liver and metabolic parameters. Following the favorable evaluation of the safety profile and pharmacokinetics in the phase Ia trial, the Company announced in July 2018 the positive results of its phase Ib study consisting of a study with multiple ascending doses and a drug interaction study. The Company is in the process of preparing the phase IIa proof-of-concept program for the treatment of patients with NASH, with or without type 2 diabetes, for which it is anticipating the filing of an Investigational New Drug (“IND”) application with the FDA in the first half of 2019.

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<sup>1</sup> Sattar N, et al. Non-alcoholic fatty liver disease. BMJ. 2014;349:g4596.

<sup>2</sup> Spengler EK, Loomba R. Recommendations for diagnosis, referral for liver biopsy, and treatment of nonalcoholic fatty liver disease and nonalcoholic steatohepatitis. Mayo Clinic Proceedings. 2015;90(9):1233–1246.

PXL065, which was originally developed by DeuteRx LLC under the name DRX-065, is derived from pioglitazone, a drug that has been the subject of the most advanced studies for the treatment of NASH, and enabled “resolution of NASH without aggravation of fibrosis” in a phase IV trial. The Company estimates, based on the preclinical results and the phase I study, that PXL065 may have a superior therapeutic profile versus pioglitazone, its parent molecule, in the treatment of NASH.

- ***Expand the portfolio by discovering, developing or acquiring additional drug candidates.*** Given the Company’s expertise in metabolic diseases, as well as its management team’s experience in drug development, the Company intends to develop additional compounds, which it may derive either from its existing programs, which were originated by Merck Serono, or which it may source externally through business development efforts.

### 6.3. Type 2 Diabetes Overview, the current treatments and their limitations, market opportunities

#### ***Type 2 Diabetes Overview***

Glucose is a simple sugar used by cells to produce energy. Digestion of food serves as the primary means through which the human body receives glucose. In a fasting state, the liver produces glucose. The production of glucose by the liver and the utilization of digested glucose are managed by insulin, a peptide hormone produced by the pancreas. Insulin secreted by islet beta cells in the pancreas stimulates cells to uptake and process glucose thereby regulating blood glucose levels.

Diabetes is a disease characterized by abnormally high levels of blood glucose and inadequate levels of insulin. There are two primary types of diabetes: type 1 and type 2. In type 1 diabetes, the pancreas produces no insulin. In type 2 diabetes, although the pancreas produces insulin, it either fails to do so at sufficient levels or the body ignores the insulin produced, a condition known as insulin resistance. According to the IDF, type 2 diabetes is the more prevalent form of the disease, affecting approximately 90% of all people diagnosed with diabetes.

In healthy individuals, the pancreas releases a natural spike of insulin at the start of a meal, which serves both to process the glucose produced through digestion and signal the liver to stop producing glucose while digestion is taking place. This allows healthy individuals to remain in glucose homeostasis. By contrast, in patients with type 2 diabetes, the liver does not receive a signal to stop making glucose, thereby resulting in excess blood glucose after eating, a condition known as hyperglycemia. High levels of blood glucose lead to attachment of glucose to certain proteins in the blood, interfering with such proteins’ ability to perform their normal function of maintaining the integrity of the small blood vessels. Over time, these small blood vessels break down and leak, resulting in adverse and sometimes fatal events including retinopathy leading to blindness; loss of kidney function; nerve damage and loss of sensation; poor circulation in the periphery, potentially requiring amputation of the limbs; and macrovascular complications in the heart and brain. According to the American Diabetes Association, 66% of deaths among diabetes patients are due to cardiovascular events.

Several hours after a meal, blood glucose levels in an untreated type 2 diabetes patient become sufficiently elevated that the pancreas releases an inordinately large amount of insulin. However, this occurs at a time when the digestion process is nearly complete and, accordingly, when blood glucose levels should fall. This excess release of insulin places undue demand on the pancreas. This may lead

to a quicker deterioration and eventually result in failure of islet beta cells, rendering the pancreas unable to produce insulin. This also leads to weight gain, which may further exacerbate the disease condition, leading to eventual reliance on injectable insulin.

Although the causes of type 2 diabetes are not fully understood, risk factors for type 2 diabetes include: excess body weight; poor diet, including excess consumption of high-fat and sugary foods; physical inactivity; aging; family history; and ethnicity. Type 2 diabetes generally affects individuals over the age of 40, although it is becoming more common in younger people, including children.

### ***Role of the Mitochondria in Type 2 Diabetes***

Recent scientific advances, reflected in numerous published studies per year in each of the last five years, have highlighted the role of mitochondrial dysfunction in the pathophysiology of type 2 diabetes, associating insulin resistance with changes in mitochondrial function and its capacity to transform nutrients into energy, also known as oxidative capacity.

The mitochondrion is the power center of the cell, generating energy through the production of adenosine triphosphate, or ATP, the primary unit of cellular energy, by oxidizing nutrients such as glucose and lipids. Reactive oxygen species, or ROS, are molecular compounds formed naturally during mitochondrial ATP production and play a crucial role in cell signaling and homeostasis. However, chronic exposure to high concentrations of glucose and lipids as a result of a high calorie diet and/or a sedentary lifestyle leads to insufficient nutrient oxidation and a low ratio of ATP production to oxygen consumption, which is associated with excess ROS formation. Excess ROS formation can contribute to mitochondrial dysfunction and cause cellular damage to tissues in critical organs including the muscles, lungs, heart, liver, brain and eyes. Excess ROS formation is also believed to damage the endothelial cells that coat blood vessel walls, and inactivate enzymes that protect against arteriosclerosis, which can result in microvascular and macrovascular complications often associated with type 2 diabetes. Furthermore, within pancreatic islet beta cells, the formation of excess ROS has been shown to lead to a decline in both cellular insulin content and secretion of insulin in response to glucose.

In addition to excess ROS formation, genetic factors, aging and reduced formation of new mitochondria in the cell contribute to mitochondrial dysfunction, as well as to insulin resistance. In turn, insulin resistance emanating from mitochondrial dysfunction may contribute to metabolic and cardiovascular abnormalities and subsequent deterioration in cardiovascular disease. Furthermore, interventions that improve mitochondrial function have been shown to improve insulin resistance.

Mitochondrial dysfunction is also associated with increases in matrix calcium ( $\text{Ca}^{2+}$ ), which together with excess ROS formation induces the mitochondrial permeability transition pore, or mPTP, to open. In turn, mPTP opening triggers programmed cell death, or apoptosis.

Taken together, these observations suggest that mitochondrial dysfunction may be a central cause of insulin resistance and associated complications.

### ***Current Therapies and their Limitations***

Treatments for type 2 diabetes are intended to re-establish glucose homeostasis. Initially, patients may be placed on an exercise regimen and diabetes-friendly diet that limits the intake of simple carbohydrates and high-fat foods, which are associated with increased blood glucose and lipid levels. However, exercise and dietary changes alone are generally insufficient to control patients' glycemic levels, and type 2 diabetes patients are often prescribed metformin, an orally-administered small molecule drug, that limits glucose production in the liver, decreases intestinal absorption of glucose

and improves insulin sensitivity by increasing peripheral glucose uptake and utilization. Metformin is also an indirect activator of AMPK. If and when the combination of exercise, diabetes-friendly diet and metformin as a monotherapy is insufficient to facilitate glucose homeostasis for patients, physicians may prescribe additional medications to the treatment regimen, including: (i) oral sulfonylureas, which trigger pancreatic beta cells to release more insulin; (ii) oral thiazolidinediones, which help muscle and fat tissue uptake and process insulin more effectively and reduce the amount of glucose released by the liver, while also acting as indirect activators of AMPK; (iii) oral DPP-4 inhibitors, which increase gut-derived hormone levels and insulin levels in order to reduce blood glucose levels; (iv) GLP-1 receptor agonists, injectable synthetic hormones that help lower blood glucose levels through increased glucose-dependent insulin secretion; (v) SGLT-2 inhibitors, which cause excess glucose to be removed from the body in urine; (vi) oral alpha-glucosidase inhibitors, which slow the rise in blood sugar after meals by stopping the breakdown of simple carbohydrates and other types of sugar in the digestive process; and (vii) amylin analogs, injectable forms of the hormone amylin, which modulates A1c levels. Patients unable to maintain glucose homeostasis on these therapies may be prescribed injectable insulin. Many type 2 diabetes patients are also prescribed statins in order to reduce heart disease risk.

While current treatments are often initially effective in helping patients maintain glucose homeostasis, they present a variety of safety issues. For example, metformin can cause lactic acidosis, a dangerous buildup of acid in the blood, in patients with liver and kidney disorders, and is therefore not a viable option for such patients, although it rarely results in hypoglycemia. By contrast, oral sulfonylureas and alpha-glucosidase inhibitors increase the risk of hypoglycemia and weight gain. Oral thiazolidinediones have been associated with fluid retention, which can aggravate congestive heart failure, as well as liver toxicity and increased risk of heart attack. Furthermore, many commonly prescribed treatments, including metformin, alpha-glucosidase inhibitors, oral DPP-4 inhibitors, GLP-1 receptor agonists and amylin analogs, are also associated with nausea, vomiting, gas, diarrhea, dizziness and weakness.

Moreover, many current treatments are limited in their ability to sufficiently delay disease course or prevent complications of type 2 diabetes. Even when existing treatments are effective in blood glucose control, they often fail to control the evolution of the disease and do not address associated co-morbidities. For example, according to Decision Resources, around 56% of patients become refractory to metformin within three years, representing approximately 25 million patients in the United States, Japan, France, Germany, Italy, Spain and the United Kingdom, which are referred to here as the G7 countries. This shortcoming is of particular importance in light of the fact that the mortality of diabetes patients is primarily linked to cardiovascular disease. Furthermore, the Company believes that there are no currently approved direct activators of AMPK. Finally, certain newer type 2 diabetes therapies are delivered in injectable form, which is associated with poorer patient compliance and increased cost.

Table 2 - Comparison of properties of main current treatments

MEDICATION CLASS	CHEMICAL NAME	KEY ATTRIBUTES	KEY LIMITATIONS	SALES (2016) <sup>(1)</sup>
<b>Biguanides</b>	<ul style="list-style-type: none"> <li>metformin</li> </ul>	<ul style="list-style-type: none"> <li>First-line therapy</li> <li>Limits glucose production</li> <li>Probable reduction of cardiovascular events (UKPDS study)</li> </ul>	<ul style="list-style-type: none"> <li>Lactic acidosis</li> <li>GI disorders</li> <li>Many contraindications: chronic renal insufficiency, acidosis, hypoxia, dehydration, etc.</li> <li>Low impact on disease course</li> <li>56% of treated patients become refractory in less than 3 years</li> </ul>	<ul style="list-style-type: none"> <li><b>metformin:</b> \$1.9 billion</li> </ul>
<b>Sulfonylureas</b>	<ul style="list-style-type: none"> <li>glyburide</li> <li>glimepiride</li> <li>glipizide</li> </ul>	<ul style="list-style-type: none"> <li>Increases insulin secretion</li> </ul>	<ul style="list-style-type: none"> <li>Increased risk of hypoglycemia</li> <li>Weight gain</li> <li>Contraindicated for patients with liver and kidney disorders</li> </ul>	<ul style="list-style-type: none"> <li><b>sulfonylureas:</b> \$288 million</li> </ul>
<b>Thiazolidinediones</b>	<ul style="list-style-type: none"> <li>pioglitazone</li> <li>rosiglitazone</li> </ul>	<ul style="list-style-type: none"> <li>Improves glucose uptake and transformation by muscles and fat tissues</li> <li>Low impact on disease course</li> </ul>	<ul style="list-style-type: none"> <li>Weight gain, fluid retention</li> <li>Liver toxicity</li> <li>Increased risk of heart attack</li> </ul>	<ul style="list-style-type: none"> <li><b>thiazolidinediones:</b> \$341 million</li> </ul>
<b>DPP-4 inhibitor</b>	<ul style="list-style-type: none"> <li>sitagliptin</li> <li>saxagliptin</li> <li>linagliptin</li> </ul>	<ul style="list-style-type: none"> <li>Increases insulin secretion</li> <li>Some cardiovascular benefits</li> </ul>	<ul style="list-style-type: none"> <li>GI disorders</li> <li>Urinary &amp; respiratory infections</li> <li>Low impact on disease course</li> </ul>	<ul style="list-style-type: none"> <li><b>DPP-4 inhibitor:</b> \$13.8 billion</li> <li><i>Januvia:</i> \$6.4 billion</li> <li><i>Janumet:</i> \$3.0 billion</li> <li><i>Tradjenta:</i> \$1.6 billion</li> <li><i>Onglyza:</i> \$899.5 million</li> </ul>
<b>GLP-1 receptor agonists</b>	<ul style="list-style-type: none"> <li>liraglutide</li> <li>vildagliptin</li> <li>exenatide</li> </ul>	<ul style="list-style-type: none"> <li>Increases glucose addiction and insulin secretion</li> <li>Slows down weight gain</li> <li>Cardiovascular protective action</li> </ul>	<ul style="list-style-type: none"> <li>GI disorders</li> <li>Acute pancreatitis</li> <li>Potential increase of risk of thyroid cancer</li> </ul>	<ul style="list-style-type: none"> <li><b>GLP-1 receptor agonists:</b> \$6.02 billion</li> <li><i>Victoza:</i> \$3.6 billion</li> <li><i>Bydureon:</i> \$419 million</li> </ul>
<b>SGLT-2 inhibitors</b>	<ul style="list-style-type: none"> <li>empagliflozine</li> <li>canagliflozine</li> <li>dapagliflozine</li> </ul>	<ul style="list-style-type: none"> <li>Increases glucose excretion</li> <li>Cardiovascular protective action</li> </ul>	<ul style="list-style-type: none"> <li>Urinary tract infections</li> <li>Increased risk of diabetic ketoacidosis</li> </ul>	<ul style="list-style-type: none"> <li><b>SGLT-2 inhibitors:</b> \$4.7 billion</li> <li><i>Invokana:</i> \$2.4 billion</li> <li><i>Forxiga:</i> \$1.3 billion</li> </ul>

<sup>(1)</sup> Decision Resources, November 2017.

Source: Company

## The Company's Market Opportunity

According to the IDF, diabetes-related expenditures in 2017 totaled close to \$436 billion in North America, Germany, Japan and France. Decision Resources estimates that diabetes treatments generated sales of \$54.6 billion in 2016 in the United States, Japan, Germany, Italy, the United Kingdom, France and Spain, and that sales in these markets are projected to increase to \$73.7 billion by 2026. Furthermore, according to the IDF, aggregate diabetes-related expenditures in the United States, China and Germany, the three highest spending countries, amounted to more than 68% of total global expenditures on diabetes, even though these countries accounted for only about 35% of the global diabetes population. In addition, the IDF estimates the aggregate diabetes-related expenditures in the three highest spending regions of Western Pacific, Middle East and North Africa, and South and Central America amounted to \$157.7 billion in 2015, and expects these expenditures to increase by 39% by 2040.

According to the IDF, it is estimated that globally 425 million individuals between the ages of 20 and 79 were affected by diabetes in 2017, with more than 90% of these individuals having type 2 diabetes. In the United States alone, 30.2 million individuals, or 9.3% of the population, suffered from diabetes in 2017, according to the IDF. Furthermore, the IDF estimates that by 2045, the number of people globally affected by diabetes will increase by 48% to 629 million.

Within certain developing regions of the world, the IDF projects diabetes prevalence to increase at even higher rates. For example, in China there were approximately 114.4 million patients in 2017, which the IDF estimates will increase to 134.3 million by 2045. In the Middle East and North Africa region, there were approximately 39 million patients with diabetes in 2017, which the IDF estimates will increase to 82 million by 2045. In Southeast Asia, the IDF estimates that 151 million individuals will suffer from diabetes in 2045, an increase of 84% compared to 2017.

Despite the limitations of current non-insulin therapies for diabetes, Decision Resources estimates that these treatments generated sales of over \$55.6 billion in 2016 in the United States, Japan, Germany, Italy, the United Kingdom, France and Spain, and that sales in these markets are projected to grow to \$73.7 billion by 2026. The total economic consequences of diabetes are even larger, with 2015 diabetes-related expenditures totaling \$521 billion in North America, the Caribbean and Europe, according to the IDF. Furthermore, according to the IDF, aggregate diabetes-related expenditures in the United States, China and Germany, the three highest spending countries, amounted to 60% of the total global expenditures on diabetes, even though these countries only accounted for 35.1% of the global diabetes population. According to Decision Resources, the diabetes monotherapy treatment market in the G7 countries is worth approximately \$1.9 billion (with the current standard of care, metformin, used for the treatment of approximately 60% of type 2 diabetes patients in the G7 countries), while the new oral combination therapies market is worth approximately \$17 billion (with sitagliptin accounting for a 50% market share within its class).

The US diabetes market is the largest diabetes market worldwide, according to Decision Resources. The Japanese market is the second largest diabetes market worldwide, according to Decision Resources. According to the same source, the Japanese diabetes market grew by a compound annual growth rate of more than 18% between 2008 and 2012 and could grow by more than 30% by 2020. Additionally, the Company believes that the Japanese diabetes market has pricing and reimbursement characteristics similar to the United States and has shown a rapid market uptake for new innovative products. This has been supported by a clear development path defined by the PMDA. The Company believes that the strength of the Japanese diabetes market has been shown in sales of sitagliptin reaching in excess of \$1.4 billion in three years, according to Decision Resources.

The Company believes that there is significant market potential for non-insulin therapies that preserve pancreatic function, reduce insulin resistance and decrease cardiovascular and metabolic disease risk



factors, such as heightened blood lipid levels and excess body weight, either acting alone or in combination with existing type 2 diabetes treatments. Based on figures published by Decision Resources, the Company believes that the potential market opportunity in the United States and the EU is approximately \$50.9 billion and the potential market opportunity in Japan is approximately \$4 billion.

#### **6.4. Imeglimin – the first type 2 diabetes treatment with the ambition of slowing disease course and its complications**

Imeglimin is a first-in-class oral drug candidate that targets the two main metabolic defects at the root of type 2 diabetes—low insulin secretion and elevated insulin resistance—by counteracting mitochondrial dysfunction.

Imeglimin was discovered at Merck Serono and has been further developed by Poxel. Since the late 1990s, Merck Serono has been interested in the role of mitochondria in the pathophysiology of diabetes, as it had been suggested that metformin could act on the mitochondria. In order to capitalize on this understanding of the role of mitochondria, Merck Serono worked with an academic team to identify new chemical structures that could restore normal functioning of the mitochondrial respiratory chain, which is impaired in type 2 diabetes patients. This initial partnership formed the basis for the development of Imeglimin.

Merck Serono filed an Investigational New Drug application, or IND, for Imeglimin on October 18, 2006 with a type 2 diabetes indication. Merck Serono transferred this IND to the Company in 2009.

The Company believes that Imeglimin is the most advanced type 2 diabetes drug candidate of its class. Certain large pharmaceutical companies have similar programs and have entered into partnerships aimed at identifying products similar to Imeglimin. The Company believes, however, that these programs are not as advanced in clinical development as Imeglimin.

##### ***Summary of Imeglimin's mechanism of action***

The Company believes that Imeglimin is able to regulate mitochondrial energy production by counteracting the mitochondrial dysfunction associated with the diabetes pathology and its associated microvascular and macrovascular complications.

The mitochondrion is the power center of the cell, generating energy through the production of ATP, the primary unit of cellular energy, by oxidizing nutrients such as glucose and lipids, and contributing to the regulation of energy balance, thereby improving metabolic function.

In the pathophysiology of diabetes, excess food and a sedentary lifestyle lead to a disequilibrium in the energy balance and are linked to the fact that the supply of nutrients is higher than the demand for energy. This disequilibrium causes an increase in the production of ROS from the mitochondrial respiratory chain, which further impairs the functioning of the chain, leading to insufficient insulin secretion in response to glucose and to impaired insulin sensitivity.

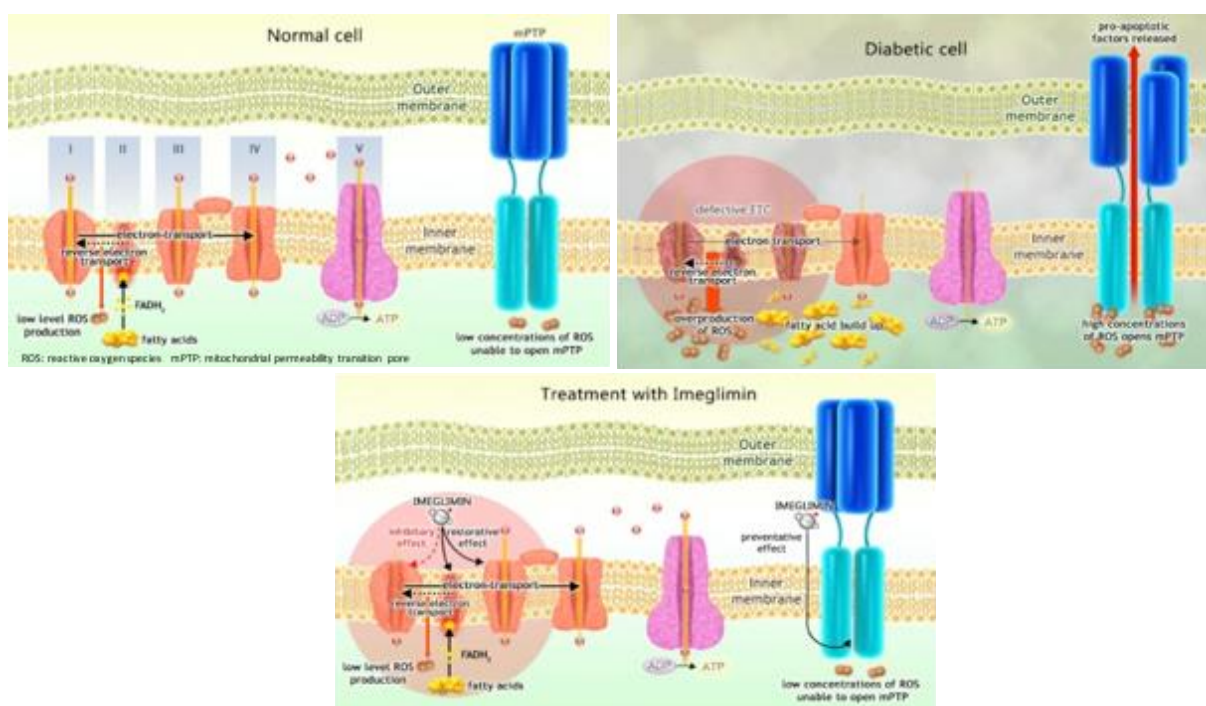
The Company believes that Imeglimin improves mitochondrial function by modulating complex activities of the mitochondrial respiratory chain and by decreasing ROS overproduction in this unhealthy context. Through this mitochondrial action, Imeglimin has been observed to restore the organs' sensitivity to glucose and insulin, and cause:

- an increase in glucose-dependent insulin secretion by the pancreas;

- a decrease in excess production of glucose by the liver; and
- an increase in absorption and use of glucose by the muscles.

Imeglimin has also been observed to prevent the mPTP from opening and to prevent cell death in the pancreas' beta cells and in human endothelial cells. Imeglimin's beneficial effect on the pancreas' beta cell mass preservation is expected to lead to a delay in disease course. Imeglimin's effect on improving endothelial dysfunction leads the Company to believe that Imeglimin may have an early vascular protective effect that may potentially delay the occurrence or decrease the progression of vascular complications in the type 2 diabetes population.

*Graph 3 - The diagrams below show Imeglimin's mechanism of action:*



Source: Company data

### **Clinical Studies**

As of the date of this document de référence, these clinical trials have obtained statistically significant results for the primary and secondary endpoints, including a reduction in HbA1c and fasting glycemia versus placebo, associated with a favorable profile in terms of safety of use. At the completion of the completed and ongoing phase I, II and III trials, Imeglimin will have been administered to approximately 2,500 subjects in 29 clinical trials in the United States, Europe, and Japan.

*Table 4 - Overview of clinical studies evaluating Imeglimin:*

PHASE	STUDY NO.	NUMBER OF PATIENTS <sup>(1)</sup>	TREATMENT DURATION	PRIMARY END POINT	DOSE	P-VALUE <sup>(2)</sup>	REGION
Phase I	EML017008-001 <sup>(3)</sup>	73	Up to 9 days	Safety / Pharmacokinetics	Up to 4000 mg	—	Europe
Phase I	EML017008-002 <sup>(3)</sup>	6	Single dose	Safety / Pharmacokinetics	1000 mg	—	Europe
Phase I	EML017008-005 <sup>(3)</sup>	51	8 days	Safety / Pharmacokinetics	1000 mg QD / 500 mg	—	Europe
Phase I	PXL008-001	15	6 days	Safety / Pharmacokinetics	1500 mg	—	Europe
Phase I	PXL008-003	16	6 days	Safety / Pharmacokinetics	1500 mg	—	Europe
Phase I	PXL008-007	14	Single dose	Safety / Pharmacokinetics	750 mg / 1500 mg	—	Europe
Phase I	PXL008-010	14	Single dose	Safety / Pharmacokinetics	750 mg / 1500 mg	—	Europe
Phase I	PXL008-011	48	Single dose or 10 days	Safety / Pharmacokinetics	500 mg / 1000 mg / 1500 mg / 2000 mg RD 4000 mg / 6000 mg / 8000 mg SD	—	Europe
Phase I	PXL008-012	9	Up to 7 days	Safety / Pharmacokinetics	Up to 8000 mg	—	Europe
Phase I	PXL008-016 <sup>(4)</sup>	49	Single dose	Cardiovascular safety	2250 mg / 6000 mg		Europe
Phase I	PXL008-022	16	Single dose	Safety / Pharmacokinetics	1000 mg		Europe
Phase I	PXL008-023	16	Single dose	Safety / Pharmacokinetics	1500 mg		Europe
Phase I	PXL008-024	16	Single dose	Safety / Pharmacokinetics	1000 mg		Europe
Phase I	DD401101	12	Single dose	Safety / Pharmacokinetics	1000 mg		Japan
Phase I	DD401102	24	Single dose	Safety / Pharmacokinetics	500 mg or 1000 mg		Japan
Phase II	EML017008-003 <sup>(3)</sup>	40	4 weeks	Change in AUC Glucose versus Placebo	1000 mg / 2000 mg QD	$P<0.0001$ / $P=0.0305$	Europe
Phase II	EML017008-004 <sup>(3)</sup>	62	8 weeks	Change in AUC Glucose versus Placebo	500 mg / 1500 mg	$P=0.086$ / $P=0.003$	Europe
Phase II	PXL008-002	78	12 weeks	Change in A1c versus Placebo	1500 mg	$P<0.001$	Europe
Phase II	PXL008-004	82	12 weeks	Change in A1c versus Placebo	1500 mg	$P<0.001$	Europe
Phase II	PXL008-006	18	7 days	Change in AUC Insulin versus Placebo	1500 mg	$P=0.035$	Europe
Phase II	PXL008-008	301	24 weeks	Change in A1c versus Placebo	500 mg / 1000 mg / 1500 mg / 2000 mg	n.s. / n.s. / $P<0.001$ / $P=0.006$	U.S. & Europe

PHASE	STUDY NO.	NUMBER OF PATIENTS <sup>(1)</sup>	TREATMENT DURATION	PRIMARY END POINT	DOSE	P-VALUE <sup>(2)</sup>	REGION
Phase II	PXL008-009	30	18 weeks	Change in AUC Glucose versus Placebo	1500 mg	P=0.001	Europe
Phase II	PXL008-014	221	24 weeks	Change in HbA1c versus Placebo	500 mg / 1000 mg / 1500 mg	—	Japan
Phase II	PXL008-017	12	7 days	Artery endothelial function	1500 mg		Europe
Phase II <sup>5</sup>	1002	46	4 weeks	PK/PD	500 mg (bid) / 1000 mg (bid) / 1500 mg (qd)	-	U.S.
Phase III	TIMES 1 <sup>4</sup>	200+	26 weeks	Change in HbA1c versus Placebo	1000 mg	-	Japan
Phase III	TIMES 2 <sup>4</sup>	~700	52 weeks	Long Term safety & Change in HbA1c	1000 mg	-	Japan
Phase III	TIMES 3 <sup>4</sup>	200+	52 weeks	Long Term safety & Change in HbA1c	1000 mg	-	Japan

<sup>(1)</sup> This column indicates the number of patients treated with Imeglimin during the studies.

<sup>(2)</sup> P-value is a conventional statistical method for measuring the statistical significance of clinical results.

<sup>(3)</sup> The clinical trials were conceived and conducted by Merck Serono before the Company was founded in 2009.

<sup>(4)</sup> Ongoing studies whose recruitment is completed

<sup>(5)</sup> Study conducted by Roivant

Source: Company data

### Phase II studies - completed:

#### Phase IIb dose-finding study (PXL008-014) - Japan -

A Phase 2b randomized, double-blind, placebo-controlled study has evaluated three doses of Imeglimin (500 mg, 1000 mg and 1500 mg) administered twice a day for 24 weeks in 299 Japanese patients for the treatment of type 2 diabetes.

Graph 5 - Clinical Plan of the PXL008-014 study:

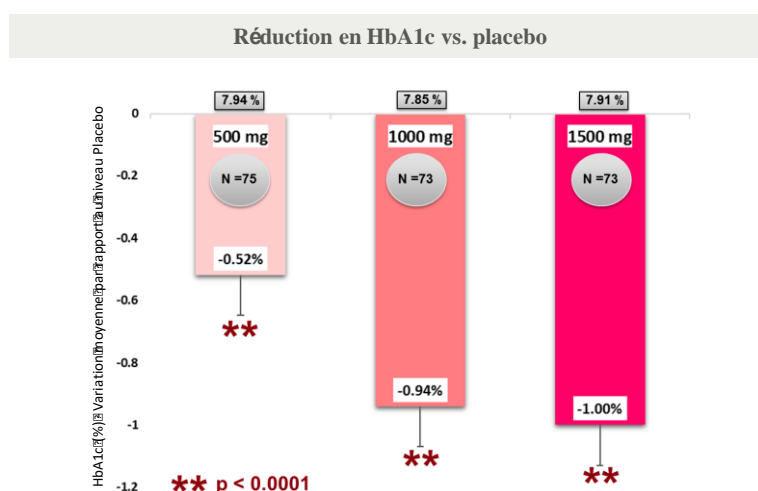


Source: Company data

This study has revealed a statistically significant ( $P<0.0001$ ) reduction in the rate of glycated hemoglobin (HbA1c), the primary endpoint for the study, against placebo in all treated groups, after

24 weeks of treatment. By comparison with placebo, the reduction in HbA1c rate was 0.52%, 0.94% and 1.00%, respectively, with doses of 500 mg, 1000 mg and 1500 mg.

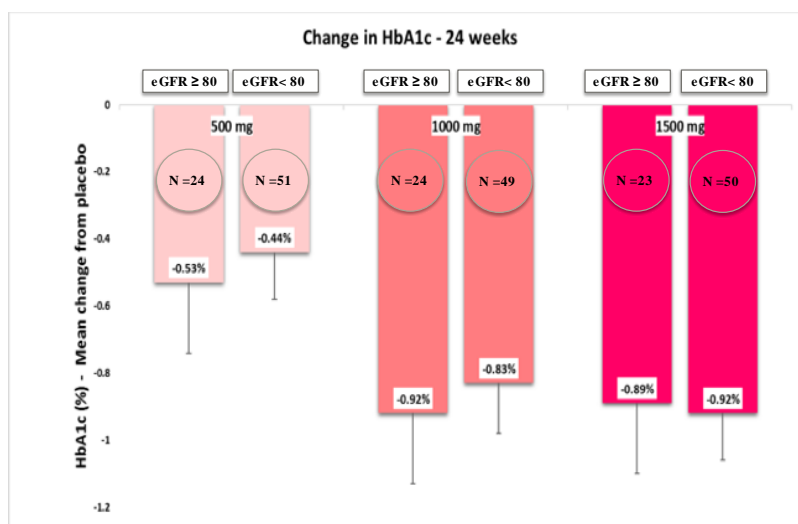
Graph 6 - Primary endpoint: reduction in HbA1c against placebo



Source: Company data

The study has also revealed a statistically significant ( $P < 0.0001$ ) improvement in secondary endpoints with the two highest doses: decrease in fasting plasma glucose and glycated albumin, and percentage of patients achieving a target HbA1c below 7% at the end of the study.

Graph 7 - Efficacy of Imeglimin in Type 2 Diabetes Patients with Renal Disorders



Source: Company data

On the whole, this study shows the safety and good tolerance of Imeglimin; reported adverse effects are coherent with those observed in the framework of phase I and II trials in the U.S. and in Europe. No serious adverse effects have been reported. No difference has been found between the treated group and the placebo group, as regards the overall incidence rate of patients with at least one adverse effect that emerged during treatment. In particular, in this study, the safety and the efficacy of Imeglimin in patients with mild or moderate chronic kidney disease (Graph 7) were similar to those

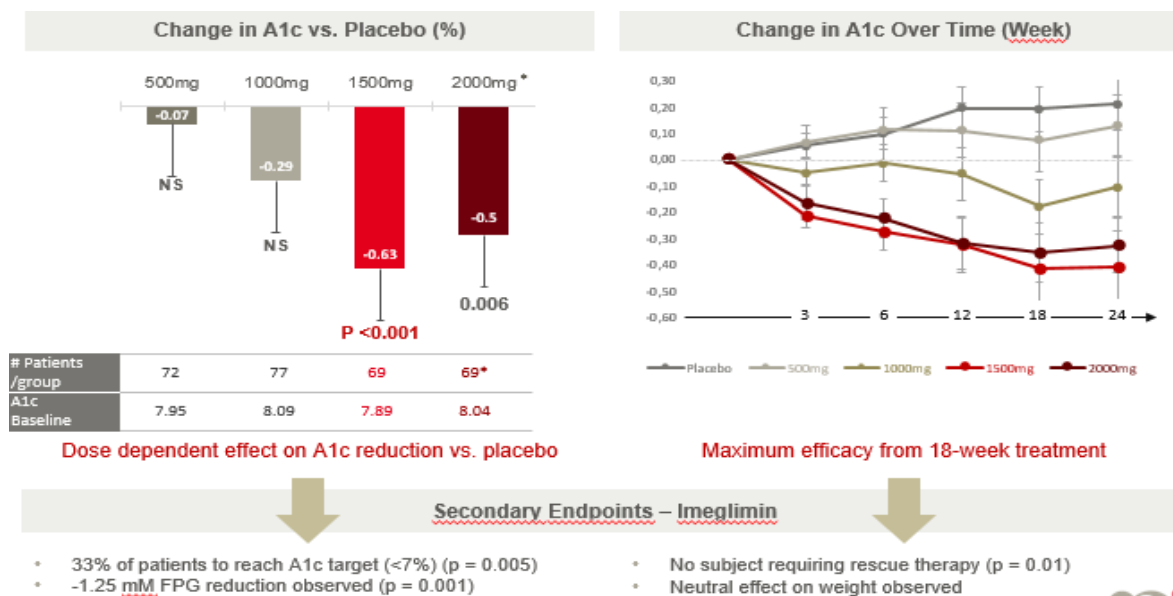
observed in patients whose renal function is normal. In addition, Imeglimin has not been associated with any weight gain.

## PXL008-008

The Company initiated a double-blind, placebo-controlled phase IIb dose-finding study in March 2013. The primary endpoint of this study was to assess the change of A1c levels versus placebo. The study, conducted across multiple sites in the United States and Europe, included 382 randomized subjects (including 301 patients administered Imeglimin and 81 administered placebo) who were either previously untreated or had previously been treated with a monotherapy. The patients were placed into five groups, with four groups treated with Imeglimin and one group treated with a placebo over 24 weeks. The previously untreated patients took a placebo during a three-week stabilization period, and subjects who had been treated using monotherapy were asked to interrupt their treatment for a period of six weeks prior to dosing, in order to wash out any residual placebo or monotherapy before randomization. The Company reported the results of this study in June 2015 at the American Diabetes Association conference.

During the phase IIb study, A1c was measured to assess the effect that each dose of Imeglimin had on controlling glycemic levels. After 24 weeks of treatment, decreases of 0.63% and 0.50% in A1c levels were observed in the groups that received the 1500 mg dose and the 2000 mg dose, respectively, as compared to the group that received the placebo. In this study, the Company observed a moderate change in A1c levels at the lowest dose (500 mg), and noted that the change in A1c levels increased until a dose of 1500 mg was attained. As anticipated, the 2000 mg dose was not observed to provide any additional benefit as compared to the 1500 mg dose. As a result, the Company considers the 1500 mg dose to be the optimal dose to attain efficacy of Imeglimin, while preserving a comparable safety profile to placebo.

Graph 8 - Results of Phase IIb study in monotherapy



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\* Excluding one subject due to blood sample error

Source: Company data



The 0.63% glucose lowering effect observed in patients who received a 1500 mg bid dose of Imeglimin is comparable to historic results of studies involving oral pharmacologic agents approved in the past 10 years.

Imeglimin showed a favorable safety profile for a drug candidate at this stage of clinical development at all doses evaluated in the study and, in particular, at the optimal dose for efficacy of 1500 mg. The frequency of adverse events in patients receiving Imeglimin was comparable to the frequency of adverse events reported in the placebo group. Most of the adverse events identified were mild and were considered by the investigator to not be directly related to the treatment. The small number of adverse events considered to be related to the treatment with Imeglimin mainly related to the gastrointestinal system. Five serious adverse events comprising instances of (i) incisional hernia; (ii) lung disorder; (iii) orchitis (inflammation of one or both testicles); (iv) sciatica (leg pain radiating along the sciatic nerve); and (v) gangrene were reported to have occurred during the trial, but these events were considered to be unrelated to the treatment and were balanced among the groups administered Imeglimin and placebo. In addition, there were no hypoglycemia or cardiovascular events considered to be related to the treatment in this trial.

In addition to safety and tolerability, a number of additional secondary endpoints were assessed, including fasting plasma glucose, the number of patients requiring rescue therapy and the number of patients reaching A1c targets below 7%.

#### **PXL008-009**

In parallel to the phase II dose-finding study described above, the Company completed a phase IIb dose-finding study to assess the characteristics of Imeglimin with regard to various efficacy parameters, including fasting and post-prandial glycemia (the level of blood glucose after eating) and the contribution of those two effects on the decline in A1c levels. The study included 59 randomized patients who had previously been treated with a monotherapy across multiple study sites in Europe. A total of 30 patients were administered Imeglimin at the optimal dose of 1500 mg and 29 patients were treated with a placebo over 18 weeks. Subjects in the study who had previously been treated with a monotherapy were asked to interrupt their treatment for a period of four weeks to wash out any residual monotherapy before participating in the study. The Company reported the results of this study in November 2015 at the World Congress on Insulin Resistance, Diabetes & Cardiovascular Disease.

The Company observed a significant improvement in patient glucose tolerance, as evidenced by a 430 mmol per liter decrease in the area under the glucose curve during the three hours after the glucose load ( $P<0.001$ ), together with a 1.22 mmol per liter decrease in fasting plasma glucose ( $P<0.022$ ). These effects resulted in a significant decrease in A1c levels of 0.62% ( $P<0.013$ ), which is consistent with the decrease observed during the phase IIb dose-finding study for the same dose.

During the glucose tolerance test, the insulin and C-Peptide (a byproduct of insulin synthesis and a universal measure of insulin secretion) secretions increased compared to placebo, and mathematical modeling of C-Peptide secretion increased in response to glucose. This demonstrated that the improvement in insulin secretion can be partly explained by an improvement in the glucose sensing of the beta cells in the pancreas, or improvement in glucose sensitivity. These results supported the positive effect of Imeglimin on insulin secretion observed during another phase II clinical study using a hyperglycemic clamp technique (PXL008-006). Similarly, mathematical modeling of the glucose, insulin or C-Peptide curves revealed that Imeglimin significantly improved several surrogate markers

of insulin sensitivity, including the Mastuda index or the Stumvoll index, that were correlated to the result obtained using the reference method of the hyperinsulinemic clamp.

The results from this trial therefore support the dual mechanism of Imeglimin in type 2 diabetes patients, improving both glucose dependent insulin secretion (by improving the beta cell glucose sensitivity) and insulin sensitivity.

In addition, Imeglimin was observed to have a favorable safety profile for a drug candidate at this stage of clinical development during this study, with 27% of treated subjects presenting at least one treatment-emergent adverse event, as compared to 59% in the placebo group. The only treatment-related adverse events reported in the trial were events of hyperglycemia (3% of patients treated with Imeglimin as compared to 14% of patients treated with placebo).

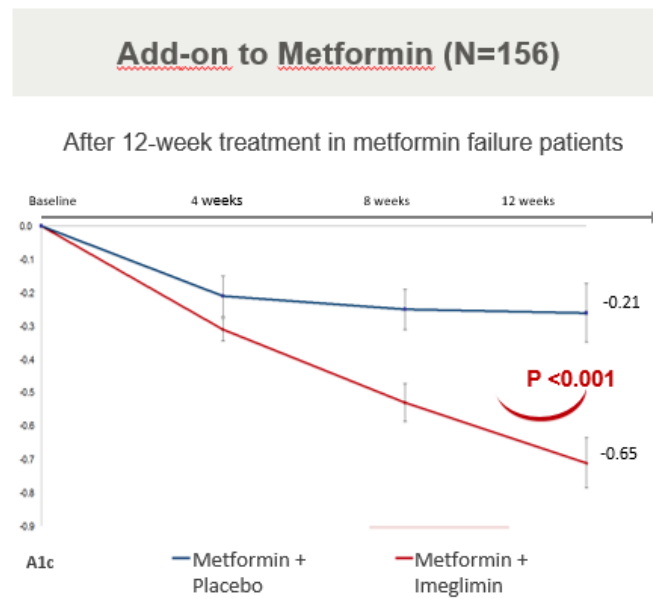
#### **PXL008-002 and PXL008-004**

The Company completed these phase II efficacy and safety studies of Imeglimin in combination with metformin and with a DPP-4 inhibitor, sitagliptin. The Company published the results of these studies in the peer-reviewed journal *Diabetes Care*, *Fouqueray et al.* 2013; 36: 565–568 and *Fouqueray et al.*, 2014; 37: 1924–1930.

The first study (**PXL008-002**) assessed the benefit of combining metformin with Imeglimin, as compared to a placebo, in subjects for whom monotherapy with metformin alone was not sufficient to control their glycemia, and assessed the safety of this combination after 12 weeks of treatment. A total of 156 type 2 diabetes patients were randomized in this study. During this study, the Company observed a 0.44% decrease in A1c levels ( $P=0.001$ ) after 12 weeks of treatment in the group administered metformin and Imeglimin, as compared to those administered metformin and placebo. A number of secondary end points were assessed, primarily fasting plasma glucose and the number of patients whose A1c value decreased by 0.5% or more by the end of the treatment. Overall, the incidence of adverse events was comparable in the two groups. The adverse events rate was 23.1% in the combined metformin and Imeglimin group and 19.2% in the group administered a combination of metformin and placebo.

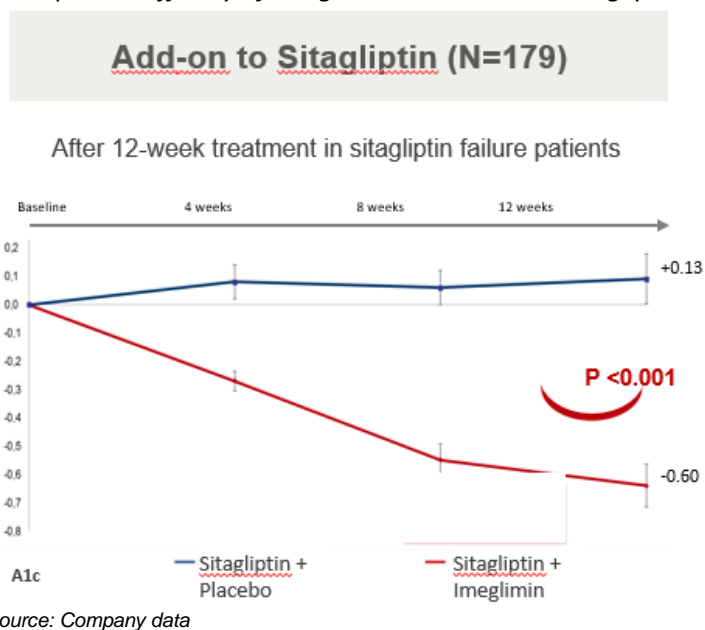


Graph 9: Efficacy of Imeglimin as complement of metformin:



The second study (**PXL008-004**) assessed the benefit of combining Imeglimin with sitagliptin, as compared to a placebo, in subjects for whom monotherapy with sitagliptin had failed, and assessed the safety of this combination. A total of 170 type 2 diabetes patients were randomized in this study. During this study, the Company observed a decrease of 0.72% in A1c levels ( $P < 0.001$ ) after 12 weeks of treatment in the Imeglimin group, as compared to the placebo group. A number of secondary end points were assessed, primarily fasting plasma glucose and the number of patients whose A1c value decreased by 0.5% or more by the end of the treatment. The incidence of adverse events was comparable in the two groups, with an adverse event rate of 14.6% in the group administered sitagliptin and Imeglimin and 22.7% in the group administered sitagliptin in combination with placebo. The Company believes that the percentage of adverse events, which was slightly higher in the placebo group, can be partially explained by the occurrence of hyperglycemia linked to lower blood glucose control in patients who were administered placebo instead of Imeglimin. In the Imeglimin group, no adverse events were considered to be related to the treatment. In addition, no episodes of hypoglycemia were reported during the treatment period among those administered with Imeglimin and sitagliptin.

Graph 10 - Efficacy of Imeglimin in addition to sitagliptin:



The reduction in A1c levels observed in these studies with the 1500 mg Imeglimin dose compare favorably to the results obtained with other approved drugs, in particular DPP-4 inhibitors. The results of these studies showed greater decreases in A1c versus baseline in those patients administered a combination of Imeglimin and metformin or a combination of Imeglimin and sitagliptin than in those administered metformin or sitagliptin alone.

#### PXL008-006

The Company also completed a phase II efficacy study of Imeglimin's effect on pancreatic beta cell function in diabetes patients. The study took place over a seven-day period. Eighteen patients were treated with Imeglimin at the dose of 1500 mg and 15 patients were treated with a placebo, for a total of 33 patients in the study. The primary endpoint of the study was insulin secretion as defined by total insulin response (which is reflected in the graph below as incremental area under the curve, or iAUC, measured in 0–45 min periods) and insulin secretion rate, or ISR. The Company observed that Imeglimin raised insulin secretory response to glucose by 112% ( $P=0.035$ ), first-phase ISR by 110% ( $P=0.034$ ) and second-phase ISR by 29% ( $P=0.031$ ). The study's secondary endpoint of beta cell glucose sensitivity was also met. Imeglimin was not observed to affect glucagon secretion and was observed to have a favorable safety profile for a drug candidate at this stage of clinical development during this study.

#### Phase I Studies

The Company conducted 15 phase I studies of Imeglimin with an aggregate of 330 subjects. These phase I studies assessed safety, tolerability and pharmacokinetics of Imeglimin in doses ranging from 100 mg to 8000 mg per day. In these studies, the Company observed that Imeglimin had a good pharmacokinetic profile with a low risk of drug interactions both alone and in combination with metformin and sitagliptin. In these studies, a favorable safety profile for a drug candidate at this stage of clinical development was observed, including among patients with renal insufficiency.

#### Clinical development plan in Japan

In October 2017, the Company and Sumitomo Dainippon launched the “TIMES” program in Japan, including three phase III studies for the development and commercialization of Imeglimin in Japan

The TIMES program will consist of the three following trials, each performed with the dose of 1000 mg administered twice a day:

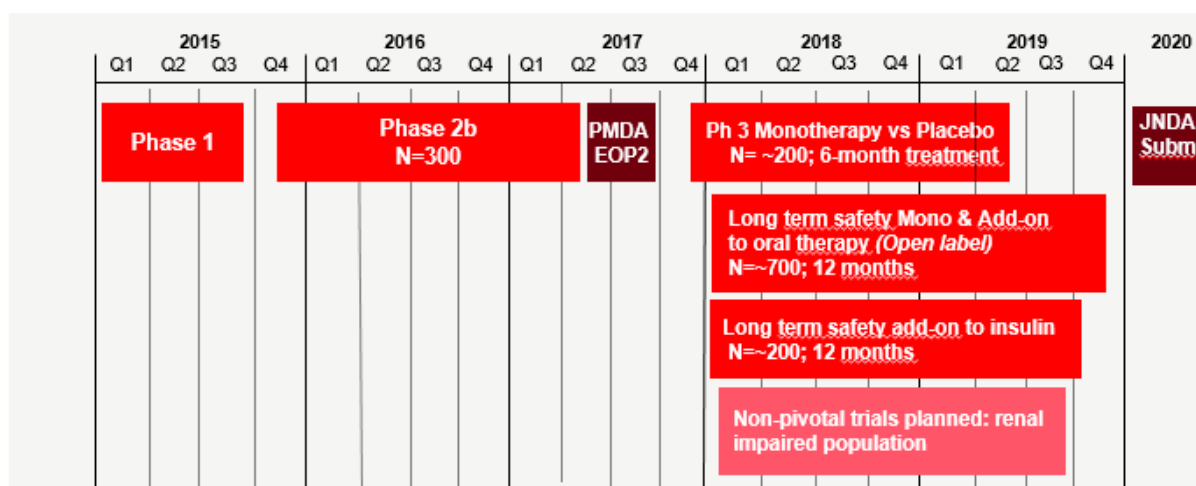
TIMES 1: Phase III, 24-week, randomized, double-blind placebo-controlled study to evaluate the efficacy, safety and tolerance of Imeglimin in Japanese patients suffering from type 2 diabetes. The reduction of glycated hemoglobin (HbA1c) will be the main evaluation criterion. The secondary evaluation criteria of the study include other standard glycemic and non-glycemic parameters.

TIMES 2: Phase III, 52-week, open and parallel-group study to evaluate the long-term efficacy, safety and tolerance of Imeglimin in Japanese patients suffering from type 2 diabetes. In this study, Imeglimin will be administered by the oral route in monotherapy or in association with existing diabetes drugs, including a DPP-4 inhibitor, a SGLT-2 inhibitor, a biguanide, a hypoglycemic sulphonylurea and a GLP-1 receptor agonist.

TIMES 3: Phase III, 16-week, randomized, double-blind placebo-controlled study with a 36-week, open-label extension period to evaluate the efficacy and safety of Imeglimin in association with insulin in Japanese patients suffering from type 2 diabetes associated with insufficient control of glycemia by insulin therapy.

Approximately 1,150 patients were enrolled in the phase III clinical studies to obtain marketing authorization for Imeglimin in Japan. The Company expects to publish the first results of TIMES 1, the randomized double-blind placebo-controlled efficacy study in monotherapy, early in the second quarter of 2019. This first publication should be followed, at mid-year, by that of the first results of the study in combination with insulin, TIMES 3, after 16 weeks of randomized, double-blind, placebo-controlled administration. The results of the study in combination with other existing diabetes medications, TIMES 2, as well as the full results of TIMES 3 (after the 36-week open-label extension period) are expected to be published in the fourth quarter of 2019.

Graph 11 - Plan of development of Imeglimin in Japan.



### Clinical development plan in the United States and Europe

The Company and Roivant Sciences have signed a strategic development and license agreement for Imeglimin in the United States, Europe and in other countries not covered by the existing partnership of Poxel in East and Southeast Asia<sup>3</sup>.

The preparatory work for the phase III program is ongoing and includes in particular studies to confirm the differentiated potential of Imeglimin on sensitive diabetes populations such as patients with renal insufficiency. It will also focus on the manufacture of treatment units that will be used in the framework of phase III trials.

The goal is to initiate the phase III program in the United States and Europe in 2019 by initially targeting type 2 diabetic patients with moderate and severe renal insufficiency.

### Manufacturing and Supply

Imeglimin is manufactured using standard raw materials over a three-step process. Merck Serono originally developed and optimized the synthesis procedure for the manufacture of Imeglimin, based on a 500 mg dosage, on an industrial scale and in compliance with standards imposed by Good Manufacturing Practices. A group of specialized subcontractors manage this molecule synthesis and tablet manufacturing process, as well as the analytical methods of controls and batch release. These subcontractors can manufacture batches of 500 Kg, making it possible to deliver up to 900,000 tablets depending on doses.

Imeglimin is formulated as a coated, oval-shaped tablet with immediate release. The Company has developed three different dose strengths: 250 mg, 500 mg and 750 mg. Imeglimin is a stable active substance and, if kept below 25°C, has a shelf life of up to 60 months (depending on the primary packaging used). Imeglimin's long shelf life has been observed during long-term stability studies in accordance with ICH recommendations.

<sup>3</sup> The agreement between Poxel and Roivant focuses on all countries not covered by the agreement between Poxel and Sumitomo Dainippon Pharma, which extends to Japan, China, South Korea, Taiwan, Indonesia, Vietnam, Thailand, Malaysia, Philippines, Singapore, Myanmar, Cambodia and Laos.

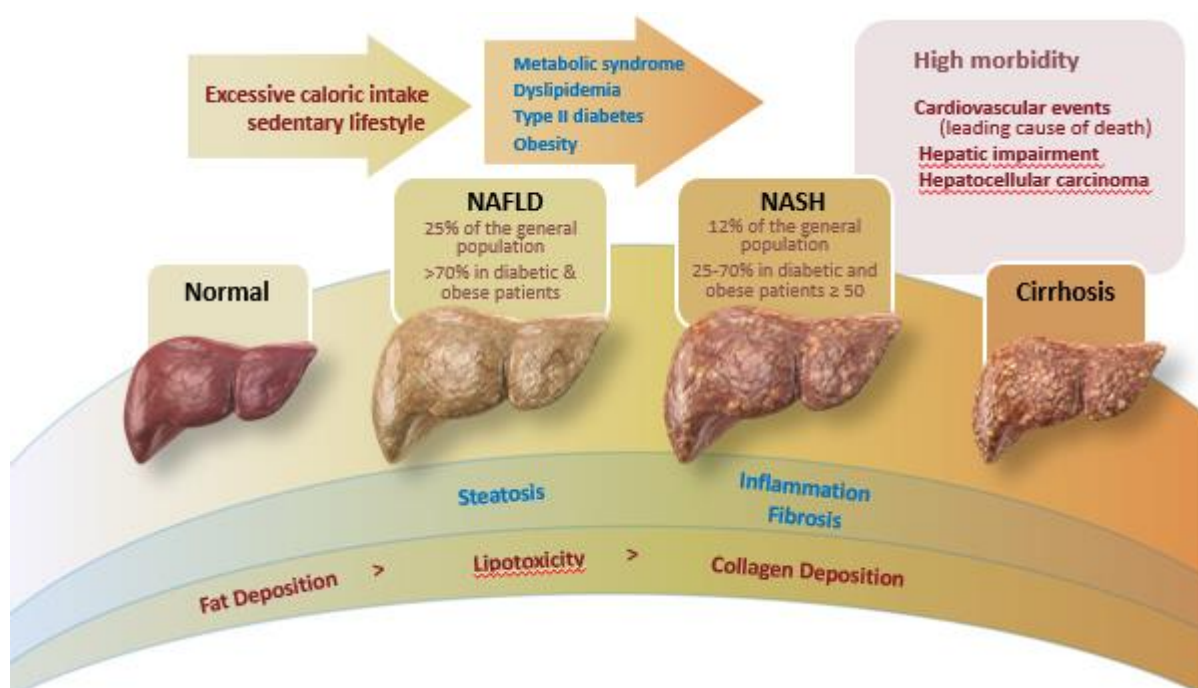
The manufacturing process for immediate-release tablets can enable the manufacturing of batches of sufficient size to perform phase III studies and for a market launch.

## 6.5. PXL770 and PXL065 Two Novel Drug-Candidates to treat patients with NASH

### Overview of NASH

NASH is a chronic and serious liver disease caused by an excessive accumulation of fat in the liver, steatosis, which induces inflammation that can gradually lead to a fibrosis and liver cirrhosis. This state when it breaks down can lead to the shutdown of liver functions and cause the death of most severely affected patients. Other conditions, such as obesity and type 2 diabetes, present in most patients suffering from NASH, are all important risk factors. The scientific community recognizes that NASH would be linked, both in developed countries and those in the process of development, to the Western diet and increased consumption of refined products containing polyunsaturated fatty acids and fructose. The main symptoms of NASH include liver steatosis, inflammation and ballooning of liver cells, fibrosis and metabolic disorders.

Graph 12 - Evolution of NAFLD and NASH and main symptoms



### Current Therapies and their Limitations

The diagnosis of NASH is complex and it is often made by default. Most patients are diagnosed based on blood tests revealing abnormal liver function tests, or liver steatosis in imaging exams.

There is no approved treatment for NASH. The standard treatment consists of lifestyle changes intended to encourage physical exercise and diet modification to reduce weight, but no efficacy to prevent disease course has been demonstrated yet.

The most commonly prescribed therapeutic solutions, such as the administration of antioxidants, antidiabetic treatments reducing insulin resistance in the body and liver gluconeogenesis, antihyperlipidemic agents, pentoxifylline (vasoactive agents) or ursodiol, aim to improve the most common comorbidities, such as obesity and T2D, and to reduce the risk of complications such as cardiovascular disease or certain forms of cancer such as hepatocellular carcinoma.

While the precise causes of the disease are still poorly understood, the various components of the pathogenesis of NASH all represent topics for research and processes that can be exploited for the development of new therapeutic targets.

To the best of the Company's knowledge, as of the date of this document de référence, in addition to the many preclinical and clinical programs in development, there are five therapeutic molecules in advanced phase III clinical development likely to obtain a marketing authorization in the next few years, as shown in the table below:

*Graph 13 - Most advanced drug-candidates under clinical development for the treatment of NASH*

		Medicinal product	Mechanism of action	Company	Development stage
Metabolism	Bile acid modulator	Ocaliva <sup>1</sup>	FXR Agonist	Intercept	Phase III
	PPARs	Elafibranor	Agonist PPAR( $\alpha$ , $\beta$ )	Genfit	Phase III
		K-877	PPAR Modulator $\alpha$	Kowa	Phase III
Inflammation		Cenicriviroc	CCR5/CCR2 Agonist	Allergan/Tobira	Phase III
Fibrosis		Selonsertib <sup>2</sup>	ASK 1 Inhibitor	Gilead	Phase III

<sup>1</sup> On February 19, 2019, Intercept Pharmaceuticals announced that the primary endpoint of the phase III "REGENERATE" study evaluating Ocaliva for the treatment of liver steatosis in NASH patients has been achieved.

<sup>2</sup> On February 11, 2019, Gilead announced that the primary endpoint of the phase III "Steallar-4" study evaluating Selonsertib in 877 patients was not achieved.

### ***The Company's Market Opportunity***

According to Decision Resources, approximately 5% and 4% of the total population in the United States and Europe (France, Germany, Italy, Spain and the United Kingdom), respectively, suffered from NASH in 2018. This is almost 40 million people suffering from NASH in the United States, France, Germany, Italy, Spain, the United Kingdom and Japan. In developing countries, China and India for example, NASH has become a liver disease with a high prevalence. It is recognized<sup>4</sup> that in approximately 20% of patients with NASH, the disease worsens and progresses to the level of liver cirrhosis in the ten years following diagnosis. In the United States<sup>5</sup>, NASH is considered one of the main causes of cirrhosis

<sup>4</sup> Source: The Natural Course of Non-Alcoholic Fatty Liver Disease, Int J Mol Sci. 2016 May; 17(5): 774., Luis Calzadilla Bertot and Leon Anton Adams.

<sup>5</sup> Source: Global Epidemiology of Nonalcoholic Fatty Liver Disease—Meta-Analytic Assessment of Prevalence, Incidence, and Outcomes, HEPATOLOGY, VOL. 64, NO. 1, 2016, Zobair M. Younossi, Aaron B. Koenig, Dinan Abdelatif, Yousef Fazel, Linda Henry, and Mark Wymer

in adults. Cases of liver cirrhosis related to NASH are the second leading cause of liver transplant in the United States, and should in the next few years become the leading cause of transplantation, ahead of hepatitis C and alcoholic cirrhosis.

PXL770 and PXL065 can be distinguished from other compounds under development for liver diseases by their mechanism of action.

### ***Description and therapeutic benefits expected from PXL770***

PXL770 is a first-in-class drug candidate, a direct activator of adenosine monophosphate-activated protein kinase (AMPK). AMPK is a key regulator of cellular energy, which activates the pathways that allow energy to be generated, and inhibits pathways which consume energy, at the level of the cell. AMPK thus allows regulation of lipid metabolism, homeostasis of glucose and inflammation. Thanks to this central metabolic role, the activation of AMPK could have an effect on many chronic metabolic diseases<sup>6</sup>, including liver diseases such as nonalcoholic steatohepatitis (NASH), as well as type 2 diabetes and the complications related to diabetes, such as diabetic kidney disease. Activation of the AMPK enzyme is indeed interesting because it could have benefits on the three main pathophysiologic processes occurring in the liver and leading to NASH: steatosis, inflammation and fibrosis.

Activation of AMPK plays a key role in the regulation of each component of the disease:

- Steatosis: AMPK regulates energy homeostasis and adjusts the available energy at the cellular level by promoting processes that generate energy (such as oxidation of fatty acids) and by stopping processes that consume energy (such as lipid production)
- Inflammation: AMPK changes the polarization of macrophages and decreases the production of pro-inflammatory cytokines
- Ballooning: AMPK improves mitochondrial function and integrity, thus restoring liver cell function and survival
- Fibrosis: AMPK reduces (i) activation of stellate cells responsible for the secretion of collagen fibers that form scar tissue and lead to fibrosis and (ii) secretion of the extracellular matrix in the liver.

By directly targeting the primary regulator of cellular energy, PXL770 is ideally positioned for the treatment of NASH. It does the following in particular:

- Improves sensitivity to insulin
- Inhibits the two main sources of steatosis
- Reduces inflammation in the liver and fat tissue
- Reduces profibrogenic pathways leading to fibrosis
- Reduces cardiovascular risks

The Company believes that PXL770 has the potential to be prescribed as monotherapy and in combination with other therapies under development in NASH that target other components of the disease, such as MPC inhibitors, FXR agonists, etc.

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<sup>6</sup> Source: Smith B. K et al., (2016) Am J Physiol Endocrinol Metab 311, E730 – E740 Day E.A et al., (2017) Trends Endocrinol Metab. 28, 545-560

### ***Clinical development***

In July 2018, the Company announced positive results of its two-part phase 1b study of PXL770, consisting of a study with multiple ascending doses and a drug interaction study.

The multiple ascending doses study was conducted in 48 subjects to evaluate the safety, tolerance and pharmacokinetics (PK) of PXL770 administered once or twice daily for 10 days, with six dose groups ranging from 60 mg to 500 mg. No serious adverse events and no adverse events leading to discontinuation of the study in subjects were observed in this study. The Company found that PXL770 was well tolerated up to the highest dose of 500 mg, without meeting the criteria for stopping the dose increase. In this study, an electrocardiogram (ECG) was performed at each dose, and PXL770 was not associated with any prolongation of the QT interval (cardiac safety measurement) or any changes in other ECG parameters. The PK (C<sub>max</sub> and SSC) of PXL770 were linear with a saturation tendency at the highest dose tested.

In addition to the study with multiple ascending doses, a drug interaction study was also conducted with rosuvastatin, a statin that is also a substrate for OATP (organic anion transporting polypeptides) transporters and that can cause pharmacokinetic interactions when co-administered with other drugs. In this study, 12 subjects received 250 mg of PXL770 and a standard dose of rosuvastatin once daily. The results demonstrated that there were no pharmacokinetic interactions between PXL770 and OATP transporter substrates.

Based on the positive results of the phase 1b study and the favorable safety and tolerance profile demonstrated in the phase 1a increasing single-dose study, the Company is now preparing for the launch of the phase IIa proof-of-concept program.

This program will consist of a randomized, double-blind, placebo-controlled, parallel-group study to evaluate the efficacy and safety of PXL770 versus placebo in approximately 100 NASH patients with or without type 2 diabetes. The primary endpoint of the study will be the change in lipid levels in the liver as a percentage relative to baseline as measured by proton density fat fraction (PDFF) MRI after 12 weeks of treatment. The secondary endpoints will explore the role of PXL770 in lipid metabolism and glycemic control.

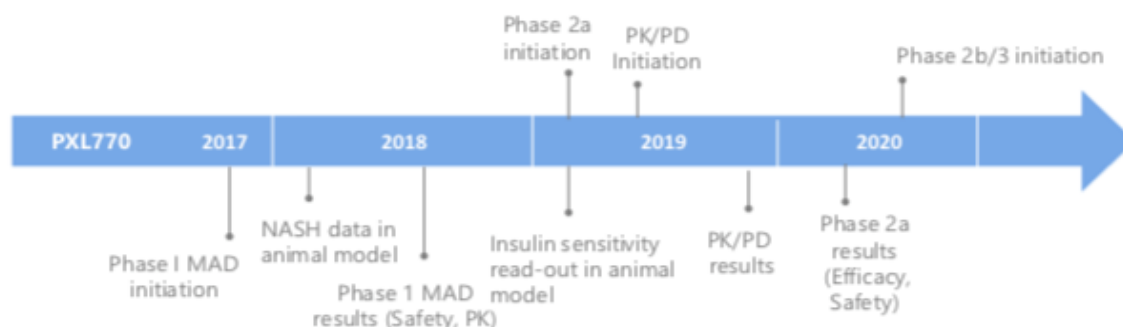
This phase IIa program will also have a mechanistic component that will evaluate the effect of PXL770 on inhibition of lipolysis (release of free fatty acids from triglycerides stored in fat tissue) and de novo lipogenesis in the liver (synthesis of triglycerides from glucose precursors).

The Company anticipates starting this phase IIa proof-of-concept study in the first half of 2019.

### ***Clinical development plan***

#### ***Graph 14 - Clinical development plan of PXL770***





## Preclinical developments

### *Preclinical studies of proof-of-concept in the mouse model “DIO-NASH”*

In February 2018, the Company announced the presentation of the results of this study<sup>7</sup>, in which PXL770 appears as a new therapeutic approach in the treatment and improvement of the main symptoms of nonalcoholic fatty liver disease (NAFLD).

In this study, the Company's research teams have evaluated the effect of PXL770 in a NASH mouse model linked to food-related obesity (diet rich in fat, fructose and cholesterol for 41 weeks), and confirmed by a biopsy at the start and at the end of the treatment. The mice were divided into three groups: a control group of mice and two groups of mice treated with PXL770 at a dose of 35 mg/kg or 75 mg/kg orally, twice a day for 8 weeks (n=12).

This NASH mouse model linked to food-related obesity reproduced the characteristics of NASH, with steatohepatitis (NAS=7), hepatic fibrosis (score=2), elevation of hepatic triglycerides (x26), and increase in plasma levels of cholesterol (x3.5) and ALT (x8) compared to mice receiving a normal diet. As expected, PXL770 increased the activity of AMPK in the liver (p-AMPK/AMPK, +128%,  $P<0.05$  and +143%,  $P<0.001$  respectively to 35 mg/kg and 75 mg/kg). Compared to the control group, PXL770 was associated with a slight reduction in body weight at a dose of 75 mg/kg (-5%,  $P<0.05$ ), as well as a reduction of the weight of the liver (-23%,  $P<0.01$ ; -33%,  $P<0.001$ ) and the weight of lipid deposits in the epididymis (-25%,  $P<0.01$ ; -37%,  $P<0.001$ ) at 35 mg/kg and 75 mg/kg, respectively. PXL770 has also reduced the plasma levels of free fatty acids (-37% and -38%,  $P<0.01$ ), cholesterol (-33% and -34%,  $P<0.01$ ) and ALT (-68% and -79%,  $P<0.01$ ) at 35 mg/kg and 75 mg/kg, respectively.

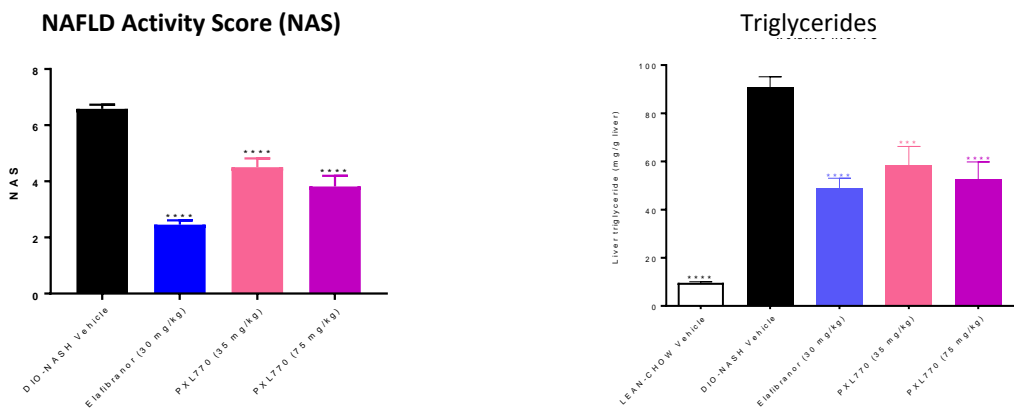
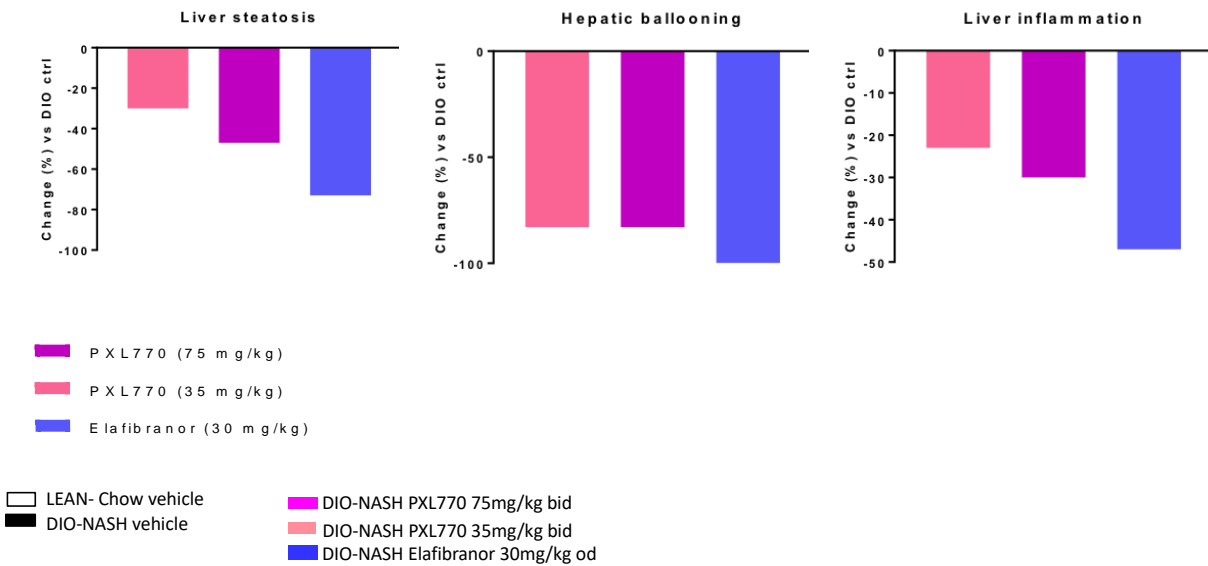
The two doses of PXL770 have significantly reduced the NAS activity score of nonalcoholic fatty liver disease (NAFLD), which measures the development of the disease according to histologic criteria (-32% and -44%, respectively at 35 mg/kg and 75 mg/kg), thanks to a reduction of steatosis, liver inflammation and hepatocyte ballooning. The benefit on liver steatosis has been confirmed by the reduction of liver triglycerides (-36%,  $P<0.001$  and -42%,  $P<0.001$ , at 35 mg/kg and 75 mg/kg, respectively). PXL770 has greatly reduced the expression of a panel of genes involved in fibrosis, such as the gene coding for the collagen type I (-65% and -68%,  $P<0.01$ ) and the gene coding for the collagen type III (-60% and -63%,  $P<0.01$ ), at 35 mg/kg and 75 mg/kg, respectively.

In conclusion, these results demonstrate the beneficial effect of the activation of AMPK in this NASH

<sup>7</sup> PXL770, a new direct AMP Kinase activator, demonstrates promising effects for treatment of non-alcoholic steatohepatitis; Pascale Gluais-Dagorn, Pascale Fouqueray, Sebastien Bolze, Sophie Hallakou-Bozec

model, as well as the potential of PXL770 as a new promising treatment option for NAFLD, and NASH in particular.

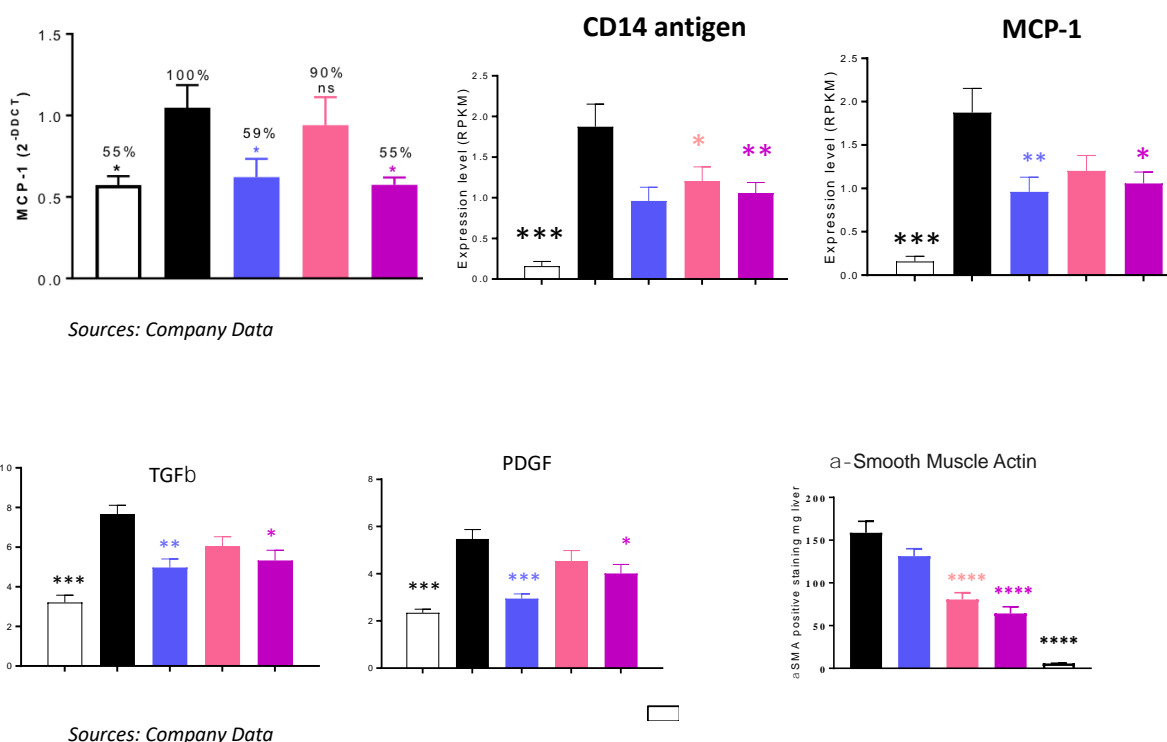
Graph 15 - PXL770 significantly improves liver steatosis and the NAS score



Sources: Company Data

Gene expression of tissues

Gene expression in liver tissue

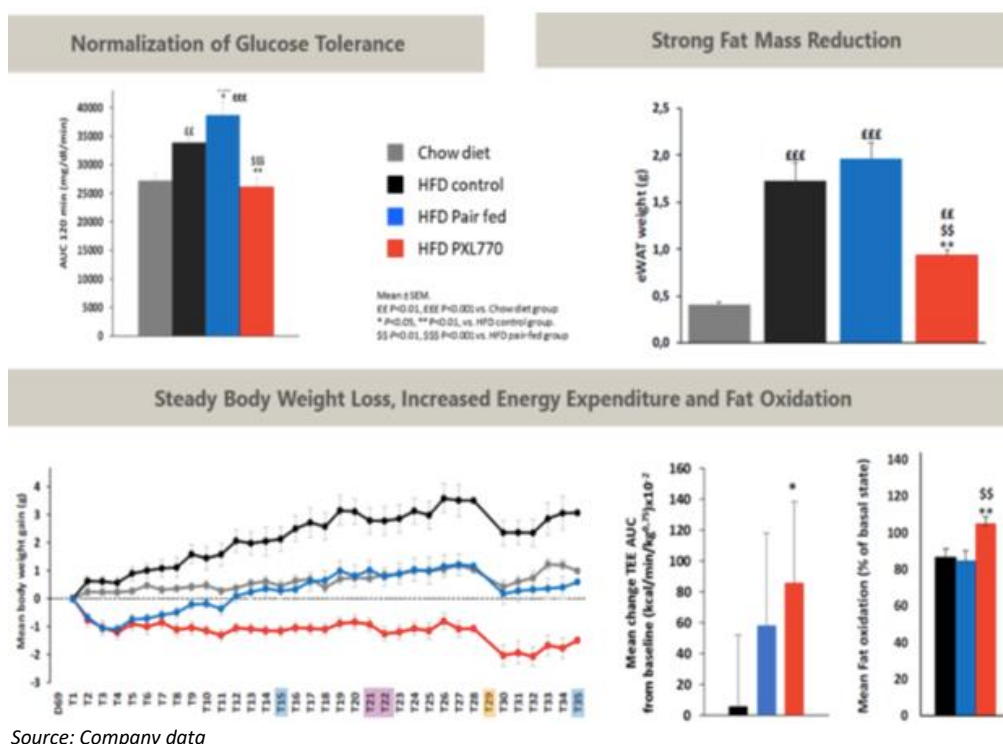


The effects of PXL770 were also studied in a HFD-induced glucose intolerance and obesity model. In this study, which was presented orally on September 14, 2018, 5-week-old mice on a hyperlipidemic diet or a normal diet were treated with 75 mg/kg of PXL770 versus control. Among the mice subjected to the hyperlipidemic diet, those treated with PXL770 gained less weight than the control group despite identical caloric intake. In the PXL770-treated group, the Company also noticed an increase in total energy expenditure and a significant increase in fat oxidation, compared to the control mice subjected to the same hyperlipidemic diet. Finally, over the 4- to 5-week treatment period, PXL770 significantly improved fasting glucose and glucose tolerance, with a 32% decrease ( $P<0.0001$ ), and significantly reduced fat mass by 53% ( $P<0.0001$ ) compared to the control mice, thus confirming the results observed in previous studies.

Finally, the inhibition induced by PXL770 on liver lipogenesis was evaluated on primary mouse and human hepatocytes, as well as *in vivo* in nine-week-old mice. PXL770 resulted in a very significant reduction in liver lipogenesis, in a dose-dependent manner, in all models tested. These results are consistent with previous studies that revealed a decrease in fatty acid synthesis following PXL770 treatment, confirming the key role of AMPK in this metabolic pathway.

Overall, these studies support the potential of PXL770 for the treatment of liver metabolic diseases, as well as other metabolic disorders such as type 2 diabetes and lipid disorders.

Graph 16 - PXL770 improves key cardiovascular risk factors associated with NASH



## Manufacturing and Supply

The active substance PXL770 is manufactured according to a synthetic pathway in several stages. Poxel initially developed the synthesis process for the manufacture of PXL770 end product, on the basis of assays at 30 mg, 125 mg and 250 mg to conduct clinical studies, on the pilot scale and in accordance with the standards imposed by Good Manufacturing Practices. This process has been optimized to reduce the number of synthesis steps and increase batch size. A group of specialized subcontractors manages this molecule synthesis and gel capsule manufacturing process, as well as the analytical methods of controls and batch release. These subcontractors can manufacture batches of several dozen kilograms of active substance and batches of 415 kg of end product to deliver at least 1,100,000 capsules depending on the dosage.

PXL770 is formulated in the form of a capsule, with immediate release. The Company has developed three different dose strengths: 30 mg, 125 mg and 250 mg. PXL770 is a stable active substance and, if stored below 25° C, has a shelf life of up to 36 months. PXL770's long shelf life has been observed during long-term stability studies in accordance with ICH recommendations.

The manufacturing process for immediate-release gel capsules can enable manufacturing of batches of sufficient size to at least perform phase I and phase II studies.

## Description and therapeutic benefits expected from PXL065

Pioglitazone is a mixture, in equal proportions, of two mirror molecules (stereoisomers) that interconvert *in vivo*. By substituting deuterium, DeuteRx successfully stabilized each stereoisomer and

defined their diametrically opposite pharmacologic properties. *In vitro* studies have revealed that PXL065 is an inhibitor that targets the MPC. Preclinical models have demonstrated the anti-inflammatory action of PXL065 and its efficacy in NASH with little or no weight gain or fluid retention, which are adverse effects associated with the S stereoisomer. The preclinical results and phase I study suggest that PXL065 has a superior therapeutic profile compared with pioglitazone in the treatment of NASH. The Company indeed found favorable safety and good tolerance of PXL065 after the first part of the phase Ia study conducted by DeuteRx, without any notable adverse events.

### ***Clinical development***

The first part of the phase Ia study conducted by DeuteRx is an open-label study evaluating the safety, tolerance and pharmacokinetics (PK) of a single dose of PXL065 compared to Actos® in healthy subjects. In this trial, twelve healthy volunteers received a single oral dose of either 45 mg of Actos® or 22.5 mg of PXL065. Following treatment, the subjects were monitored in a hospital setting for 36 hours after taking the drug, and were then seen externally on Days 4 and 7 for follow-up assessments. Based on these results, a PK model was generated to predict the dose of PXL065 that will produce the same exposure to R-pioglitazone as the 45 mg dose of Actos®, as well as the number of days of use of the drug required to achieve this equilibrium. In addition, exposure to PPAR $\gamma$  agonist metabolites was compared with equivalent doses of PXL065 and Actos.

*Graph 17 - Safety, Tolerance and Pharmacokinetics*



Source: Company data

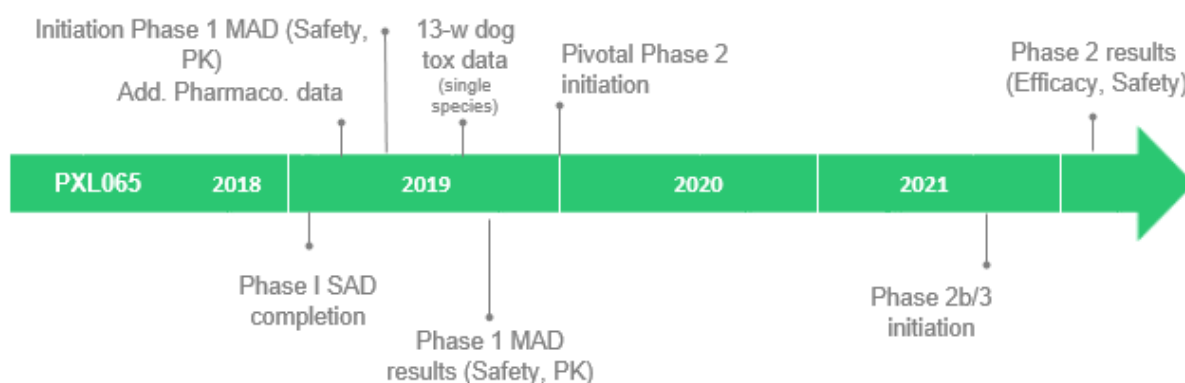
The phase I study found that PXL065 has a favorable safety and tolerance profile. No adverse effects were reported. After a single dose of PXL065, the relative exposure to R-pioglitazone was increased by more than 3-fold compared to Actos®. Total exposure to the PPAR $\gamma$ , M-III and M-IV agonist metabolites decreased by 50% compared with Actos®.

Based on the modeling, a 15 mg dose of PXL065 should provide the same exposure to R-pioglitazone as a 45 mg dose of Actos®. The PK results and simulations in humans, associated with preclinical animal studies, suggest that PXL065 could potentially have the same efficacy on NASH as pioglitazone, but with fewer PPAR $\gamma$  receptor-related adverse effects, such as weight gain and fluid retention.

The Company initiated the second part of the phase Ia study to test different doses of PXL065 and to evaluate the safety and pharmacokinetic profile of the product. This phase Ia study will be followed by a phase Ib study aimed at evaluating the safety of use and the pharmacokinetic profile of the product after repeated administration of PXL065. The Company expects to publish the results of the second part of the phase Ia study and the phase Ib study in the first half of 2019, and to launch the

phase II program by the end of 2019. This phase II program will evaluate the efficacy and safety of PXL065 in patients with NASH, particularly with the evaluation of adverse effects such as weight gain. The primary endpoint will include the effect of the product on ballooning, inflammation and fibrosis. On the regulatory side, PXL065 will benefit from a 505(b)(2) registration process with the FDA. This system could enable the Company to benefit from the large volume of data available on Actos® and thus enable the Company to reduce the work remaining before registration.

*Graph 18 - Clinical development plan of PXL065*



*Source: Company data*

## Preclinical developments

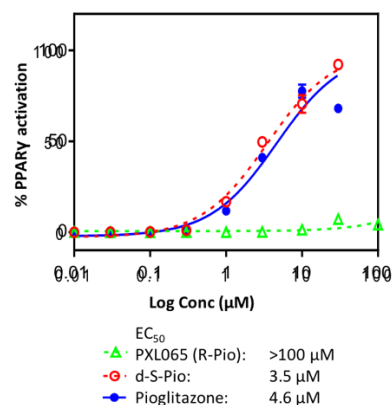
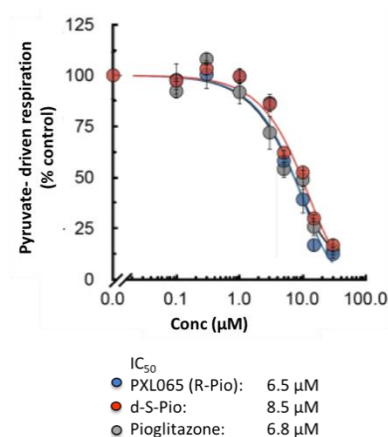
The preclinical data have highlighted key aspects related to the pharmacokinetic (PK) and pharmacodynamic (PD) roles of stereoisomers belonging to the class of thiazolidinediones (TZD), as well as their potential relevance for the treatment of NASH. Representatives of TZDs include rosiglitazone, pioglitazone and lomeglitazone, all being mixtures of R and S stereoisomers exhibiting interconversion between each stereoisomer. Studies in animals and/or humans have revealed that these compounds have variable efficacy in the treatment of NASH.

The main observations presented were 1) the comparison between the pronounced stereoselectivity of the PK of pioglitazone as a function of the species, and that of other TZDs, 2) the comparison of unexpected differences in activity on the peroxisome proliferator-activated receptor (PPAR) among the eight stereoisomers present in pioglitazone and its two active metabolites, and 3) the stabilization of the stereoisomers of pioglitazone by deuterium substitution to characterize and identify R-pioglitazone as the stereoisomer of choice for NASH treatment.

The data demonstrated that each stereoisomer of pioglitazone and its active metabolites have different PPAR $\gamma$  activity. Other data show that PXL065 is a mitochondrial pyruvate carrier (MPC) inhibitor, with no PPAR $\gamma$  activity in a cofactor recruitment assay. Studies of PXL065 in murine models have demonstrated the liver benefits of pioglitazone in patients with NASH. In preclinical models, PXL065 was associated with reduced or no weight gain and fluid retention, these adverse effects being mainly associated with the S stereoisomer of pioglitazone that acts on the PPAR  $\gamma$ receptor.

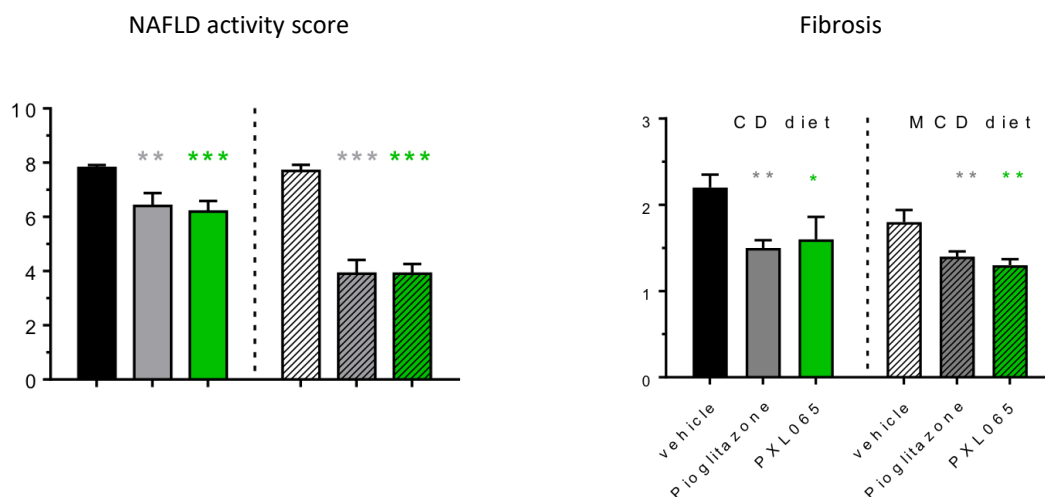
Inhibition of the MPC in HepG2 cells

PPAR $\gamma$ agonist



Source: Company data

In addition, the Company also observed that PXL065 was as effective as pioglitazone in a NASH mouse model. In particular, the Company has observed that PXL065 was as effective as pioglitazone on the NAS as well as on fibrosis.



Source: Company data

## PXL065 - Manufacturing and supply

The PXL065 active substance is manufactured from Pioglitazone. Poxel started development of the synthesis process for manufacture of the PXL065 end product, at doses of 7.5 mg to 30 mg to conduct clinical studies, on the pilot scale and in accordance with the standards imposed by Good Manufacturing Practices. A group of specialized subcontractors manages this molecule synthesis and gel capsule manufacturing process, as well as the analytical methods of controls and batch release.

PXL065 is formulated in the form of a capsule, with immediate release. The Company has developed three different dose strengths: 7.5 mg, 22.5 mg and 30 mg. The manufacturing process for immediate-release gel capsules can allow for the manufacturing of batches of sufficient size to perform phase I clinical studies, and is being scaled up for phase II clinical studies.

## 7. ORGANIZATIONAL STRUCTURE

### 7.1. Legal organization chart

As of the date of this document de référence, the Company holds 100% of its subsidiary created in 2018, Poxel Japan.

### 7.2. Group Companies

**POXEL S.A.:** Parent company of the Group, based in Lyon (Department 69).

**POXEL JAPAN KK:** incorporated in March 2018 and domiciled in Tokyo, a wholly owned subsidiary of Poxel, engaged in research and development activity.

**POXEL INC:** incorporated in January 2019 and domiciled in Burlington (Massachusetts), a wholly owned subsidiary of Poxel, engaged in research and development activity.

### 7.3. Group financial flows

As part of the launch of its subsidiary's business activity, the Group has implemented agreements related to the organization of financial flows and the movement of products within the Group, in line with the following structure:

- Charging back of intercompany services: an intra-group agreement was signed between the Company and Poxel Japan KK, concerning reciprocal service provision between the Company (research and management services) and its subsidiary (research services and administrative services).
- Financial flows: a cash facility agreement was signed between the Company and Poxel Japan KK, to determine the conditions governing cash advances made by the Company to its subsidiary.

As of December 31, 2018:

- Amounts paid by Poxel to its subsidiary totaled €318,000 for chargebacks on services and €1,000 for interest on current account advances;
- The amounts invoiced by Poxel Japan KK to its parent company totaled €534,000 for chargebacks on services.



## 8. REAL PROPERTY AND EQUIPMENT

### 8.1.1. Rented real property

The Company's registered office is located in premises occupied under a commercial lease, as described below:

Address	259/261 Avenue Jean Jaurès, Immeuble le Sunway, 69007 Lyon, France
Surface area	400 square meters of office space, one parking space. Starting in 2018, additional lease for 455 square meters in offices and five parking spaces.
Duration	July 1, 2015 - June 30, 2024 (with authorization for triennial leave) / April 1, 2018 - March 31, 2027 (with authorization for triennial leave).
Annual rent excluding VAT	€92,000 for the offices, and €1,500 for the parking space / €98,000 for the additional lease.

The company also occupies offices under a 12-month sub-lease agreement, automatically renewable every year:

Address	47 rue de Liège, 75008 Paris
Surface area	17 square meters of office space
Term	January 1, 2018 – December 31, 2018
Annual rent excluding VAT	€14,000

In Japan, the Company occupies offices under a two-year contract:

Address	1F & 3F Otemachi building office number 303, Tokyo
Surface area	17 square meters of office space
Term	January 15, 2018 – January 15, 2020
Annual rent excluding VAT	€46,000

### 8.1.2. Other property, plant and equipment

The main property, plant and equipment owned by the Company are set out in Note 4 to the financial statements prepared in accordance with IFRS, appearing in Section 20.1 "Financial statements prepared in accordance with IFRS for the year ended December 31, 2018" of this *document de référence*.

## 8.2. Environmental issues

### 8.2.1. Social and environmental information

The nature of the Company's business does not result in any significant risk to the environment.

### 8.2.2. Information relating to societal sustainable development commitments

Refer to "Non-financial information" set out in Section 26.3 of this *document de référence*.

## 9. OPERATING AND FINANCIAL REVIEW

The reader is invited to read the following information relative to the financial position and the results of the Group in conjunction with the *document de référence* as a whole and, in particular, the Group's consolidated financial statements prepared in accordance with IFRS for the year ended December 31, 2018, presented in Section 20.1 of this *document de référence*.

The comments on the financial statements presented in chapters 9 and 10 of the *document de référence* are established solely on the basis of the IFRS consolidated financial statements presented in Section 20.1 "Financial statements established using IFRS standards for the financial year ended" of this *document de référence*.

### 9.1. General presentation

#### 9.1.1. General presentation

The Company was incorporated on March 11, 2009 and has as its object the research and development of new therapeutic strategies and new pharmaceutical specialties. Its research focuses on the development of innovative molecules for the treatment of metabolic diseases, including type 2 diabetes and nonalcoholic steatohepatitis (NASH).

The activities pursued by the Company over the course of the various financial years presented can be grouped into a single segment: development of innovative molecules for the treatment of metabolic diseases, in particular type 2 diabetes and nonalcoholic steatohepatitis (NASH).

In 2017, the Company signed a strategic partnership contract with Sumitomo Dainippon Pharma for the development and marketing of Imeglimin, a drug-candidate for the treatment of type 2 diabetes for Japan, China and eleven other Asian countries. In 2018, we also signed a strategic development and license agreement with Roivant Sciences for the development and marketing of Imeglimin in the United States, Europe and other countries not covered by our existing partnership with Sumitomo Dainippon Pharma.

The Company relies on low fixed costs and widely uses sub-contractors, in particular for conducting pre-clinical and clinical trials, while protecting its intellectual property rights.

Since its creation, the Company has been funded by:

- the contracts of strategic partnerships signed in 2017 with Sumitomo Dainippon Pharma and 2018 with Roivant Sciences (see Sections 22.2 "Contract with Sumitomo Dainippon Pharma" and 22.3 "Contract with Roivant Sciences GmbH" of this *document de référence*);
- capital increases, in particular the initial public offering (IPO) of the Company at the beginning of 2015, as well as the private placements made in July 2015 with investors in the United States and in July 2016 with investors in the United States and Europe;
- the subsidy provided by Merck Serono at the time of creation of the Company (see Section 22.1 "Contract with Merck Serono" of this *document de référence*);
- refunds received pursuant to the research tax credit;
- innovation aid and grants of Bpifrance Financement (see Note 11.2 to the IFRS financial statements set out in section 20.1 "Financial statements established using IFRS standards for the financial year ended" of this *document de référence*);

- a non-convertible debenture loan subscribed by Kreos (see Section 10.1.2.1 “Issuance of non-convertible bonds for the benefit of Kreos Capital IV (UK) Limited” of this *document de référence*), and
- a grant from the European Regional Development Fund (ERDF) for the Greater Lyon project (see Section 10.1.3 “Financing by repayable advances and subsidies” of this *document de référence*).

The research and development costs and times for the Company's products and the pursuit of its clinical development program are in part beyond the Company's control and will continue to create significant financing needs in the future. The Company will continue to incur operating losses.

No significant revenue is expected from the sale of the Company's drug-candidates until the development programs that are currently underway achieve success and the Company obtains regulatory approval to put them on the market, which is expected to take several years and is uncertain. In the light of its programs of developments such as defined in the date of drafting the present *document de référence*, the Company considers that it will cover its financing needs for at least 24 months following the filing date of the present *document de référence*. However, the Company anticipates that it may seek additional funding for the development of its business, which could be obtained through a combination of capital transactions, debt, partnerships or licenses, the absence of which could affect all or part of its activities (see Chapter 4 “Risk factors” of this *document de référence* for further information).

#### **9.1.2. Sales revenue and operating income**

The Company is not yet in the marketing phase of its products. Therefore, it does not have recurrent sales revenue.

Nevertheless, in 2017 and 2018, the Group signed strategic partnerships that led to a recognition of revenue:

- in 2017, we signed a partnership agreement with Sumitomo Dainippon Pharma for the development and marketing of Imeglimin, a drug-candidate for the treatment of type 2 diabetes for Japan, China and eleven other Asian countries.
- in 2018, we also signed a strategic development and license agreement with Roivant Sciences for Imeglimin in the United States, Europe and other countries not covered by our existing partnership with Sumitomo Dainippon Pharma.

#### *Contract with Sumitomo Dainippon Pharma*

The contract stipulates:

- an initial payment of €36,031 K to the Company, which pays the license and the exclusive rights granted to Sumitomo Dainippon Pharma as well as the co-development;
- the reimbursement by Sumitomo Dainippon Pharma of external costs of development incurred by the Company as part of Phase III and in the conditions laid down in the contract;
- payments linked to the achievement of the development and sales objectives can reach 29.25 billion yen (approximately €219 million), as well as two-digit royalties on the net sales.

The Company analyses the license granted and the co-development as two separate performance obligations:

- The obligation of performance is satisfied immediately for the license, as this is a case of a static license.
- The obligation of performance is satisfied continuously for the co-development. The nature of the services related to the co-development corresponds to the research work. As of December 31, 2018 the remaining performance obligations amount to €36,190 K.

The contract price is composed of fixed payments and of variable considerations considered as highly likely, that is to say the initial payment and reimbursement of direct costs. Therefore, the corresponding income incorporates the initial payment and refunds. The milestone payments will be integrated into the price of the contract when they become highly probable. The royalties collected in the framework of the operation of the license by Sumitomo Dainippon Pharma will be recognized to the extent that they become payable, that is to say when Sumitomo Dainippon Pharma carries out sales.

The price of the transaction has been allocated to the two obligations of performance following the residual method, because the price of the license is uncertain. The price of the specific obligation of co-development has been established on the basis of the estimated costs for the satisfaction of the obligation of performance plus a margin in line with the practices of the market. This has led to allocation of the full price of the transaction to the obligation of performance of co-development. This allocation reflects the savings of the contract since the highly probable payments aim to ensure a reasonable margin on the research and development work, the license being essentially paid via the future amounts, not highly probable at year-end.

The income allocated to the service of research and development is recognized according to the progress on the basis of the estimate of the direct costs, internal and external, for any phase of co-development. This is a method that best represents the progress of the work. The Company expects to achieve a positive margin on this contract.

As such, the Company recognized €66,412 K of revenue in 2018, compared with €5,290 K in 2017.

#### *Contract with Roivant Science*

This contract is analyzed as the assignment to Roivant of an exclusive license for Imeglimin. No other performance obligation has been identified.

The contract price on the transaction date was valued at \$10 million. This price is made up of a non-refundable fixed payment of \$35 million, less \$25 million granted by the Company in the form of a firm commitment to take part in financing Roivant's development program.

This amount was recognized in full as revenue on the date the license was granted for a value of \$10 million net.

The part of the initial payment having for counterpart the undertaking to participate to the financing of the research program of Roivant have been treated as a current liability. The remaining amount to be paid at the closure being equal to 13 646k€ is entirely classified as a current liability (see note 14.3). The license agreement also provides for the payment by Roivant of development, regulatory and marketing milestone payments as well as fees based on Imeglimin sales in the areas covered by the license. These payments fall within the category of variable consideration to which the Company is entitled for transferring the license to Roivant.

- Since milestone payments based on development and regulatory milestones were not considered as highly probable as of December 31, 2018, no revenue was recognized in this respect in 2018. These payments will be considered as highly probable when the development of Imeglimin is advanced sufficiently to achieve the technical and regulatory milestones defined.
- Milestone payments based a level of sales and fees from Imeglimin sales benefit from the exception provided by IFRS 15 relating to intellectual property license rights. Payments and fees will be recognized as revenue as and when they become due, depending on the sales recorded by Roivant.

The Company has benefited from the CIR (research tax credit) since its incorporation. The CIR is a tax credit awarded to companies that significantly invest in research and development (the eligible expenses include, in particular, wages and salaries, consumables, expenses of sub-contracting with certified bodies and intellectual property expenses). Companies must substantiate, upon request by the French tax authorities, the amount of the CIR receivable and the eligibility of the activities taken into account to benefit from this measure.

The CIR is recognized as income for the financial year concerned and recorded as a reduction of the research and development expenses in the income statement, in accordance with IAS 20.

### **9.1.3. Research and development – Subcontracting**

Research and development are at the heart of the Company's business. Research and development costs generally increase as clinical development progresses, because of the increase in size and the length of the last stages of the clinical trials and the potential demands of the regulatory bodies (FDA, EMA). The Company therefore expects that clinical studies will be continued in the future with significant amounts. The Company cannot determine with certainty the length and the costs of these future clinical trials and the extent to which the Company may generate income based on these projects (see Section 4 "Risk factors" of this *document de référence* for further information).

Because of the risks and uncertainties linked to regulatory approvals and the research and development process, the six capitalization criteria established by IAS 38 to capitalize development expenses are not deemed to be satisfied until marketing authorization (MAA) is obtained. Therefore, the in-house development expenses incurred before obtaining marketing authorization, consisting mostly of the costs of clinical studies (mainly subcontracted) are expensed as incurred, under "R&D costs".

The contract signed in 2009 with Merck Serono provides, in the case of signature of a partnership agreement relating to drug-candidates covered by patents assigned or licensed in license, that Poxel is liable to pay a percentage of the income of the partnership for such products, whose rate is a function of the product and its stage of development at the time of the partnership. Under this contract, the company paid a percentage of the initial payment described in Chapter 22.1 to Merck Serono in 2017 and created a provision thereof in 2018. This payment was recognized as research and development costs in 2017 and 2018.

The Company's internal research and development structure consists of 24 highly qualified people. A significant part of studies is subcontracted to external laboratories (CRO).

The main research and development expenses are:

- the costs of subcontracting of preclinical and clinical studies on Imeglimin and PXL770;

- personnel expenses for the 24 members of the R&D team. These expenses include salaries and social charges together with any share-based payments for the R&D team employees;
- the purchase of biological raw materials, operating costs for the R&D team (premises, specific equipment) and conferences and travel expenses; and
- intellectual property fees, including patent protection costs.

In 2018, the Company dedicated €58.1 million to developing its two main projects, Imeglimin and PXL770, compared with €24.1 million in 2017 (see Chapter 6 “Business Overview” of this *document de référence* for further information).

The Company also devotes a sizable part of its resources to protecting its intellectual property: by filing patents or applying for international patents (see Section 11 “Research and development, patents, licenses and other intellectual property rights” of this *document de référence*).

#### **9.1.4. General and administrative expenses**

The Company has set itself up to minimize general and administrative expenses, in order to focus its resources on research and development. The general and administrative expenses are primarily composed of:

- the salaries of the non-scientific team;
- external advisers’ fees;
- the Company’s operating expenses;
- travel expenses; and
- share-based payments.

The Company expects its general and administrative expenses to increase in respect of the support functions for the development of its research and development activities.

#### **9.1.5. Financial expenses and income**

Financial income is mostly composed of interest related to deposits of cash and cash equivalents in term deposit accounts and in money market funds, as well as foreign exchange gains linked to transactions denominated in US dollars and Japanese yen.

Financial expenses in 2017 and 2018 mainly consist of:

- interest calculated on repayable advances; and
- foreign exchange losses due to operations denominated in US dollars and in yen.

In 2017, they also included interest on the loan taken out with Kreos, which was paid back in 2017.

#### **9.1.6. Main factors affecting the business**

As the outcome of such research and the commercial development of the results of this research will only come about over time, the historical results of the Company primarily reflect the research and development expenses.

Considering the stage of development of the Company, the key factors that have an influence on its business, its financial position, the results of its operations, its development and its prospects are:

- the magnitude of the R&D programs and compliance with the timeline for progress;

- the Company's ability to fund these programs;
- signing of partnership agreements;
- obtaining subsidies and repayable advances; and
- the existence of tax incentive measures for companies that perform technical and scientific research activities (research tax credit).

## 9.2. Post year-end events

N/A

## 9.3. Comparison of the financial statements for the last two financial years

### 9.3.1. Creation of operating income and net income

Revenue for the financial years ended December 31, 2017 and December 31, 2018 breaks down as follows:

REVENUE (Amounts in K€)	12/31/2018 Audited	12/31/2017 Audited
Revenue	74 605	5 290
Sumitomo Contract	66 412	5 290
Roivant Contract	8 192	

The operational products reflect the license agreements and partnership concluded by the Company.

In 2018, revenue reflected the contract signed with Sumitomo Dainippon Pharma in October 2017 and the contract signed with Roivant Sciences GmbH in February 2018.

The revenue recognized under the Sumitomo Dainippon Pharma contract breaks down as follows:

- €22,125 K: the 2018 share (€1,730 K in 2017) of the initial payment made in November 2017 (€36,031 K spread over the duration of the contract on the basis of the progress of the costs incurred, the balance of €12,077 K is recognized under deferred income as of December 31, 2018);
- €44,196 K: chargeback to Sumitomo Danippon Pharma of Phase III development costs (€3,559 K in 2017), recognized as the advancement of the external costs incurred by the Company in 2018.

#### 9.3.1.1. Operating expenses by function

##### R&D costs

In 2018, the Company devoted most of its research and development efforts to the Imeglimin and PXL770 projects (see Section 6 "Business overview" of this *document de référence* for further information).

R&D costs increased by €34 million between 2017 and 2018. They can be analyzed as follows:

<b>RESEARCH AND DEVELOPMENT (Amounts in K€)</b>	<b>12/31/2018 Audited</b>	<b>12/31/2017 Audited</b>
Subcontracting, studies and research	52 195	18 951
Personnel expenses	3 617	3 273
Share-based payments	686	546
Travel, Missions and Receptions	589	459
Intellectual property fees	256	340
Compensation Interm. Fees	661	481
Other Charges	88	46
<b>Research and development costs</b>	<b>58 092</b>	<b>24 096</b>

The costs of subcontracting, studies and research increased by €33.2 million.

(1) The major part of the increase in subcontracting costs is related to the TIMES program for which expenses of €46 million were recorded in 2018. This amount also includes the fees to be paid to Merck Serono under the contract signed with Roivant Sciences GmbH, for which a provision was created according to the Company's best estimate on the balance sheet date.

(2) The change in personnel expenses is primarily linked to the reinforcement of the clinical research teams.

#### **General and administrative expenses**

General and administrative expenses rose by €1.4 million (+21%) between 2017 and 2018. They can be analyzed as follows:

<b>GENERAL AND ADMINISTRATIVE EXPENSES (Amounts in K€)</b>	<b>12/31/2018 Audited</b>	<b>12/31/2017 Audited</b>
Compensation Interm. Fees (1)	2 388	2 103
Personnel expenses (2)	1 845	1 579
Share-based payments	1 195	1 190
Travel, Missions and Receptions (3)	688	445
Other Charges	1 410	902
<b>General and Administrative expenses</b>	<b>7 527</b>	<b>6 219</b>

In 2018, the change in fees was primarily due to market studies conducted. Fees directly related to the acquisition of the portfolio of products under development from DeuteRx were recognized, depending on their destination, as assets or deducted from the issue premium for the share directly linked to the capital increase.

The change in personnel costs and travel expenses is related to the strengthening of the administrative team.

The increase in other expenses is primarily correlated to the change in personnel: leasing of premises and additional equipment, maintenance expenses and related insurance policies (up €0.3 million), acquisition of new software licenses (up €0.1 million), increase in the CFE business tax (up €0.1 million).



## Operating expenses by nature

Operating expenses by nature during the relevant years can be analyzed as follows:

<b>RESEARCH AND DEVELOPMENT</b> <b>(Amounts in K€)</b>	<b>12/31/2018</b> <b>Audited</b>	<b>12/31/2017</b> <b>Audited</b>
Subcontracting, studies and research	52 195	18 951
Personnel expenses	3 617	3 273
Share-based payments	686	546
Travel, Missions and Receptions	589	459
Intellectual property fees	256	340
Compensation Interm. Fees	661	481
Other Charges	88	46
<b>Research and development costs</b>	<b>58 092</b>	<b>24 096</b>

The subcontracting, studies and research includes the preclinical and clinical development costs delegated to third parties.

The fees related to intellectual property (€265 K in 2018 against €340 K in 2017) correspond to the costs of external consultants.

The fees related to the general and administrative expenses (€2,388 K in 2018 against €2,103 K in 2017) correspond to the costs incurred in connection with the statutory audit, accounting and legal services, as well as to the fees related to transactions on the company's capital and partnerships.

Staff costs include remuneration (other than payments in shares) of employees and consultants. As of December 31, 2018, the Group employed 33 persons.

The cost of travel and reception correspond to the costs incurred for the travel of staff participants in scientific, medical, financial conferences or those related to business development.

### 9.3.1.2. Financial income (expense)

<b>INCOME AND FINANCIAL EXPENSES</b> <b>(Amounts in K€)</b>	<b>12/31/2018</b> <b>Audited</b>	<b>12/31/2017</b> <b>Audited</b>
Kreos interest		-47
Other financial expenses	-28	-34
Financial income	368	64
Foreign exchange (losses) and gains	724	-379
<b>Total income and financial expenses</b>	<b>1 064</b>	<b>-396</b>

In 2018, financial income was mainly composed of:

- interests related to the accretion of repayable advances (€28 K in 2018 against €34 K in 2017);
- income from cash investments. The Company's cash investment policy favors the absence of risk on principal and, wherever possible, guaranteed minimum performance;
- foreign exchange gains, mainly related to changes in the dollar exchange rate in 2018.

In 2017, financial expenses included interest on the loan taken out with Kreos, which was paid back in full in 2017.

### 9.3.1.3. Corporate income tax

The Company recorded a corporate income tax expense of €77 K.

As of December 31, 2018, the Company had €105,991 K of tax loss carryforwards that may be carried forward indefinitely in France (against €107,552,000 as of December 31, 2017). French law provides that, for financial years ending on or after December 31, 2012, the allocation of these losses is subject to a maximum of €1 million, plus 50% of the portion of net earnings exceeding this amount. The unused balance of the loss can be carried forward to future financial years and may be carried forward under the same conditions without any limit in time.

The tax rate applicable to the Company for its profits excluding long-term capital gains, is the applicable rate in France, i.e., 33.33%. The tax rate voted for subsequent years is 31% in 2019, 28% in 2020, 26.5% in 2021 and 25% as from 2022.

The tax rate applicable to the Company for its long-term capital gains related to intellectual property is the applicable rate in France, i.e. 15% in 2017 and 2018. The tax rate voted for subsequent years is 15%.

Deferred tax assets are recorded as tax loss carry forwards when it is probable that the Company will have future taxable income against which the unused tax losses can be offset. In 2018, the Company charged €1,508 K of prior tax loss carryforwards against revenues generated by partnership contracts signed during the year, which constitute non-recurring revenues. The Company believes that to date, the likelihood of generating taxable profits does not allow it to recognize all or part of the balance of its loss carryforwards as assets.

### 9.3.1.4. Earnings per share

The basic loss per share is calculated by dividing the net loss attributable to shareholders of the Company by the weighted average number of outstanding shares for the year.

<b>BASE LOSS PER SHARE (Amounts in K€)</b>	<b>12/31/2018 Audited</b>	<b>12/31/2017 Audited</b>
Net income/(loss) for the year	13 525	-22 298
Weighted average number of shares outstanding	24 833 331	23 033 299
<b>Basic earnings per share (€/share)</b>	<b>0,54</b>	<b>(0,97)</b>
<b>Diluted earnings per share (€/share)</b>	<b>0,53</b>	<b>(0,97)</b>

## 9.3.2. Balance Sheet Analysis

### 9.3.2.1. Non-current assets

<b>NON-CURRENT ASSETS (Amounts in K€)</b>	<b>12/31/2018 Audited</b>	<b>12/31/2017 Audited</b>
Intangible assets	16 577	
Tangible fixed assets	296	143
Other non-current financial assets	372	356

<b>Total non-current assets</b>	<b>17 246</b>	<b>500</b>
---------------------------------	---------------	------------

In 2018, under the contract signed with DeuteRx, the Company acquired an innovative drug-candidate under clinical development for the treatment of NASH (DRX-065), as well as other programs for the treatment of metabolic diseases for a non-refundable sum of €15,780 K, of which €8,914 K paid in shares and \$8 million (€6,866 K) paid in cash, as well as additional variable payments. This acquisition is recognized as an intangible asset for an amount of €16,572 K, which includes €791 K of acquisition costs.

Tangible fixed assets primarily include office supplies and computer equipment. The Company has not made any significant investments in 2017.

Non-current financial assets are composed of:

- the cash portion of the liquidity agreement signed with Oddo Corporate Finance (€78 K in 2018 versus €130 K in 2017);
- sureties concerning operating lease contracts for premises and deposits relating to wage portage contracts (€294 K in 2018 against €234 K in 2017).

### 9.3.2.2. Current assets

<b>CURRENT ASSETS</b> <b>(Amounts in K€)</b>	<b>12/31/2018</b> <b>Audited</b>	<b>12/31/2017</b> <b>Audited</b>
Suppliers and related accounts	14 262	4 902
Other receivables	7 271	7 187
Cash and cash equivalents	66 737	54 163
<b>Total current assets</b>	<b>88 270</b>	<b>66 253</b>

Receivables (€14,262 K) correspond to €14,216 K in 2018 and €4,877 K in 2017 to the chargeback to Sumitomo Dainippon Pharma of research expenses incurred under the Imeglimin phase III TIMES program in Japan. The amount of these receivables is recognized as and when the program costs advance.

The other receivables include mainly:

- research tax credits recorded during the reference financial years (€3,539 K in 2018, €3,122 K in 2017) and which were refunded during the following financial year;
- deductible VAT or VAT credits;
- an advance paid in the framework of the phase III study of Imeglimin and accounted on December 31, 2018 for €1.2 million, charged back to Sumitomo Dainippon Pharma, and the consideration for which consisted in advances received for the same amount.
- prepaid expenses

The cash and cash equivalents consist of short-term bank deposits (€7.3 million of bank accounts and €59.4 million of term deposits) and monetary SICAVs.

### 9.3.2.3. Equity

<b>SHAREHOLDERS' EQUITY</b> <b>(Amounts in K€)</b>	<b>12/31/2018</b> <b>Audited</b>	<b>12/31/2017</b> <b>Audited</b>
Capital	517	463
Share issuance and contribution premiums	127 996	106 951
Conversion reserve	-5	
Reserves - group share	-86 251	-65 788
Net Income - group share	13 525	-22 298
<b>Shareholders' equity</b>	<b>55 782</b>	<b>19 327</b>

As of December 31, 2018 share capital amounted to €517,136.54, divided into 25,856,827 fully paid-up and fully subscribed ordinary shares.

The net changes in the Company's equity during the 2017 and 2018 financial years are mainly the result of a combination of:

- the Group's earnings; and
- positive changes related to the funds raised.

### 9.3.2.4. Non-current liabilities

<b>NON-CURRENT LIABILITIES</b> <b>(Amounts in K€)</b>	<b>12/31/2018</b> <b>Audited</b>	<b>12/31/2017</b> <b>Audited</b>
Commitments toward personnel	279	230
Non-current financial liabilities	359	555
<b>Non-current liabilities</b>	<b>638</b>	<b>785</b>

Non-current financial debts correspond to the non-current portion of the repayable advances granted by public bodies (see Note 13.2 to the IFRS financial statements set out in Section 20.1 "Financial statements established using IFRS standards for the financial year ended" of this *document de référence*).

Since 2011, the Company has benefited from two repayable advance programs, with a maximum amount of €250 K for the first and €950 K for the second; with drawdowns made between 2011 and 2016 (see Section 10.1.3 "Financing by repayable advances and subsidies" of this *document de référence*). The first of these advances was repaid in full in financial year 2018.

Employee benefit obligations correspond to the provision for retirement indemnities.

### 9.3.2.5. Current liabilities

<b>CURRENT LIABILITIES</b> <b>(Amounts in K€)</b>	<b>12/31/2018</b> <b>Audited</b>	<b>12/31/2017</b> <b>Audited</b>
Current financial liabilities	13 873	936
Trade payables and related accounts	20 742	9 008
Tax and social security liabilities	1 129	899
Other creditors and accrued liabilities	13 334	35 714
<b>Current liabilities</b>	<b>49 096</b>	<b>46 640</b>

The current financial liabilities are composed of:

- in 2018, the balance to be paid at the end of the obligation to participate in the financing of Roivant Sciences' development plan, amounting to 13,646k €. Indeed, under the Roivant Sciences' contract, the Company received an initial payment of \$35 million and has also committed to contribute \$25 million to the financing of the development of Imeglimine in the United States and Europe. The portion of the initial payment that is counterpart to the obligation to participate in the financing of Roivant's development plan has been treated as a debt;
- the current portion of the repayable advances granted by public bodies for an amount of €218 K in 2018 versus €181 K in 2017 (see Section 10.1.3 "Financing by repayable advances and subsidies" of this *document de référence*);
- bank credit facilities of €751 K in 2017;

The policy liability corresponds to:

- for €12.1 million, deferred income relating to the initial payment of €36 million received under the Sumitomo Dainippon Pharma contract (versus €34.3 million in 2017). The corresponding turnover is recognized and spread over the duration of the contract.
- in 2018, the Company's contribution to the financing of the development of Imeglimin in the United States and Europe for a total amount of \$25 million, which presented a balance of €13.7 million as of December 31, 2018.
- in 2017 and 2018, payments received of €1.3 million, and charged back to Sumitomo Dainippon Pharma by the Company in the framework of the phase III study of Imeglimin (the consideration corresponds to advances paid for the same amount).

## 10. LIQUIDITY AND CAPITAL RESOURCES

The reader is invited to refer also to Notes 10, 12 and 14 to the annual financial statements drawn up according to IFRS standards contained in section 20.1 “IFRS accounts established for the financial year ended December 31, 2018”.

### 10.1. Information on the capital, liquidity and funding sources

As of December 31, 2018, the net amount of cash and cash equivalents held by the Company (sum of the cash and cash equivalent assets and of the current bank loans as liabilities) amounted to €66,737 K against €53,412 K as of December 31, 2017 and the net amount of cash (sum of the cash and cash equivalent assets and of the current bank loans as liabilities) amounted to € 52,506 k as of December 31, 2018 and €52,672 k as of December 31, 2017, and the amount of net cash (sum of cash and cash equivalents in assets and financial liabilities) amounted to €52.506 at 31 December 2018 and €52,672 at 31 December 2017.

Since its creation, the Company has been funded by:

- the strategic partnership contracts signed in 2017 with Sumitomo Dainippon Pharma and in 2018 with Roivant;
- capital increases, in particular the initial public offering (IPO) of the Company at the beginning of 2015, as well as the private placements made in July 2015 with investors in the United States and in July 2016 with investors in the United States and Europe;
- the subsidy granted by Merck Serono when the Company was created;
- refunds received pursuant to the research tax credit;
- innovation grants and subsidies from BpiFrance Financement;
- a venture loan agreement Kreos; and
- a FEDER subsidy from Grand Lyon.

#### 10.1.1. Capital financing

The Company has received a total of €134,005 K (before deducting expenses related to the equity transactions) through the contribution by the founders and equity transactions carried out between 2009 and 2018.

In 2017 and 2018, the Company raised around €22 million through the following events:

Periods	Gross amounts raised in K€	Activities
Jan.-Nov. 2017	546	Conversion of 177,200 Founder Warrants/warrants by employees and board members
February 2018	12 167	Emission of 1,431,399 shares at a price of €8.5 per share under the contract with Roivant Sciences

May 2018	20	Conversion of 400 Founder Warrants by employees
August 2018	8 914	Emission of 1,290,000 shares at a price of €6.91 per share as part of the contract signed with DeuteRx
<b>At December 31, 2018</b>	<b>134 005</b>	

### 10.1.2. Debt financing

#### 10.1.2.1. Issuance of non-convertible bonds for the benefit of Kreos Capital IV (UK) Limited

On July 25, 2014, the Company entered into a venture loan agreement intended to allow the Company to benefit from financing in the form of non-convertible bonds representing a loan for a maximum amount of €8 million for which Kreos Capital IV (UK) Limited agreed to subscribe in two tranches, as follows:

- €5 million (“Tranche A”) subscribed as of July 25, 2014, repayable over 33 months (no repayment of capital for the first 9 months); and
- €3 million (Tranche B), in one or several drawdowns, subject to the condition that the Company obtains additional financing of at least €12 million (in capital, through the issuance of convertible bonds, a subordinated shareholder loan or a license agreement with a pharmaceutical company) by March 31, 2015 and repayable over 36 months. This tranche 2 could be subscribed until April 30, 2015. It was not used by the Company.

The bonds have a fixed 11.25% coupon and include various fees to be paid by the Company.

Under the Venture Loan Agreement, the Company was also to issue to Kreos Capital IV (Expert Fund) Limited, a Kreos subsidiary, a maximum of 220,000 warrants for class A preferred shares, 137,500 of which were issued at the time Tranche A was released and a maximum of 82,500 of which were to be issued at the time Tranche B was released in its entirety (see Note 4 of Section 21.1.4.1 “Stock subscription warrant plan” of this *document de référence* for a more detailed description of the procedures for exercising these warrants).

Finally, in order to guarantee all obligations entered into by the Company under the Venture Loan Agreement, it has granted various security interests relating to its intellectual property and its cash such as pledges over bank accounts, receivables and certain intellectual property rights, which were removed upon repayment of this debt (see Section 11.2.4 “Patents that are pledged” and Section 11.4 “Other intellectual property items” of this *document de référence* for the details of these pledges).

The debt was repaid in the 2017 financial year.

### 10.1.3. Financing by repayable advances and subsidies

#### Repayable advances:

Since 2011, the Company has benefited from two repayable advance programs, with a maximum amount of €250 K for the first (PXL770) and €950 K (Imeglimin – New Formulation) for the second, with more significant drawdowns in 2012 and 2013.

In 2016, the Company received the balance of the second advance for an amount of €150 K, with the amount finally reaching €850 K

The first of the two advances was repaid in full during the financial year 2018.

The table below sets forth movements relating to those two advances between 2014 and 2017 and specifies their precise breakdown per income concerned:

	PXL770	Imeglimin (New Formulation)	Total
<b>At December 31, 2016</b>	<b>111</b>	<b>733</b>	<b>845</b>
(+) Collection of funds			
(-) Refund of expenses	-73	-69	-142
Subsidies			
Financial expenses	5	28	33
(+/-) Other movements			
<b>At December 31, 2017</b>	<b>43</b>	<b>692</b>	<b>736</b>
(+) Collection of funds			
(-) Refund of expenses	-45	-143	-188
Subsidies			
Financial expenses	2	27	28
(+/-) Other movements			
<b>At December 31, 2018</b>		<b>577</b>	<b>577</b>

The repayment schedule for these advances is described in note 14.2 to the financial statements prepared in accordance with IFRS set out in section 20 “Financial information concerning the assets, financial position and the results of the company” of this *document de référence*.

The balance as of December 31, 2018 is summarized as follows:

	PXL770	Imeglimin (New Formulation)	Total
<b>At December 31, 2018</b>		<b>577</b>	<b>577</b>
Portion less than one year		218	218
Portion one to five years		359	359
Portion over five years			

#### Subsidies:

The Company received:

- a FEDER and Grand Lyon non-repayable innovation support subsidy consisting of two subsidies of a maximum amount of €218 K each, or a total of €437 K, as part of the “new therapeutic approaches in the treatment of chronic infections caused by the hepatitis B virus (Natheb project)” program, of which €281 K has been recognized as income; Poxel contributed to this approach by



providing its knowledge of the target which is mobilized in type 2 diabetes as well as in hepatitis B.

- a non-repayable OSEO innovation support subsidy in the amount of €233 K as part of the “Development and selection of a new AMPK activator drug for the treatment of diabetes” program.

The table below summarizes the cash flows generated by these subsidies:

Subsidy	Amount received or to be received (unaudited)
FEDER/Grand Lyon Subsidy (NATHEB project)	Total of €281 K received between 2011 and 2016
OSEO subsidy (PXL <sub>770</sub> )	€233 K received in 2012

#### 10.1.4. Financing through the research tax credit

<b>RTC receivable at December 31, 2016</b>	<b>1 918</b>
Income recognized as a deduction from R&D costs	3 122
Collection of funds	-1 918
<b>RTC receivable at December 31, 2017</b>	<b>3 122</b>

<b>RTC receivable at December 31, 2017</b>	<b>3 122</b>
Income recognized as a deduction from R&D costs	3 539
Collection of funds	-3 122
<b>RTC receivable at December 31, 2018</b>	<b>3 539</b>

The Company has benefited from the CIR (research tax credit) since its incorporation. The above amounts represent a CIR receivable at the close of each financial year.

Since 2008, the calculation of the CIR is based on a rate of 30% of the eligible expenses for the year. Where it cannot be deducted from the tax payable, the CIR is refunded by the tax authorities during the fourth financial year following the period for which it was recognized. Since 2010, small and medium-sized companies can obtain an immediate refund. Thus, the Company obtained the refund of the 2016 and 2017 CIRs in 2017 and 2018 respectively and will request the refund of 2018 CIR in 2019.

Since 2009, the cumulative amount of the CIR is €26.7 million.

#### 10.1.5. Off-balance sheet commitments

##### 10.1.5.1. Real estate leases

In 2015, in relation with its activities, the Company moved its headquarters and entered into a commercial lease in Lyon with an effective date of July 1, 2015. It has a duration of nine whole and

consecutive years, until June 30, 2024, and the Company retains the possibility to terminate it every three years only.

In November 2017, the Company entered into a commercial lease enabling it to enlarge the office space at its headquarters, effective from April 1, 2018. Its term is nine complete and consecutive years, until March 31, 2027. The Company has the possibility to provide notice to terminate only every three years.

The Group also signed a sub-lease for office premises in Paris for a term of 12 months, renewable annually, effective from January 1, 2013, and a lease for premises in Japan, effective from January 15, 2018, with a two-year undertaking.

As of December 31, 2018, the amount of the future rent and expenses relating to the lease of the Group's headquarters and the sub-lease of the Paris office until next three-year period is €1,174 K (refer to Note 25.1 to the IFRS financial statements set out in Section 20 "Financial information concerning the assets, financial position and the results of the company" of this *document de référence*).

#### **10.1.5.2. Obligations under the Merck Serono agreement**

In accordance with the MS Transfer and License Agreement signed with Merck Serono on March 19, 2009 and amended on July 30, 2009, June 22, 2010, May 23, 2014 and November 28, 2014, Merck Serono transferred certain patents and granted Poxel a license for other patents and know-how for the research, development and marketing of pharmaceutical products. This license is exclusive and covers a list of 25 molecules by program, selected by Poxel.

In exchange for the rights that were granted to Poxel under the MS Agreement, Poxel was to pay Merck Serono the following compensation:

- royalties on net sales of the products covered by the patents transferred or licensed by Merck Serono at a high single-digit rate for Imeglimin, and at a low single-digit rate for the other projects;
- a percentage of the revenue from any partnership agreement relating to the drug-candidates covered by the patents, granted or granted under license, sold or licensed, at a low double-digit rate near the bottom of the range.

#### **10.1.5.3. Obligation under the Sumitomo Dainippon Pharma contract**

On October 30, 2017 the Company signed a license with Sumitomo Dainippon Pharma ("SDP") for the co-development and marketing of Imeglimin, a drug-candidate for type 2 diabetes.

Under this contact, SDP has an exclusive marketing right for Japan, China, South Korea, Taiwan and nine other countries in South-Eastern Asia, for all human and veterinary indications, including type 2 diabetes.

The two parties will co-finance certain development activities within the limit of €1.2 million for the Company. SDP will support the development costs above this limit, as well as the marketing costs.

#### **10.1.5.4. Obligation under the Roivant Science GmbH contract**

On February 9, 2018 we signed an exclusive contract with Roivant Sciences GmbH ("Roivant") for development and marketing of Imeglimin, an oral drug-candidate developed by us for treatment of

type 2 diabetes, in the United States, in Europe and in other countries not covered by the partnership existing in East and South-Eastern Asia between us and Dainippon Pharma.

Roivant will take in charge the costs of development and marketing of Imeglimin, and the Company will participate in the financing of the program for the development of up to \$25 million (approximately €20 million) for two years.

As this amount is in counterpart to the obligation to participate in the financing of Roivant's development plan, it has been treated as a debt. The balance to be paid at the closure, amounting to 13,646 k € is fully classified as current financial debts.

This agreement provides that, until the Company has fully paid its obligation to participate in the financing of Roivant's development plan, and in the event that the Company's immediately available cash, less expected disbursements within 30 days, is less than 3 times the amount of such residual obligation, for at least 10 consecutive days, then, the Company would be required to establish an irrevocable letter of credit with a leading bank for the benefit of Roivant for the residual amount of such obligation calculated on such date. Roivant may return this letter of credit for collection if the Company defaults in the repayment of its obligation, or in the event of termination of the contract at Roivant's initiative and under certain conditions. If the Company is unable to obtain a letter of credit, or if it is cancelled, then the amounts due to Roivant by the Company on that date will be immediately payable.

At the closure date, the Company is in compliance with the terms of the contracts on the basis of its available cash balances amounting to 66,737 thousand euros.

#### **10.1.5.5. Obligations under the DeuteRx agreement**

The Company entered into an acquisition agreement with DeuteRx, on August 29, 2018, in relation to DRX-065, a drug-candidate in clinical development for the treatment of nonalcoholic steatohepatitis (NASH), a portfolio of other deuterated drug-candidates for the treatment of rare metabolic diseases, and a variety of related industrial and intellectual property rights pertaining to DeuteRx.

This agreement specifies, for the entire product portfolio, the issue of up to 4 million shares in the Company in favor of DeuteRx, and milestone payments linked to the attainment of development, regulatory and sales targets, amounting to a maximum of \$545 million, part of which may be paid through the issue of shares in the Company. It also provides for the payment of royalties, at a low single-digit rate, on sales. The first milestone payment corresponds to the Company's decision to commence the phase III clinical development program for the drug-candidates covered under that agreement and will be made exclusively through the issue of shares in the Company.

#### **10.1.5.6. Obligations under other agreements**

In the ordinary course of its business, the Company regularly uses the services of subcontractors and enters into research and partnership arrangements with various contract research organizations, or CROs, who conduct preclinical or clinical trials and studies in relation to the drug-candidates, primarily Imeglimin and to a lesser extent, PXL770. The cost of the services rendered by the CROs is counted as an operating cost when it they are engaged, or, depending on the nature, according to their stage of completion at the date of this *document de référence*. The Company's commitment to its subcontractors is presented in section 5.2.3 of this *document de référence*.

## 10.2. Cash flows

Table of cash flows (Amount in euros)	31/12/2018		31/12/2017
Net cash from operating activities before working capital changes	15 116		-20 377
(-) Change in working capital requirements	19 860		-28 503
<b>Cash flows from operations</b>	<b>-4 744</b>		<b>8 126</b>
<b>Cash flows from investment activities</b>	<b>-7 608</b>		<b>213</b>
<b>Cash flows from financing activities</b>	<b>25 676</b>		<b>-496</b>
<b>Increase (Decrease in cash)</b>	<b>13 325</b>		<b>7 843</b>
Cash and cash equivalents at beginning of period	53 412		45 569
Cash and cash equivalents at end of period	66 737		53 412

The annual variation of the cash flow during the year ended December 31, 2018 is explained in the following manner:

- Cash flows generated by operations are negative and amount to €8.9 million, which reflects positive operating cash flow of €15.4 million, offset by an increase in working capital requirement (WCR) of €19.9 million.
- Investment flows are negative and amount to -€7.6 million, in relation to the acquisition of a product portfolio pursuant to the contract entered into with DeuteRx, financed partly in cash and partly through the issue of securities (refer to note 4.1 to the IFRS financial statements set out in section 20.1 "Financial statements established using IFRS standards for the financial year ended" of this *document de référence*).
- Cash flows related to financing operations are positive and amount to €25.7 million, following:
  - various capital increases which took place over the financial year,
  - initial payment of \$25m in accordance with the contract with Roivant Sciences, for which a partial repayment has occurred during the financial year,
  - the repayment of conditional cash advances.

### 10.2.1. Cash flows used in operating activities

The changes in cash flow from operations for the financial years ended December 31, 2018 and 2017 amounted to +€4 744 K and +€8,126 K respectively. The 2018 financial year ended with operating profit of €12.5 million, due to the recognition of revenue from contracts signed with Sumitomo Dainippon Pharma and Roivant Sciences. The 2017 financial year ended with an operating loss of -

€20,377 K, mainly related to the end of the phase IIb study and the preparation of the phase III study of Imeglimin in Japan.

In 2018, the WCR increased by €19 860 K (against a reduction of €28,503 K in 2017), due to:

- an increase in receivables of €9,360 K (chargebacks related to the Sumitomo Dainippon Pharma contract)
- a decrease in other creditors and accrued liabilities of €22 380 K, which is explained by the write-down of deferred income recognized under the Sumitomo Dainippon Pharma contract (impairment of €22,224 K).
- an increase in trade payables of €11,734 K, essentially due to the increase in costs incurred under the TIMES phase III program for Imeglimin in Japan

### 10.2.2. Cash flows related to investment activities

The Company uses subcontractors for the achievement of many of the operations related to research, and only in-sources control and project management. Therefore, the model chosen does not require significant investments.

In 2018, investment flows are mainly related to the acquisition of a product portfolio pursuant to the contract signed with DeuteRx (refer to note 4.1 of the notes to the IFRS financial statements set out in section 20.1 “Financial statements established using IFRS standards for the financial year ended” of this *document de référence*). This investment, amounting to a total of €16,572 K, was financed in the amount of €7,658 K in cash, and in the amount of €8,914 K through the issue of shares.

In 2017, the flow of investments corresponds mainly to the acquisition of tangible fixed assets. The interest received as cash investments (€90 K) as well as the repayment of the deposits of the Kreos contract are deducted from that amount.

The changes in cash flow from investment activities for the years ended December 31, 2018 and December 31, 2017 amounted respectively to -€7,608 K and +€213 K.

### 10.2.3. Cash flows from financing activities

The breakdown of cash flows from financing activities are set out below.

(Amounts in K€)	12/31/2018 Audited	12/31/2017 Audited
Capital increase and share premium net of expenses	12 172	546
Subscription of warrants	41	24
Interest paid	5	-20
Collection of repayable advance payment/loan	13 646	
Repayments of borrowings and conditional advances	-188	-1 046
<b>Cash flows from financing activities</b>	<b>25 676</b>	<b>-496</b>

In 2018, financing flows were mainly related to:

- transactions involving the Company's share capital, described in section 18.3 "Recent transactions with regard to the share capital of the Company" of this *document de référence*,
- the obligation to participate to the financing of the development program of Roivant as described in Section 22.3 "Contract with Roivant Sciences GmbH" of this *document de référence*.

In the light of its development programs, as defined at the time of drafting this *document de référence*, the Company considers that its financing needs are covered for at least 24 months following the date of filing of this *document de référence*. Therefore, the Company anticipates that it may seek additional funding in the framework of the development of its activity, which could be obtained by the combination of capital operations or signatures of partnerships or licenses.

The Company's present and future financing needs depend on a number of factors, including:

- the progress of clinical studies for its drug candidates;
- the potential number of new drug candidates that could be identified;
- costs related to the protection of intellectual property;
- the time and cost required to obtain the necessary regulatory approvals for drug candidates; and
- the amount of income that could be generated, directly or indirectly, by current or future partnership arrangements concerning one or more of the Company's drug-candidates.

For more information about the associated risks, refer to section 4 "Risk Factors" of this *document de référence*.

### 10.3. Borrowing conditions and financing structure

Information related to the financing of the Company's activities is set out in section 10.1 "Information on the capital, liquidity and funding sources" of this *document de référence*.

### 10.4. Possible restrictions on the use of funds

None

### 10.5. Sources of financing expected for future investments

With nearly €66.7 million in cash and cash equivalents as of December 31, 2018 the Group believes it has the resources needed to finance its operational expenditure for at least 24 months from the date of filing of this *document de référence*

## 11. RESEARCH AND DEVELOPMENT, PATENTS AND LICENSES AND OTHER INTELLECTUAL PROPERTY RIGHTS

### 11.1. Research and development

Research and development (R&D) activities are at the heart of the Company's business. Since its creation in 2009, the majority of the Company's resources have been devoted to R&D activities, allowing the Company to have two innovative drug-candidates currently under development, Imeglimin and PXL770, both first in their respective classes, Glimins on the one hand and AMPK activators on the other.

To be successful in its R&D activities, the Company relies on several key factors:

- A team primarily made up of researchers and developers, who all have significant experience in the pharmaceutical industry. Each member of this team is encouraged to develop and innovate within the Company, so that they contribute positively to the Company's development. This concerns not only inventions of new drug candidates, but also any improvement to an existing product (through a new formulation for example), a synthesis procedure for this product, or even a clinical study design. Every innovation discovered within the Company belongs to it, in return for fair remuneration of the inventors.
- A business-oriented R&D strategy: right from the start of the development of the strategy, a qualitative market analysis is performed to confirm that the innovation arising from the strategy will meet an unsatisfied need in that market and present an attractive profile in terms of profitability. This was clearly implemented at the time when the Imeglimin and direct APMK activator programs were implemented within the Company, and more recently for the acquisition of the MPC inhibitor program, and this analysis is regularly updated to ensure that innovation continues to meet market needs.
- Qualified and experienced subcontractors: once the R&D strategy is developed, a requirements specification is developed to enable implementation by one or more subcontractors (contract research organizations, university professors, university hospital centers). Through each employee's significant experience, several subcontractors who have recognized expertise in the specific field are contacted and a selection is made based on previously defined objective criteria (incorporating quality aspects, successful experience, cost and timing, at a minimum). If necessary, several interviews and audits can be organized to ensure that implementation of the activity meets the program.
- Finally, the Company relies on scientific advisors consisting of recognized experts, to analyze the results obtained and discuss the next steps in R&D.

The Company has established three committees of experts for its programs:

- i. A Scientific Diabetes Committee composed of seven members, reputed diabetologists and opinion leaders in the United States and Europe, who have been involved in the analysis of the clinical results obtained on Imeglimin since the origin of the Company and make recommendations on future studies to be carried out. These members are:
  - Professor Harold Lebovitz: Harold is currently a professor of medicine at SUNY Health Science Center in Brooklyn (USA), where he also previously served as chief of the Endocrinology Division and Director of the Clinical Research Center.

- Professor Michael Roden: Michael is an endocrinologist, professor of medicine and Director of the Heinrich Heine Metabolic Diseases Department in Düsseldorf, Germany. He is also Scientific Director of the German Diabetes Center (DDZ), and Director of the Karl Landsteiner Institute for Endocrinology and Metabolism in Vienna, Austria.
  - Professor Silvio Inzucchi: Silvio is currently a professor of medicine at the Yale University School of Medicine in New Haven (USA), where he serves as Clinical Director of the Endocrinology Department, and attending physician at Yale-New Haven Hospital, where he is Director of the Diabetes Center.
  - Professor Guntram Schernthaner: Guntram serves as Head of the Department of Medicine at Rudolfstiftung Hospital in Vienna, Austria.
  - Professor Clifford Bailey: Clifford is a professor and Director of Diabetes Research at Aston University in Birmingham (England).
  - Professor Ele Ferannini: Ele is Professor of Internal Medicine, Honorary Associate Investigator and Member of the CNR (National Research Council) at the Institute of Clinical Physiology, Pisa (Italy).
  - Professor Rury R. Holman: Rury is Professor of Medicine and Director of the Diabetes Clinical Trials Unit at the Oxford University (United Kingdom) School of Medicine.
- ii. A second Scientific Committee on Diabetes, consisting of four members, reputed diabetologists and opinion leaders, in Japan, who make recommendations on product development strategy in Japan and who take part in the analysis of clinical results of studies conducted in Japan. At the present time, the four members of this committee are:
- Professor Masato Kasuga: Masato is currently President of the National Center for Global Health and Medicine, based in Tokyo, Japan.
  - Professor Kohjiro Ueki: Kohjiro is currently Professor at the University of Tokyo, Japan, in the Diabetology Department.
  - Professor Wataru Ogawa: Wataru is Professor of Medicine and Head of the Clinical, Diabetes and Metabolic Diseases Department of the University of Kobe (Japan)
  - Professor Hirotaka Watada: Hirotaka is Professor of Medicine in the Department of Medicine, Metabolism and Endocrinology at the University of Juntendo, Tokyo (Japan) School of Medicine.
- iii. A Scientific Committee on NASH, composed of three members, reputed diabetologists and opinion leaders in the United States and Europe, who are involved in the analysis of the results obtained on PXL770 and PXL065 and who make recommendations on future studies to be carried out. At the present time, the following committee members collaborate with the Company on the two NASH products in development:
- Professor Kenneth Cusi: Ken is Director of the Endocrinology, Diabetes and Metabolism Department at the University of Florida (United States) School of Medicine.
  - Professor Vlad Raziu: Vlad is Professor of Medicine at Université Pierre et Marie Curie in Paris and works at the Hôpital de la Pitié Salpêtrière (France).



- Professor Stephen Harrison: Stephen is Professor of Medicine and Director of the Clinical Research Unit of Pinnacle in San Antonio (United States).

Finally, *ad hoc* experts are frequently enrolled for the development of the Company's products:

- Bioenergy expert: Professor Eric Fontaine;
- Toxicology expert: Professor Gerd Bode; and
- Regulatory expert: Mark Cerpial.

## 11.2. Patents and patent applications

### 11.2.1. General presentation

Intellectual property is a major issue for Poxel, as it helps to protect and promote the discoveries made by the Company and thus to make Poxel a key player in the treatment of type-2 diabetes among all pharmaceutical groups.

Poxel owns 25 patent families, covering its three main programs: Imeglimin, AMPK activators, whose most advanced drug-candidate is PXL770, and MPC inhibitors, whose most advanced drug-candidate is PXL065. In addition, the Company has a license for 22 families of patents owned by Merck Serono (including 21 still in force) concerning both Poxel's two main programs, but also other programs for the treatment of diabetes. The license for the patents held by Merck Serono is granted to the Company for the term of the patents, subject to performance by the Company of its contractual obligations.

Poxel's patent portfolio can be separated into four families:

- patents to protect Imeglimin;
- patents relating to AMPK activators;
- patents relating to MPC inhibitors;
- patents aimed at protecting Poxel's other programs, including GLP-1 agonists, FxR agonists, glucokinase activators and 11-beta-hydroxysteroid dehydrogenase type-1 inhibitors. These programs are still in the research phase.

Among these four families, there are a number of sub-families: product patents, synthesis procedure patents, combination patents and new therapeutic application patents.

Poxel's patent portfolio includes patents that the Company owns, patents licensed to Poxel, as well as jointly owned patents. Families of patents involving Imeglimin were the subject of a sub-license to Sumitomo Dainippon Pharma for Japan and South-Eastern Asia, and to Roivant Sciences for the United States, Europe and all other countries not covered by the partnership with Sumitomo Dainippon Pharma. The family of patents involving the FxR agonist was the subject of a license to ENYO Pharma. The Company has purchased all worldwide rights for seven patent families related to the MPC inhibitor program from DeuteRX.

Patents held by the Company (solely or in co-ownership)

Imeglimin			
Poxel Reference	Title	Sub-family	Priority
B2820	Application of Imeglimin in the treatment of type-2 diabetes and its related pathologies	Products	26.01.2000 FR
B896	Imeglimin synthesis procedure	Synthesis procedure	10.04.2003 FR
B897	Combination of Imeglimin with insulin secretagogue products (sulfonylureas, gliptins, glinides, GLP-1 receptor agonists)	Association	13.01.2006 FR
B899	Combination of Imeglimin with insulin sensitizing products (metformin, thiazolidinediones)	Association	13.01.2006 FR
B900	Combination of Imeglimin with PPARα agonists (fibrates)	Association	13.01.2006 FR
B901	Application of Imeglimin for cicatrization	New therapeutic applications	13.01.2006 FR
B902	Optimization of the first stage of the Imeglimin synthesis procedure	Synthesis procedure	02.02.2008 DE
B903	New Imeglimin synthesis procedure using a basic method	Synthesis procedure	23.05.2008 EP
B904	New Imeglimin synthesis procedure using granulometry	Synthesis procedure	29.07.2008 EP
B923	Application of Imeglimin for cancer and inflammation	New therapeutic applications	12.12.2008 EP
B944	New Imeglimin synthesis procedure based on preferential crystallization	Synthesis procedure	26.03.2009 EP
B1042	Application of Imeglimin in the prevention of type-1 diabetes	New therapeutic applications	09.06.2010 EP
B1043	Application of Imeglimin in the prevention of type-2 diabetes	New therapeutic applications	09.06.2010 EP
B1053	Application of Imeglimin for the treatment of diseases associated with ischemia and/or reperfusion	New therapeutic applications	17.07.2009 FR
B1100	New Imeglimin synthesis procedure using tartaric acid	Synthesis procedure	01.12.2010 EP
B1561	Combination of Imeglimin with insulin	Association	12.12.2008 EP

**APMK activators**

<sup>8</sup> This patent is held jointly by the Company and by Inserm. Its conditions are regulated by a memorandum of understanding signed by the parties on January 22, 2010. The scope of this patent, regarding the use of Imeglimin and its derivatives in a pathology other than type-2 diabetes, is not used by the Company at present. In case of commercial exploitation of this patent, the Company will pay to Inserm lump-sum amounts upon completion of certain steps, as well as royalties less than or equal to 1% on net sales of products covered by the patent in the application domain only.

Poxel Reference	Title	Sub-Family	Priority
B993	Application of new AMPK activators in the treatment of Type 2 diabetes and its related pathologies	Products	12.29.2009 EP
B1361	Application of new AMPK activators in the treatment of Type 2 diabetes and its related pathologies	Products	06.29.2012 EP

MPC inhibitors, including PXL065			
Poxel Reference	Title	Sub-family	Priority
DEU-005	Deuterium-enriched Pioglitazone	Products	09.26.2007 US
DEU-013	Treatment methods for neurological, metabolic and other disorders, using an enantiomer of deuterium-enriched Pioglitazone	New therapeutic applications	01.15.2014 US
DEU-015	Combination therapy based on an enantiomer of deuterium-enriched 5-(benzyl)-5-deutero-thiazolidine-2.4-diones, for the treatment of medical disorders	New therapeutic applications	03.20.2015 US
DEU-018	Treatment methods for bacterial infections and fungal infections, using deuterium-enriched Pioglitazone	New therapeutic applications	03.20.2015 US

MPC inhibitors, not including PXL065			
Poxel Reference	Title	Sub-family	Priority
DEU-010	Treatment methods using deuterium-enriched 2.4-thiazolidinediones	Products	03.14.2013 US
DEU-016	5-deutero-thiazolidine-2.4-dione compounds and treatment methods for medical disorders	Products	03.20.2015 US
DEU-017	5-deutero-thiazolidine-2.4-dione compounds and treatment methods for medical disorders	Products	03.20.2015

#### 11.2.1.1. Patents held by Merck Serono, for which Poxel has a license

See Section 22.1 “Merck Serono agreement” of this *document de référence* for further information on the transfer and license agreement entered into with Merck Serono.

APMK activators
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Merck Reference	Title	Sub-Family	Priority
P05/204 (case 7067)	Application of new AMPK activators in the treatment of Type 2 diabetes and its related pathologies	Products	08.18.2005 EP
P06/101 (case 7071)	Application of new AMPK activators in the treatment of Type 2 diabetes and its related pathologies	Products	07.13.2006 FR
P08/050 (case 7107)	Application of new AMPK activators in the treatment of Type 2 diabetes and its related pathologies	Products	04.11.2008 EP
P08/063 (case 7108)	Application of new AMPK activators in the treatment of Type 2 diabetes and its related pathologies	Products	05.05.2008 EP
P08/089 (case 7125)	Application of new AMPK activators in the treatment of Type 2 diabetes and its related pathologies	Products	06.16.2008 EP

GLP-1 Agonists			
Merck Reference	Title	Sub-Family	Priority
P08/028 (case 7105)	Application of new GLP-1 agonists in the treatment of Type 2 diabetes and its related pathologies	Products	03.05.2008 EP
P08/026 (case 7116)	Application of new GLP-1 agonists in the treatment of Type 2 diabetes and its related pathologies	Products	03.05.2008 EP
P08/027 (case 7117)	Application of new GLP-1 agonists in the treatment of Type 2 diabetes and its related pathologies	Products	03.05.2008 EP
P08/062 (case 7124)	Application of new GLP-1 agonists in the treatment of Type 2 diabetes and its related pathologies	Products	04.29.2008 EP

Fxr Agonists			
Merck Reference	Title	Sub-Family	Priority
P08/151 (case 7123)	Application of new Fxr agonists in the treatment of Type 2 diabetes and its related pathologies	Products	04.18.2008 EP

<b>11beta-hydroxysteroid dehydrogenase type 1 inhibitors (11βHSD1)</b>			
<b>Merck Reference</b>	<b>Title</b>	<b>Sub-Family</b>	<b>Priority</b>
P05/219 (case 7073)	Application of new 11βHSD1 inhibitor structures in the treatment of Type 2 diabetes and its related pathologies	Products	12.16.2005 EP
P06/159 (case 7102)	Application of new 11βHSD1 inhibitor structures in the treatment of Type 2 diabetes and its related pathologies	Products	03.11.2006 EP
P08/168 (case 7101)	Application of new 11βHSD1 inhibitor structures in the treatment of Type 2 diabetes and its related pathologies	Products	12.21.2006 EP
P07/113 (case 7106)	Application of new 11βHSD1 inhibitor structures in the treatment of Type 2 diabetes and its related pathologies	Products	05.11.2007 EP
P08/137 (case 7130)	Application of new 11βHSD1 inhibitor structures in the treatment of Type 2 diabetes and its related pathologies	Products	09.01.2008 EP

<b>Glucokinase activators</b>			
<b>Merck Reference</b>	<b>Title</b>	<b>Sub-Family</b>	<b>Priority</b>
P07/103 (case 7118)	Application of new glucokinase activator structures in the treatment of Type 2 diabetes and its related pathologies	Products	10.09.2007 EP
P07/104 (case 7119)	Application of new glucokinase activator structures in the treatment of Type 2 diabetes and its related pathologies	Products	10.09.2007 EP
P08/007 (case 7120)	Application of new glucokinase activator structures in the treatment of Type 2 diabetes and its related pathologies	Products	01.24.2008 EP
P08/020 (case 7127)	Application of new glucokinase activator structures in the treatment of Type 2 diabetes and its related pathologies	Products	02.25.2008 EP
P08/023 (case 7128)	Application of new glucokinase activator structures in the treatment of Type 2 diabetes and its related pathologies	Products	02.27.2008 EP
P08/024 (case 7129)	Application of new glucokinase activator structures in the treatment of Type 2 diabetes and its related pathologies	Products	03.01.2008 EP

#### 11.2.1.2. Geographic coverage

The choice of the countries in which the protection will apply depends above all on the market potential of each of these countries. Poxel has drawn up two lists (List A and List B) of countries/groups of countries adapted to the significance of the invention protected by the patent. The lists are as follows:

List A	List B
Europe (list as defined by the European Patent Organization)	Europe (limited to France, Germany, Italy, United Kingdom and Spain)
Australia	United States Japan
Israel	
Brazil	
Japan	
Canada	
Mexico	
China	
Eurasia (limited to Russia)	
South Korea	Japan
Taiwan	
South Africa	
United States	
India	

#### 11.2.2. Nature of the patents per group

##### 11.2.2.1. Imeglimin group

- A family of patents involving Imeglimin and its derivatives for the treatment of type-2 diabetes and its related pathologies.
- This patent family is of considerable importance as it protects Imeglimin as such, and as a drug, in particular for the treatment of type-2 diabetes. These patents were issued in a very large number of countries, a very much higher number than that of the list adopted by Poxel and therefore offering very broad territorial coverage. Poxel is the owner of this patent family.

A study of the freedom to exploit the rights to Imeglimin in Europe and in the USA was conducted in October 2011 by Becker et Associés, Industrial Property Consultants. Ten patents or patent applications were identified as covering molecules that are structurally close to Imeglimin. None of these patents was identified as liable to restrict the freedom to exploit the rights to Imeglimin in Europe, the USA and Japan. It should be noted that these 10 patents or patent applications were all filed after the date of filing of the patent covering Imeglimin.

- Patents concerning the synthesis of Imeglimin and its derivatives.  
Six families of patents cover various processes for the synthesis of Imeglimin. These patents are at different stages in the patent issuance procedure. Poxel is the owner of these six patent families.

- Patents concerning the combination of Imeglimin and its derivatives with products already on sale for the treatment of diabetes and its related pathologies.

Four families of patents protect Imeglimin and its derivatives in combination with other diabetes products. Through its unique mechanism of action, Imeglimin is a drug-candidate which has the ability to be combined with any treatment for diabetes or related pathologies. Through targeted studies, Poxel has demonstrated that Imeglimin makes it possible to increase the effectiveness of diabetes treatments that are currently commonly prescribed. The stages of advancement of issuance of these patents vary by country. Poxel is the owner of these four families of patents.

- Patents concerning Imeglimin and its derivatives for new therapeutic applications  
Four families of patents protect the use of Imeglimin and its derivatives in the treatment of pathologies other than type-2 diabetes. Poxel has discovered that, in addition to its action on type-2 diabetes, Imeglimin is very promising in the prevention of types-1 and -2 diabetes, cancer, inflammations and scarring. The stages of advancement in issuance of the patents protecting these discoveries vary by country. The Company is the owner of these four families of patents.

In addition to these four families of patents held by the Company itself, various collaborations put in place between Poxel and Inserm have made it possible to identify a patented innovation, the rights to which were then assigned to Poxel. Indeed, one of the collaborations highlighted an unexpected effect of Imeglimin in the treatment of ischemia-reperfusion. This collaboration led to the filing of a family of patents jointly owned with Inserm. These patents are currently being examined in the various countries selected by the Company.

#### **11.2.2.2. AMPK activators group**

- Patent covering new molecules and their therapeutic uses

Poxel benefited from a license to Merck Serono's rights pertaining to five families of patents for innovative structures serving as AMPK activators. These structures were used as the basis for Poxel's research to develop other drug-candidates. The stages of advancement of issuance of these patents vary by country.

Poxel's research has also invented and developed new interesting structures that are promising as AMPK activators. Two families of patents have been filed to protect these inventions. PXL770, which is protected by one of these families of patents, is currently a highly promising clinical candidate.

#### **11.2.2.3. MPC inhibitors group**

- Patent covering new molecules and their therapeutic uses

The Company has purchased all worldwide rights for seven patent families from DeuteRX. These patent families encompass "deuterated thiazolidinediones" and the treatment methods for metabolic diseases, particularly certain indications, including NASH, type-2 diabetes and adrenoleukodystrophy. Four of these patents include the rights to combinations and/or treatment methods with PXL065.

#### **11.2.2.4. Other groups**

- Patents covering new molecules and their therapeutic uses

The Company benefited from a license to Merck Serono's rights over four other programs involving the treatment of diabetes: GLP-1 agonists, FxR agonists, 11-beta-hydroxysteroid dehydrogenase type-

1 (11 $\beta$ HSD1) inhibitors and glucokinase activators. The stages of advancement of issuance of the licensed patents vary by country.

### 11.2.3. Table summarizing the patent families held by Poxel or licensed to Poxel

#### 11.2.3.1. Imeglimin family

- Patent covering Imeglimin and its derivatives for the treatment of type-2 diabetes and its related pathologies

Merck reference	Title	Priority date*	Expiration date	Status	
				Countries where the patent is issued	Countries where the patent application is in progress
P00/44 or 7023	Application of Imeglimin in the treatment of type-2 diabetes and its related pathologies	1/26/2000	1/26/2020	France	
			1/25/2021	List A (except Taiwan and Israel) + Armenia, Azerbaijan, Belarus, Kyrgyzstan, Kazakhstan, Republic of Moldavia, Tajikistan, Turkmenistan, Indonesia, Singapore, Argentina, Hong-Kong	
			8/29/2027	Brazil	

\*: The patent priority date is the date which corresponds to the first filing made in a country. The patent is generally filed internationally a year after the priority date, which gives rise to a bundle patent providing protection in each country for 20 years (or approximately 21 years as from the priority date). When a product obtains regulatory approval, the corresponding patents can benefit in most countries from an extension of their protection period for up to five years.

\*\*: The term "Issued" means that the patent has been granted by the patent office of the country concerned.

- Patents concerning the synthesis of Imeglimin and its derivatives

Poxel Reference	Title	Priority date	Expiration date	Status	
				Countries where the patent is issued	Countries where the patent application is in progress
B896	Imeglimin synthesis procedure	4/10/2003	4/6/2024	Australia, Canada, China, Europe, India, France, Japan, South Korea, Mexico, Russia, Taiwan, United States, South Africa	Brazil
B902	Optimization of the first stage of the Imeglimin synthesis procedure	2/2/2008	1/15/2029	Australia, Canada, China, Russia, Europe, Israel, Japan, South Korea, Mexico, United States, South Africa, India	Brazil
B903	New Imeglimin synthesis procedure using a basic method	5/23/2008	4/24/2029	South Africa, Australia, Russia, Europe, Israel, Japan, Mexico, South Korea	Brazil, India
B904	New Imeglimin synthesis procedure using granulometry	7/29/2008	7/28/2029	Australia, Canada, China, Russia, Europe, Israel, Mexico, United States, South Africa, South Korea, Japan, Brazil, India	
B944	New Imeglimin synthesis procedure based on preferential crystallization	3/26/2009	3/26/2030	List B	



B1100	New Imeglimin synthesis procedure using tartaric acid	12/1/2010	11/30/2031	Canada, China, Russia, Europe, Israel, Japan, South Korea, Taiwan, United States, South Africa, Australia, Mexico	Brazil, India
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**Patents concerning the combination of Imeglimin and its derivatives with products already on sale for the treatment of diabetes and its related pathologies**

Poxel Reference	Title	Priority date	Expiration date	Status	
				Countries where the patent is issued	Countries where the patent application is in progress
B897	Combination of Imeglimin with insulin secretagogue products (sulfonylureas, gliptins, glinides, GLP-1 receptor agonists)	1/13/2006	12/18/2026	Australia, Canada, Russia, France, Europe, Israel, India, Japan, Mexico, United States, South Africa	Brazil
B899	Combination of Imeglimin with insulin sensitizing products (metformin, thiazolidinediones)	1/13/2006	12/18/2026	Australia, Canada, Russia, Europe, Israel, India, Japan, South Korea, Mexico, United States, South Africa	Brazil
B900	Combination of Imeglimin with PPARα agonists (fibrates)	1/13/2006	12/18/2026	Russia	
B1561	Combination of Imeglimin with insulin	12/12/2008	11/13/2029	Australia, Russia, Europe, Japan, Mexico, United States, United States (div), South Africa, Canada, Israel, South Korea	India, Brazil

\* • The term “div” means that the filing of a divisional patent application has been undertaken with the patent offices concerned in order to divide the initial application for the patent concerned into several patent applications

**- Patents covering Imeglimin and its derivatives for new therapeutic applications**

Poxel Reference	Title	Priority date	Expiration date	Status	
				Countries where the patent is issued	Countries where the patent application is in progress
B901	Application of Imeglimin for cicatrization	1/13/2006	12/18/2026	Australia, Canada, Russia, France, Israel, South Korea, Mexico, United States, South Africa, Europe	Brazil
B923	Application of Imeglimin for cancer and inflammation	12/12/2008	12/11/2029	Japan, Europe, United States	
B1042	Application of Imeglimin in the prevention of type-1 diabetes	6/9/2010	6/9/2031	List B	
B1043	Application of Imeglimin in the prevention of type-2 diabetes	6/9/2010	6/9/2031	Australia, Canada, Japan, South Korea, Taiwan, South Africa, Israel, Mexico	Brazil, Europe

- Patent held jointly with INSERM

Poxel Reference	Title	Priority date	Expiration date	Status	
				Countries where the patent is issued	Countries where the patent application is in progress
B1053	Application of Imeglimin for the treatment of diseases associated with ischemia and/or reperfusion	7/17/2009	7/16/2030	List B	

### 11.2.3.2. AMPK activators family

- Patents covering new molecules and their therapeutic uses

Merck reference	Title	Priority date	Expiration date	Status	
				Countries where the patent is issued	Countries where the patent application is in progress
P05/204	Application of new AMPK activator structures in the treatment of type-2 diabetes and its related pathologies	8/18/2005	7/28/2026	Australia, Canada, Russia, Europe, Japan, Mexico, Singapore, South Africa	
P06/101	Application of new AMPK activator structures in the treatment of type-2 diabetes and its related pathologies	7/13/2006	6/12/2027	Australia, Canada, Europe, Israel, Japan, United States	
P08/050	Application of new AMPK activator structures in the treatment of type-2 diabetes and its related pathologies	4/11/2008	3/17/2029	Australia, Canada, China, Eurasia, Europe, Hong-Kong, Israel, India, Japan, Mexico, Malaysia, New Zealand, Philippines, Singapore, Ukraine, United States, South Africa, South Korea, Indonesia	Brazil, Colombia, Ecuador
			4/17/2029	Argentina	
P08/063	Application of new AMPK activator structures in the treatment of type-2 diabetes and its related pathologies	5/5/2008	4/30/2029	Argentina	
			4/8/2029	Australia, Canada, China, Colombia, Eurasia, Europe, Hong-Kong, Israel, Japan, Mexico, New Zealand, Philippines, Singapore, Ukraine, United States, South Africa, South Korea, Indonesia, India, Malaysia	Brazil
P08/089	Application of new AMPK activator structures in the treatment of type-2 diabetes and its related pathologies	6/16/2008	6/16/2029	Argentina	
			5/19/2029	Australia, China, Colombia, Eurasia, Europe, Hong Kong, Israel, Japan, Mexico, New Zealand, Philippines, Singapore, United States, United States (div), South Africa, Canada, Indonesia, South Korea, Malaysia, India	Brazil

Poxel Reference	Title	Priority date	Expiration date	Status	
				Countries where the patent is issued	Countries where the patent application is in progress
B993	Application of new AMPK activator structures in the treatment of type-2 diabetes and its related pathologies	12/29/2009	12/28/2030	Australia, Canada, China, Russia, Europe, Israel, India, Japan, South Korea, Mexico, South Africa, Taiwan, United States	Brazil
B1361	Application of new AMPK activator structures in the treatment of type-2 diabetes and its related pathologies	6/29/2012	6/28/2033	South Africa, Australia, Canada, South Korea, Russia, Europe, Japan, United States, China, Israel	Brazil, India, Mexico

### 11.2.3.3. MPC inhibitors group: Patents covering new molecules and their therapeutic uses (including PXL065)

Poxel Reference	Title	Priority date	Expiration date	Status	
				Countries where the patent is issued	Countries where the patent application is in progress
DEU-005	Deuterium-enriched Pioglitazone	09/26/2007	09/19/2028	United States, United States (div.)	United States (div.)
DEU-013	Treatment methods for neurological, metabolic and other disorders, using an enantiomer of deuterium-enriched Pioglitazone	01/15/2014	01/15/2035	United States	United States (div), Europe
DEU-015	Combination therapy based on an enantiomer of deuterium-enriched 5-(benzyl)-5-deutero-thiazolidine-2.4-diones, for the treatment of medical disorders	03/20/2015	03/18/2036		United States
DEU-018	Treatment methods for bacterial infections and fungal infections, using deuterium-enriched Pioglitazone	03/20/2015	03/18/2036		United States

#### 11.2.3.4. MPC inhibitors group: Patents covering new molecules and their therapeutic uses (excluding PXL065)

Poxel Reference	Title	Priority Date	Expiration date	Status	
				Countries where the patent is issued	Countries where the application is in progress
DEU-010	Treatment methods using deuterium-enriched 2.4-thiazolidinediones	03/14/2013	03/14/2034	United States, United States (div.), Europe	United States (div.), Canada, Japan
DEU-016	5-deutero-thiazolidine-2.4-dione compounds and treatment methods for medical disorders	03/20/2015	03/18/2036		United States
DEU-017	5-deutero-thiazolidine-2.4-dione compounds and treatment methods for medical disorders	03/20/2015	03/18/2036		United States

#### 11.2.3.5. Other groups

##### - GLP-1 agonists group: Patents covering new molecules and their therapeutic uses

Merck reference	Title	Priority date	Expiration date	Status	
				countries where the patent is issued	countries where the patent application is in progress
P08/026	Application of new GLP-1 agonist structures in the treatment of type-2 diabetes and its related pathologies	3/5/2008	1/15/2029	Australia, China, Russia, Israel, Japan, South Korea, Mexico, United States, United States (div), South Africa, Canada, Europe, India, Japan (div)	Brazil
P08/027	Application of new GLP-1 agonist structures in the treatment of type-2 diabetes and its related pathologies	3/5/2008	1/15/2029	Australia, Canada, China, Russia, Europe, Israel, Japan, Mexico, United States, United States (div), South Africa, South Korea, India	Brazil
P08/028	Application of new GLP-1 agonist structures in the treatment of type-2 diabetes and its related pathologies	3/5/2008	1/15/2029	Australia, China, Russia, Europe, Israel, Japan, Mexico, United States, United States (div), South Africa, Canada, South Korea, India	Brazil
P08/062	Application of new GLP-1 agonist structures in the treatment of type-2 diabetes and its related pathologies	4/29/2008	3/31/2029	Spain, Germany, France, Great Britain, Italy, Japan, United States, United States (div)	

**FxR agonists group: Patent covering new molecules and their therapeutic uses**

Merck reference	Title	Priority date	Expiration date	Status	
				Countries where the patent is issued	Countries where the application is in progress
P08/151	Application of new FxR agonists in the treatment of Type 2 diabetes and its related pathologies	04/18/2008	30/08/2029	Australia, Canada, China, Colombia, Eurasia, Europe, Hong Kong, Indonesia, Japan, Mexico, New Zealand, Singapore, Ukraine, USA, South Africa, Israel, Japan (div.), Malaysia, India, South Korea	Argentina, Brazil

**- 11-beta-hydroxysteroid dehydrogenase type-1 (11 $\beta$ HSD1) inhibitors group: Patents covering new molecules and their therapeutic uses**

Merck reference	Title	Priority date	Expiration date	Status	
				Countries where the patent is issued	Countries where the patent application is in progress
P05/219	Application of new 11- $\beta$ -HSD1 inhibitor structures in the treatment of type-2 diabetes and its related pathologies	12/16/2005	11/22/2026	Australia, Russia, Europe, Mexico, United States, United States (div), South Africa, Canada, China, Israel, South Korea, Japan, India	Brazil, Singapore
P06/159	Application of new 11- $\beta$ -HSD1 inhibitor structures in the treatment of type-2 diabetes and its related pathologies	11/3/2006	10/5/2027	Australia, Canada, Europe, Israel, Japan, United States, United States (div)	
P06/168	Application of new 11- $\beta$ -HSD1 inhibitor structures in the treatment of type-2 diabetes and its related pathologies	12/21/2006	11/22/2027	Australia, Canada, Europe, Israel, Japan, United States	
P07/113	Application of new 11- $\beta$ -HSD1 inhibitor structures in the treatment of type-2 diabetes and its related pathologies	11/5/2007	10/1/2028	Australia, China, Russia, Europe, Israel, Japan, South Korea, Mexico, Ukraine, United States, South Africa, Canada, India	Brazil
P08/137	Application of new 11- $\beta$ -HSD1 inhibitor structures in the treatment of type-2 diabetes and its related pathologies	9/1/2008	8/5/2029	Australia, China, Russia, Europe, Israel, Japan, Mexico, United States, South Africa, Canada, South Korea, Brazil	

**- Glucokinase activators group: Patents covering new molecules and their therapeutic uses**

Merck reference	Title	Priority date	Expiration date	Status	
				Countries where the patent is issued	Countries where the patent application is in progress
P07/103	Application of new glucokinase activator structures in the treatment of type-2 diabetes and its related pathologies	10/09/2007, 1/23/2008	8/13/2028	List B	
P07/104	Application of new glucokinase activator structures in the treatment of type-2 diabetes and its related pathologies	10/9/2007	9/9/2028	List B	
P08/007	Application of new glucokinase activator structures in the treatment of type-2 diabetes and its related pathologies	1/24/2008	12/23/2028	List B	
P08/020	Application of new glucokinase activator structures in the treatment of type-2 diabetes and its related pathologies	2/25/2008	2/2/2029	Switzerland, Germany, Spain, France, Great Britain, Italy, Japan, Japan (div)	
P08/023	Application of new glucokinase activator structures in the treatment of type-2 diabetes and its related pathologies	2/27/2008	2/3/2029	Israel, South Africa	
P08/024	Application of new glucokinase activator structures in the treatment of type-2 diabetes and its related pathologies	3/1/2008	2/5/2029	List B	

#### 11.2.4. Patents that are pledged

None

### 11.3. Collaboration, research, services and license agreements granted by the Company or granted to it

See Section 22.1 “Merck Serono agreement” of this *document de référence* for a detailed description of the agreement entered into with Merck Serono.

### 11.4. Other intellectual property items

The Company holds the following Poxel word marks:

- Mark No. 3718962 registered in France;
- Mark No. 3964725 registered in the United States;
- International mark No. 1036175, designating Switzerland and Japan.



Poxel's logo and the attached slogan are protected in France under figurative mark No. 3719440:



Poxel owns the URL of its website: [www.poxelpharma.com](http://www.poxelpharma.com).

Moreover, Poxel also owns the following domain names:

poxel.com	imeglimin.be	imeglimine.be
	imeglimin.biz	imeglimine.biz
	imeglimin.eu	imeglimine.eu
	imeglimin.fr	imeglimine.fr
	imeglimin.info	imeglimine.info
	imeglimin.net	imeglimine.net
	imeglimin.org	imeglimine.org

## 12.TREND INFORMATION

### 12.1. Principal trends since the close of the last financial year

During the first few months of 2019, the following information was provided by the Company:

#### 12.1.1. Press release of January 7, 2019: Poxel presents new data on PXL065 at the NASH-TAG 2019 Conference

- The presentation revealed different properties of the stereoisomers of pioglitazone and other thiazolidinediones (TZDs)
- Data obtained on PXL065 suggest a more favorable profile than pioglitazone and other TZDs for the treatment of NASH

On January 7, 2019, POXEL SA, a biopharmaceutical company specializing in the development of innovative treatments for metabolic diseases, including type 2 diabetes and nonalcoholic steatohepatitis (NASH), announced the oral presentation of data on PXL065, the R stereoisomer of pioglitazone stabilized by deuterium substitution at the NASH-TAG 2019 Conference. The presentation, entitled "PXL065, Pioglitazone (pio), and Thiazolidinediones (TZDs): Unraveling Pio's Superior Efficacy for NASH and the Role of Stereoisomers", was given on January 5, 2019 in Park City, Utah, United States.

The presentation highlighted key aspects related to the pharmacokinetic (PK) and pharmacodynamic (PD) roles of stereoisomers belonging to the class of thiazolidinediones (TZD), as well as their potential relevance for the treatment of NASH. Representatives of TZDs include rosiglitazone, pioglitazone and lobeglitazone, all being mixtures of R and S stereoisomers exhibiting interconversion between each stereoisomer. Studies in animals and/or humans have revealed that these compounds have variable efficacy for the treatment of NASH.

The main observations presented were 1) the comparison between the pronounced stereoselectivity of the PK of pioglitazone as a function of the species, and that of other TZDs, 2) the comparison of unexpected differences in activity on the peroxisome proliferator-activated receptor (PPAR) among the eight stereoisomers present in pioglitazone and its two active metabolites, and 3) the stabilization of the stereoisomers of pioglitazone by deuterium substitution to characterize and identify R-pioglitazone as the stereoisomer of choice for NASH treatment.

The data presented demonstrated that each stereoisomer of pioglitazone and its active metabolites have different PPAR $\gamma$  activity. Other data show that PXL065 is a mitochondrial pyruvate carrier (MPC) inhibitor, with no PPAR $\gamma$  activity in a cofactor recruitment assay. Studies of PXL065 in murine models have demonstrated the liver benefits of pioglitazone in patients with NASH. In preclinical models, PXL065 was associated with reduced or no weight gain and fluid retention, these adverse effects being mainly associated with the S stereoisomer of pioglitazone that acts on the PPAR $\gamma$  receptor.

*"The beneficial effects of TZDs in NASH have historically been associated with PPAR $\gamma$  receptor activation, but it is possible that they are rather due to a mitochondrial modulation effect,"* says Thomas Kuhn, CEO of Poxel. "Given that the mechanism of action of PXL065 involves inhibition of the MPC mitochondrial carrier, PXL065 is expected to have beneficial effects on hepatocyte ballooning, inflammation and steatosis, three key therapeutic targets for NASH."

The therapeutic efficacy of pioglitazone (Actos\*), a drug approved for the treatment of type 2 diabetes, has been demonstrated for the treatment of NASH, including in patients with advanced fibrosis. However, its PPAR $\gamma$  receptor-related adverse effects, such as weight gain, bone fractures and

fluid retention, limit its therapeutic use and potential. PXL065 offers a novel approach for the treatment of NASH and could potentially maintain the pharmacologic benefits of pioglitazone required for the treatment of NASH, such as a reduction of steatosis, inflammation, hepatocyte ballooning, and fibrosis in the liver, while reducing PPAR $\gamma$ -associated adverse effects that appear to be associated with the S stereoisomer of pioglitazone.

#### **About the results of PXL065**

PPAR $\gamma$  activity and inhibition of the MPC mitochondrial carrier were measured *in vitro*. Single and multiple dose PK studies were conducted in mice, rats and dogs. Weight gain and edema were evaluated in C57BL/6J mice, and the efficacy on NASH was evaluated in DIO-NASH mouse models.

A single-dose phase study was conducted to evaluate the safety, tolerance and PK of 22.5 mg of PXL065 compared to 45 mg of Actos®. In humans, PK results and modeling indicate that the efficacy of 15 mg of PXL065 on NASH may be potentially similar to that of 45 mg of Actos® with little or no weight gain or fluid retention. As part of the phase I program, the ongoing study with additional single doses will be followed by a study with multiple ascending doses.

#### **About NASH**

Nonalcoholic steatohepatitis (NASH) is a metabolic disease whose origin is poorly understood and which is becoming a global epidemic. It is characterized by an accumulation of lipids in the liver, causing inflammation and fibrosis. The disease may remain silent for a long period of time, but when its course accelerates, it can lead to severe lesions and liver cirrhosis, which can significantly alter liver function, progressing to liver failure or liver cancer. Typical risk factors for NASH are obesity, high blood lipid levels (such as cholesterol and triglycerides) and diabetes. There is currently no available treatment.

#### **About PXL065**

PXL065, formerly known as DRX-065, is the R stereoisomer of pioglitazone stabilized by deuterium substitution. Pioglitazone is a drug that has been the subject of the most advanced studies for the treatment of NASH and allowed for the “resolution of NASH without aggravation of fibrosis” in a phase IV1 trial. Pioglitazone is the only drug recommended by the American Association for the Study of Liver Diseases (AASLD) and the European Association for the Study of the Liver (EASL) in protocols for the treatment of biopsy-proven cases of NASH. However, the use of pioglitazone has been restricted in NASH due to the adverse effects of PPAR $\gamma$ , including weight gain, bone fractures and fluid retention.

Pioglitazone is a mixture, in equal proportions, of two mirror molecules (stereoisomers) that interconvert *in vivo*. By substituting deuterium, DeuteRx successfully stabilized each stereoisomer and defined their diametrically opposite pharmacologic properties. *In vitro* studies have revealed that PXL065 is an inhibitor that targets the MPC. Preclinical models have demonstrated the anti-inflammatory action of PXL065 and its efficacy in NASH with little or no weight gain or fluid retention, which are adverse effects associated with the S stereoisomer. The preclinical and phase I study results suggest that PXL065 has a superior therapeutic profile compared with pioglitazone in the treatment of NASH.

#### **12.1.2. Press release of January 15, 2019: half-year review of the liquidity contract with ODDO Corporate Finance**

Under the liquidity contract concluded by POXEL with ODDO Corporate Finance on December 31, 2018, the following assets were included in the liquidity account:

- Number of shares: 38,100 shares

- Cash balance of the liquidity account: €78,080.26

In the last half-year balance sheet, as of June 29, 2018, the following assets were included in the liquidity account:

- Number of shares: 25,201 shares
- Cash balance of the liquidity account: €148,793.57

During the execution of this contract, the following resources were included in the liquidity account:

- Number of shares: 0 shares
- Cash balance of the liquidity account: €250,000.00

#### 12.1.3. Press release of January 29, 2019: Poxel publishes its 2019 financial agenda

On January 29, 2019, POXEL SA (Euronext - POXEL - FR0012432516), a biopharmaceutical company focused on the development of innovative treatments for metabolic disorders, including type 2 diabetes and non-alcoholic steatohepatitis (NASH), announced today the publication of its financial agenda for 2019.

Event	Date *
Cash and revenues 2018	February 12, 2019
Annual Results 2018	March 21, 2019
Cash and revenues for the first quarter of 2019	April 8, 2019
Cash and revenues for the first half of 2019	July 15, 2019
Half year results 2019	August 26, 2019
Cash and revenues for the third quarter of 2019	October 7, 2019
Cash and revenues 2019	February 12, 2020

\* Subject to change.

#### 12.1.4. Press release of February 12, 2019: Poxel publishes its financial report for the fourth quarter and fiscal year 2018

On February 12, 2019, Poxel, a biopharmaceutical company focused on the development of innovative treatments for metabolic disorders, including type 2 diabetes and non-alcoholic steatohepatitis (NASH), today announced its cash position and sales for the fourth quarter of 2018 and for the twelve months ended December 31, 2018.

At December 31, 2018, cash and cash equivalents were €66.7 million (\$76.4 million).

Poxel reported revenues of €19.6 million for the quarter ended on December 31, 2018, and revenues of €74.6 million for the 2018 financial year, up from revenues of €5.3 million in 2017.

Millions EUR	Q1 2018	Q2 2018	Q3 2018	Q4 2018	2018 12 months	Q1 2017	Q2 2017	Q3 2017	Q4 2017	2017 12 months
Roivant Agreement	8,1	-	-	0,1	8,2	-	-	-	-	-
Sumitomo Agreement	10,2	19,2	17,5	19,5	66,4	-	-	-	5,3	5,3
<b>Total revenues</b>	18,3	19,2	17,5	19,6	74,6	-	-	-	5,3	5,3

Figures not audited

The revenue reflects a portion of the EUR 36 million upfront payment received from Sumitomo Dainippon Pharma relating to the strategic corporate partnership announced on October 30, 2017 and the USD 35 million (EUR 28 million) upfront payment associated with the corporate partnership announced with Roivant Sciences on February 12, 2018, net of Poxel's financial contribution to Roivant. In addition, the revenue also reflects the Imeglimin Phase 3 program costs in Japan incurred during the twelve months ended December 31, 2018 that were re-invoiced to Sumitomo Dainippon Pharma. Both the upfront payment from Sumitomo Dainippon Pharma and re-invoiced costs of the Phase 3 Trials of IMeglimin for Efficacy and Safety (TIMES) program are recognized according to the percentage of completion for this program.

*"I am very pleased to report that we made substantial progress advancing the Company in 2018. Our significant accomplishments include signing an agreement with Roivant Sciences for Imeglimin in the US, Europe and the rest of the world not covered in the agreement with Sumitomo Dainippon Pharma, fully enrolling all three Imeglimin Phase 3 TIMES trials with over 1,100 patients in Japan, advancing PXL770 for the treatment of NASH and acquiring PXL065, a second clinical-stage program for the treatment of NASH" said Thomas Kuhn, CEO of Poxel.*

*"This year will be very important for Imeglimin beginning early in the second quarter with the Phase 3 TIMES 1 monotherapy double-blind placebo-controlled randomized efficacy top-line results, which will be followed by top-line data for the TIMES 3 16-week double-blind placebo-controlled randomized part of the study expected mid-year. For the TIMES 2 and the full TIMES 3 data, including the additional 36-week open-label part of the study, top-line results are anticipated during the fourth quarter of 2019. In parallel to leading the Phase 3 TIMES program, we have been working very closely with our partner Sumitomo Dainippon Pharma in preparing for the Japanese New Drug Application for Imeglimin for the treatment of type 2 diabetes, which is targeted for 2020," said Thomas Kuhn, CEO of Poxel. "For the United States and Europe, we are collaborating with Roivant Sciences and Metavant, a company formed by Roivant Sciences to develop innovative therapies for metabolic disorders, on advancing the Imeglimin clinical program. This program will initially target patients with type 2 diabetes and moderate-to-severe chronic kidney disease (CKD stages 3b/4) and includes a dedicated clinical trial that is currently ongoing".*

*"In addition, PXL770 for the treatment of NASH is expected to enter a Phase 2a program during the first quarter of 2019. For PXL065, we plan to initiate the Phase 2 program for the treatment of NASH during second half of 2019 following the completion of the Phase 1 program," continued Thomas Kuhn. "We have expanded our presence in NASH and are one of only a few biotech companies with two clinical programs in development in this therapeutic area. The underlying pathophysiological mechanisms that contribute to the development and progression of nonalcoholic fatty liver disease and NASH are highly complex and support the need for the development of novel therapies acting on different targets. Both of our programs have the potential to be developed as a monotherapy or in combination together or with other agents".*

**12.1.5.** Press release of March 18, 2019: Poxel announces its participation in the Oppenheimer 29<sup>th</sup> Healthcare Conference

On March 18, 2019, Poxel, a biopharmaceutical company focused on the development of innovative treatments for metabolic disorders, including type 2 diabetes and non-alcoholic steatohepatitis (NASH), announced today that it will participate in the 29th Annual Healthcare Conference (Oppenheimer 29th).

The Oppenheimer 29th Healthcare Conference will be held on March 19-20, 2019 at the Westin New York Grand Central Hotel in New York City. The Company invites investors to a general presentation of its activities on Tuesday, March 19, from 3:55 p.m. to 4:25 p.m. New York time, in the Consulate Room and will be available to participate in one-on-one meetings. The presentation at the Oppenheimer Healthcare Conference will be webcast live..

**12.1.6.** Press release of March 21, 2019: Poxel announces its 2018 annual results and reviews its activities

- Implementation of the strategic partnership for Imeglimine with Roivant Sciences, with payments linked to the achievement of regulatory development and sales objectives, up to \$600 million, and royalties on revenues
- Investment of Roivant in Poxel's capital of \$15 million (approximately €12 million) by subscribing for new ordinary shares at a price of €8.5 per share
- Imeglimine Phase III TIMES program conducted in Japan in partnership with Sumitomo Dainippon Pharma as planned, first results are expected in early second quarter 2019
- Expansion of the product portfolio targeting metabolic diseases through the acquisition from DeuteRx LLC of PXL065 (DRX-065), a new drug-candidate in the clinical stage for NASH, as well as other programs
- Ongoing clinical development of PXL770 and PXL065 for the treatment of NASH

On March 21, 2019, Poxel, a biopharmaceutical company focused on the development of innovative treatments for metabolic disorders, including type 2 diabetes and non-alcoholic steatohepatitis (NASH), announced today its results for the year ended December 31, 2018 and presented a review of its activities.

*"We made significant progress in the development of the Company in 2018, including: the signature of an agreement with Roivant Sciences for Imeglimine in the United States, Europe and other countries of the world not covered by the agreement with Sumitomo Dainippon Pharma, the completion of recruitment for the three Phase III TIMES studies, with more than 1,100 patients enrolled in Japan, the continued development of PXL770 for the treatment of NASH and the acquisition of PXL065, a second program in clinical development for the treatment of NASH"* explains Thomas Kuhn, Chief Executive Officer of Poxel.

*"This year will be a particularly important year for Poxel, with several significant milestones, each representing significant value creation potential. For Imeglimine, the main milestones are the announcement of the results of the Phase III program, starting with the results of TIMES 1, which we expect to publish at the beginning of the second quarter of 2019, followed by those of TIMES 2 and TIMES 3, which will be announced during 2019. In parallel to the progress of the TIMES Phase III program, we worked closely with our partner Sumitomo Dainippon Pharma to prepare the submission of the registration dossier for Imeglimine in Japan for the treatment of type 2 diabetes. This key milestone is expected in 2020, with a product launch planned for 2021"* continues Thomas Kuhn, Chief Executive Officer of Poxel.

*"For our two clinical programs for the treatment of NASH, the main milestones will be the launch of a Phase IIa program for PXL770, which will include a study to evaluate the efficacy and safety of the product, as well as a separate study to evaluate its pharmacokinetic and pharmacodynamic profile. The first results should be published this year"* says Thomas Kuhn. *"For PXL065, we plan to launch a pivotal Phase II program in the treatment of NASH in the fourth quarter of 2019 or early 2020, following the Phase I study, the results of which are expected between mid-year and the third quarter of 2019".*

**Highlights for Poxel in 2018**

## **Imeglimine**

Imeglimine is the first oral drug-candidate to act simultaneously on all three key organs involved in diabetes: pancreas, liver and muscles. Following the success of Phase I and II clinical development in more than 1,200 patients in the United States, Europe and Japan, Imeglimine is currently in a Phase III study in Japan. Several important milestones were achieved in 2018, the main ones are detailed below.

### **Signing of a strategic partnership agreement for Imeglimine in the United States, Europe and other countries around the world**

- The strategic agreement with Roivant covers the development and commercialization of Imeglimine in the United States, Europe and other countries of the world not covered by the partnership agreement between Poxel and Sumitomo Dainippon Pharma
- Actions carried out in 2018 with Metavant, a subsidiary of Roivant, in preparation for the Phase III program include the ongoing study of patients with type 2 diabetes with moderate to severe chronic renal failure, as well as the manufacture of treatment units for Phase III.
- Metavant aims to launch the Phase III program in 2019.

### **Progress of the TIMES Phase III program**

- More than 1,100 patients were enrolled in three pivotal studies evaluating the efficacy and safety of Imeglimine as part of the Phase III TIMES (Trials of IMeglimin for Efficacy and Safety) program in Japan.
- The announcement of the results of the TIMES Phase III program is expected in 2019, starting with the first results of the TIMES 1 study, scheduled for early in the second quarter. The first results of the TIMES 3 study, after 16 weeks of treatment, randomized, double-blind versus placebo, are expected at mid-year, and the results of the TIMES 2 study as well as the complete results of the TIMES 3 study are expected in the fourth quarter of 2019.
- The purpose of the multicenter, randomized, double-blind, placebo-controlled study, TIMES 1, is to evaluate Imeglimine as monotherapy in more than 200 Japanese patients with type 2 diabetes. The open-label study TIMES 2 aims to evaluate the long-term efficacy and safety of Imeglimine as monotherapy or in combination with existing anti-diabetic drugs in approximately 700 Japanese patients with type 2 diabetes. The randomized, double-blind, placebo-controlled, open-label, open-label trial, TIMES 3, aims to evaluate the efficacy and safety of Imeglimine in combination with insulin in more than 200 Japanese patients with type 2 diabetes associated with inadequate insulin glycemic control.

### **Data presented at the 78th scientific conference of the American Diabetes Association**

- Data demonstrating the protective effect of Imeglimine on beta cells of the pancreas were presented at the 78th scientific conference of the American Diabetes Association. These data show that Imeglimine protects and preserves human beta cells from cell death induced by glucose and fructose toxicity, by inhibiting the opening of the mitochondrial Permeability Transition Pore (mPTP). These data highlight the potential of Imeglimine to delay the onset and progression of type 2 diabetes by preserving beta cell mass.

## **PXL770**

PXL770 is a direct activator of adenosine monophosphate activated protein kinase (AMPK), the first of its kind. AMPK plays an essential role as the main regulator of cellular energy, and its activity offers the opportunity to target a wide range of therapeutic indications in chronic metabolic diseases, including liver diseases such as NASH.

- Preclinical proof-of-concept data presented at the 2018 Global NASH Congress highlighted the new approach of PXL770 in the treatment of non-alcoholic hepatic steatosis (NAFLD), improving the main symptoms of the disease. PXL770 was associated with a significant reduction in hepatic steatosis and NAS score after 8 weeks of treatment, compared to controls, as well as a significant reduction in the expression of a panel of key genes associated with fibrosis.
- Data presented at the AASLD (American Association for the Study of Liver Diseases) meeting in November 2018 demonstrated a beneficial effect of PXL770 on both adipose tissue and liver by direct activation of AMPK in a DIO-NASH animal model.
- Data from the Phase I clinical program, presented at the AMPK Scientific Congress - From Mechanisms to New Therapies - in October 2018, showed that PXL770 had a favorable pharmacokinetic, safety and tolerability profile, as well as a favorable heart safety profile in animal models.
- The PXL770 Phase IIa program is expected to start in the first quarter of 2019. The twelve week Phase IIa efficacy and safety study will measure the evolution of liver fat mass based on MRI evaluation of the lipid fraction per proton density (MRI-PDFF). It will also evaluate the effects of PXL770 on key metabolic pathways involved in the pathophysiology of NASH, as well as safety and other metabolic and non-metabolic parameters in approximately 100 patients at risk of developing NASH.
- The Phase IIa program will also include a separate pharmacokinetic and pharmacodynamic study, which is expected to begin in the second quarter of 2019.

#### **PXL065 (DRX-065)**

PXL065 (R-pioglitazone stabilized by deuterium substitution) is a pyruvate mitochondrial transporter (PMT) inhibitor. PXL065 is the R stereoisomer (single isomer) of pioglitazone.

- On August 30, 2018, Poxel obtained from DeuteRx the worldwide exclusive ownership of PXL065, a drug-candidate in clinical development for the treatment of NASH, as well as other programs, including deuterated drug-candidates for the treatment of rare and specialty metabolic diseases.
- Poxel made an upfront payment to DeuteRx of €6.8 million (US\$8 million), and 1.29 million new ordinary shares of Poxel, representing 4.99% of Poxel's capital. DeuteRx may also receive milestone payments related to the achievement of development, regulatory and sales objectives, and royalties on net sales.
- Data presented at the AASLD congress in November 2018 suggest that PXL065 may have the same efficacy on NASH as pioglitazone, but with reduced adverse side effects.
- On November 26, 2018, Poxel launched the second part of the Phase Ia study of PXL065, in which 6 healthy subjects were enrolled in each group, with the primary objective of evaluating safety and tolerance and the secondary objective of evaluating the effect-dose relationship.
- Following Phase I, which includes a multiple increasing dose study, Poxel plans to initiate a pivotal Phase II program for the treatment of NASH in the fourth quarter of 2019 or early 2020.

#### **Development of the company**



- In September 2018, Poxel appointed Dr. Takashi Kaneko as Medical Vice President and President of Poxel Japan K.K. The Company also opened a Japanese subsidiary in Tokyo.

### IFRS results for the 2018 financial year

Poxel generated revenues of €74.6 million during the twelve months ended 31 December 2018, compared with €5.3 million for the same period in 2017.

2018 revenue includes a portion of the €36 million upfront payment received from Sumitomo Dainippon Pharma as part of the strategic partnership announced on October 30, 2017, and the \$35 million (€28 million) upfront payment received from Roivant Science as part of the strategic partnership announced on February 12, 2018, net of the \$25 million (€20.5 million) fixed contribution from Poxel as part of this agreement. Revenues also reflect the re-invoicing to Sumitomo Dainippon Pharma of Phase III development costs for Imeglimine in Japan in fiscal year 2018. The upfront payment received from Sumitomo Dainippon Pharma and the re-invoicing of costs for Phase III of the Trials of IMeglimin for Efficacy and Safety (TIMES) program are recognized based on the progress of costs incurred in this program.

### Income statement

Poxel dedicates most of its financial resources to its research and development (R&D) activities, which raised a total of €54.5 million in 2018, compared with €21 million in 2017. R&D expenses in 2018 mainly reflect the costs of the Phase III clinical trial of Imeglimine's TIMES program, most of which was re-invoiced to Sumitomo Dainippon Pharma. On a lesser scale, these expenses also represent the costs incurred by the Company in connection with the two clinical programs for PXL770 and PXL065 for the treatment of NASH. The 160% increase in R&D expenses in 2018 compared to the previous year is mainly due to the TIMES Phase III programme, which started at the end of December 2017.

R&D expenses are net of the research tax credit (*crédit d'impôt recherché - CIR*), which represents income of €3.6 million in 2018, compared with €3.1 million in 2017.

General and administrative expenses amounted to €7.5 million in 2018, compared with €6.2 million in 2017.

The financial result is positive and amounts to €1.1 million in 2018, compared to a loss of €0.4 million in 2017. The financial result for 2018 consists of investment income and foreign exchange gains.

Net income for the year ended on December 31, 2018 represents a net profit of €13.5 million, compared with a net loss of €22.3 million in 2017.

### Simplified income statement (in thousands of euros)

	12/31/2018	12/31/2017
<b>Revenues</b>	<b>74 605</b>	<b>5 290</b>
Net research and development expenses*	(54 540)	(20 973)
General and administrative expenses	(7 527)	(6 219)
Operating result	12 538	(21 902)
Financial result	1 064	(396)
Income tax expense	(77)	
<b>Net Result</b>	<b>13 525</b>	<b>(22 298)</b>

\* Net of the research tax credit (*credit d'impôt recherche*)

The audit procedures have been carried out and the auditors' report is in progress

## Cash position

On December 31, 2018, cash and cash equivalents amounted to €66.7 million (\$76.4 million), compared to €53.4 million (\$64.1 million) on December 31, 2017.

This amount includes the upfront payment and investment from Roivant Sciences received in February 2018 for a total amount of \$50 million, as well as the acquisition of DeuteRx's deuterated drug-candidates for an upfront payment of \$8 million.

### 12.1.7. Press release of April 1st, 2019: Poxel announces the launch of the PXL770 Phase Ila, a direct AMPK activator, in the treatment of NASH

- The Phase Ila program will include two separate studies
- The Phase Ila study, which assesses the efficacy and safety of PXL770 has started. Its results are expected in the first half of 2020.
- The pharmacokinetics and pharmacodynamics study is expected to start in the second quarter of 2019. Its results are expected in the second half of 2019.

On April 1st, 2019, Poxel, which is a biopharmaceutical company focused on the development of innovative treatments for metabolic disorders, including type 2 diabetes and non-alcoholic steatohepatitis (NASH), announces today the launch of its Phase Ila clinical program for PXL770, a direct activator of adenosine monophosphate activated protein kinase (AMPK), in the treatment of NASH.

The Phase 2a twelve-week, multicenter, randomized, double-blind, placebo-controlled, parallel group study, which will assess efficacy and safety, has been initiated. In this study, three doses of PXL770 versus placebo will be administered. Approximately 100 nonalcoholic fatty liver disease (NAFLD) patients who likely have NASH are expected to be included in this study across clinical sites in the US. The primary endpoint of the study will measure the change in liver fat mass based on magnetic resonance imaging-estimated proton density fat fraction (MRI-PDFF), a novel imaging-based biomarker that allows fat mapping of the entire liver. The study will also assess the effects of PXL770 on other metabolic and non-metabolic biomarkers as well as safety and tolerability. In addition, the effect of PXL770 on hepatic *de novo* lipogenesis (DNL) and glucose tolerance, will be investigated. Data results from the Phase 2a study are anticipated in the first half of 2020.

In addition to the Phase 2a study, a separate four-week PK/PD study is expected to be initiated during the second quarter of 2019. During this study, PXL770 will be administered to approximately 32 patients. This study will assess the PK profile of PXL770 in NAFLD patients and its effects on hepatic and metabolic parameters in the target population. Data results from this study are expected during the second half of 2019.

"AMPK is a major regulator of energy metabolism and its activation is expected to show beneficial effects in metabolic diseases, such as NASH," said Pascale Fouqueray, MD, PhD, EVP, Translational Medicine and Early Clinical Development at Poxel. "Supported by positive preclinical mechanistic and efficacy results in a DIO-NASH model, we believe that PXL770 is uniquely positioned to treat the underlying root causes of fatty liver diseases as well as to specifically target each step of the pathophysiology of the disease, including liver steatosis, inflammation, ballooning and fibrosis. PXL770 may also provide benefits for co-morbidities, including those related to cardiovascular disease."

*"By targeting the master regulator of cellular energy, PXL770 has a unique and differentiated profile compared to other drug candidates in development for the treatment of NASH," said Thomas Kuhn, CEO of Poxel. "With the acquisition of PXL065, a mitochondrial pyruvate carrier inhibitor, we have*

*expanded our presence in NASH, and we are one of only a few biotechnology companies with two clinical programs in development for this disease. The underlying pathophysiological mechanisms that contribute to the development and progression of NAFLD and NASH are highly complex and support the need for the development of novel therapies that act on different targets. Both of our programs have the potential to be developed as monotherapy or in combination together or with other agents.”*

Poxel previously announced data results from a Phase 1b multiple ascending dose trial and a drug-drug interaction study of PXL770 in a press release titled, “*Poxel Announces Favorable Results for PXL770 Phase 1b Multiple Ascending Dose Trial and Drug-Drug Interaction Study.*”

**12.2. Known tendency, uncertainty, request for commitment or events reasonably likely to affect the prospects of the Company**

None

### **13. PROFIT FORECASTS OR ESTIMATES**

The Company does not communicate any profit forecast or estimates.

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

### 14.1. General information on founders, management and directors

The Company is a French société anonyme à Conseil d'administration (public limited company with a Board of Directors), where the positions of Chairman and CEO are separate.

A descriptive summary of the main provisions of the bylaws of the Company and the internal regulations of the Board of Directors and specialized Committees (the “**Committees**”) are set out respectively in Sections 21.2 “Certificate of incorporation and bylaws” and 16.316.3 “Specialized Committees” of this *document de référence*.

#### 14.1.1. Composition of the Board of Directors and the Committees

At the date of this *document de référence*, the Board of Directors of the Company is composed as set forth in the table below.

First name, last name, position (nominated for three years)	Independent director	Date of nomination, renewal and term
Pierre Legault Chairman of the Board of Directors and director	No	Nomination: GM of 1/29/2016 Term: OGM ruling on the financial statements for the financial year ended 12/31/2018
Thomas Kuhn Director and Chief Executive Officer	No	Nomination: GM of 6/23/2010 Renewals: GM of 4/15/2014, GM of 6/30/2017 Term: OGM ruling on the financial statements for the financial year ended 12/31/2019
Thierry Hercend Director	No	Nomination: GM of 6/23/2010 Renewals: GM of 4/15/2014, GM of 6/30/2017 Term: OGM ruling on the financial statements for the financial year ended 12/31/2019
Khoso Baluch Director	Yes	Nomination: GM of 10/31/2012 Renewals: GM of 4/15/2014, GM of 6/30/2017 Term: OGM ruling on the financial statements for the financial year ended 12/31/2019
Richard Kender Director	Yes	Nomination: GM of 1/8/2015 Renewal: GM of 6/21/2018 Term: OGM ruling on the financial statements for the financial year ended 12/31/2020
Pascale Boissel Director	Yes	Nomination: Board meeting of 3/5/2015 (ratification by GM of 6/16/2015) Renewal: GM of 6/30/2017 Term: OGM ruling on the financial statements for the financial year ended 12/31/2019
Janice Bourque Director	Yes	Nomination: GM of 1/29/2016 Term: OGM ruling on the financial statements for the financial year ended 12/31/2018
Kumi Sato Director	Yes	Nomination: GM of 6/30/2017 Term: OGM ruling on the financial statements for the financial year ended 12/31/2019
Thibaut Roulon Observer	--	Nomination: GM of 3/28/2014 Renewal: GM of 6/30/2017

		Term: OGM ruling on the financial statements for the financial year ended 12/31/2019
Bpifrance Participations Permanent representative: Laurent Higuieret Observer	--	Nomination: GM of 7/25/2014 Renewal: GM of 6/30/2017 Term: OGM ruling on the financial statements for the financial year ended 12/31/2019
Bpifrance Investissement Permanent representative: Olivier Martinez Observer	--	Nomination: GM of 6/30/2017 Term: OGM ruling on the financial statements for the financial year ended 12/31/2019
Andera Partners Permanent representative: Raphaël Wisniewski Observer	--	Nomination: GM of 6/30/2017 Term: OGM ruling on the financial statements for the financial year ended 12/31/2019

At the date of this *document de référence*, the Company's Committees are made up as indicated in the table below:

First name, last name, position	Audit Committee	Compensation Committee	Business Development Committee	Scientific Advisory Committee	Appointments and Governance Committee	Strategic and Pricing Committee
Pierre Legault Chairman of the Board of Directors and director	Member	Member	Member	Member	Member	Member
Thomas Kuhn Director and Chief Executive Officer	Member*	Member*	Member	Member	Member*	Member
Thierry Hercend Director	--	--	--	Chairman	--	--
Khoso Baluch Director	--	Chairman	Member	Member	--	
Richard Kender Director	Member	Member	Chairman	--		Member
Pascale Boissel Director	Chairman	--	--	--	Member	
Janice Bourque Director	Member	--	--	--	Chairman	
Kumi Sato Director			Member			

\* As observer

Directors (the “**Directors**”) are appointed for a renewable term of three years. The Chairman is appointed for the length of his tenure as director.

The Company complies with the provisions of Article L. 225-37-4 Sub-paragraph 6 of the French Commercial Code relating to the diversity policy applied to members of the Board of Directors with regard to criteria such as age, gender or qualifications and professional experience. In fact, the members of the Board of Directors come from a variety of backgrounds, in terms of both geography (France, United States, Japan, Canada) and experience. Members of the Board of Directors are renowned professionals in the industry in which the Company operates and have significant financial, strategic and scientific expertise. The Company's objective is to maintain a policy of diversity in terms of experience and parity of Board members for future renewal of the terms of office of Board members

or the nomination of new Board members. The Board of Directors has applied these principles to the composition of its Committees, in particular the Audit Committee and the Governance and Compensation Committee. As of the Ordinary General Meeting of Shareholders of June 30, 2017, the Company's Board of Directors consists of eight members, of which three women. Finally, the Company supports a balanced representation of women and men in positions of greater responsibility. In particular, women represent approximately 50% of the Company's employees in the most senior positions, representing nearly 10% of the workforce.

The business address of the Chairman of the Board of Directors and the CEO is the Company's registered office.

The business addresses of the other Directors are as follows:

- Mr. Thierry Hercend: 3 rue Angelique Verien, 92200 Neuilly-sur-Seine;
- Mr. Khoso Baluch: 4439 Woods Edge Court, Chantilly, VA 20151, USA;
- Ms. Pascale Boissel: 31 avenue des cottages - 69300 Caluire;
- Mr. Richard Kender: 8775 W. Orchid Island Circle Vero Beach, Florida 32963, USA;
- Ms. Janice Bourque: Hercules Capital Inc., 31 St. James Avenue, Suite 790, Boston, MA 02116, USA.
- Ms. Kumi Sato: Cosmo Public Relations Corporation, Azabukaisei Building., 1-8-10 Azabudai, Minato-ku, Tokyo 106-0041 Japan

The expertise and management experience of these persons stem from various employment and management positions they hold and which they have previously held (refer to Sections 14.1.2 "Other current corporate offices and positions held in the last five years" and 14.1.3 "Directors' biographies" of this *document de référence*).

There are no family ties between the people listed above.

Over the last five years, none of these people:

- has been convicted of fraud;
- has been associated in his capacity as a manager or director in a bankruptcy, receivership or liquidation;
- has been subject to a disqualification from management;
- has been subject to incriminations or official public sanctions imposed by statutory or regulatory authorities.

#### **14.1.2. Other current corporate offices and functions**

At the date of this *document de référence*, the other current corporate offices or functions held by the directors, as well as the corporate offices or functions held by the directors during the last five financial years but having ended, are:

Name	Current corporate offices		Positions held in the last five years	
	Companies	Nature of mandate or position	Companies	Nature of mandate or position
Pierre Legault	Syndax Pharmaceuticals *  Clementia  Urovant  Stone Sunny Isles Inc.  Artios Pharma	Member of the Board of Directors  Member of the Board of Directors  Member of the Board of Directors  CEO  Member of the Board of Directors	<i>Prosidion Ltd</i> <i>OSI Pharmaceuticals, Inc.</i> <i>Forest Laboratories</i> <i>NPS Pharmaceuticals</i> <i>Regado Biosciences</i> <i>Oreo Real Estate</i> <i>Tobira Therapeutics</i> <i>Nephrogenex</i> <i>Iroko Pharmaceuticals</i> <i>Armo Biosciences</i> <i>Sempra</i>	<i>Chairman - CEO</i> <i>Director of Finances and Treasurer</i> <i>Member of the Board of Directors</i> <i>Member of the Board of Directors</i> <i>Member of the Board of Directors</i> <i>Member of the Board of Directors</i> <i>Member of the Board of Directors</i> <i>Member of the Board of Directors</i> <i>Member of the Board of Directors</i> <i>Member of the Board of Directors</i> <i>Member of the Board of Directors</i> <i>Chairman and Member of the Board of Directors</i>
Thomas Kuhn	Poxel Japan KK  Poxel Inc.	CEO  Chairman	None	
Thierry Hercend	Andera Partners	Venture Partner	<i>Oncoethix</i> <i>Genticel</i> <i>Complix</i> <i>Inotrem</i> <i>Gamamabs</i> <i>Greywolf</i>	<i>Member of the Board of Directors</i> <i>Chairman of the Supervisory Board</i> <i>Member of the Board of Directors</i> <i>Chairman of the Board of Directors</i> <i>Chairman of the Board of Directors</i> <i>Member of the Board of Directors</i>
Khoso Baluch	CorMedix *	CEO and Member of the Board of Directors	<i>Vedim Pharma S.A. (Spain)</i> <i>UCB Pharma Ltd (Spain)</i> <i>UCB Inc. (United States)</i>	<i>Manager</i>  <i>Manager</i>  <i>Member of the Board of Directors, Senior Vice-President and President of the region of Europe</i>



Name	Current corporate offices		Positions held in the last five years	
	Companies	Nature of mandate or position	Companies	Nature of mandate or position
			<p>UCB Pharma Ab (Sweden)</p> <p>UCB A.E (Greece)</p> <p>UCB Pharma A.S (Norway)</p> <p>UCB Pharma Sp. z.o.o. (Poland)</p> <p>UCB Pharma Ltd</p> <p>UCB</p>	<p>Chairman of the Board of Directors</p> <p>Chairman of the Board of Directors</p> <p>Chairman of the Board of Directors</p> <p>Chairman of the Management Committee</p> <p>Member of the Board of Directors</p> <p>Vice-President and President of the EMEA region of UCB</p>
Richard Kender	<p>Seres Therapeutics *</p> <p>Abide Therapeutics</p>	<p>Member of the Board of Directors</p> <p>Member of the Board of Directors</p>	<p>INC Research</p> <p>Merck &amp; Co., Inc.</p>	<p>Member of the Board of Directors</p> <p>Vice President</p>
Pascale Boissel	<p>Enyo Pharma</p> <p>Novadiscovery</p>	<p>CFO</p> <p>CFO</p>	Bioaster	Deputy-Chief Executive Officer - Administrative and Financial Director
Janice Bourque	<p>Hercules Capital *</p> <p>The Village Bank</p> <p>Springboard Enterprises</p> <p>TBS Technologies LLC</p> <p>Forsyth Institute</p> <p>Crystal Lake Conservancy</p> <p>Hyde Community Center</p> <p>173 Lincoln St Condo Association</p> <p>Commodore Builders</p> <p>Rhia Ventures</p>	<p>Managing Director, Life Sciences</p> <p>Member of the Board of Directors</p> <p>Member of the Life Science Committee</p> <p>Member of the Consultation Committee</p> <p>Member of the Board of Directors</p> <p>Co-Chairman</p> <p>Member of the Board of Directors</p> <p>Trustee</p> <p>Member of the Board of Directors</p> <p>Member, Investment Advisory Board</p>	None	

Name	Current corporate offices		Positions held in the last five years	
	Companies	Nature of mandate or position	Companies	Nature of mandate or position
Kumi Sato	COSMO	Chairman - CEO	None	

(\*): Listed companies in France and/or other countries

### 14.1.3. Biographies of the Directors



#### **Pierre Legault**

##### *Chairman of the Board of Directors*

Pierre Legault has served as a member of the Company's Board of Directors since January 2016 and as Chairman of the Board of Directors since March 2016. He has over 35 years of experience working in the pharmaceutical and biotechnology industry. Pierre Legault has also been a director of the Artio Pharma Company since February 2018. He is also a director of Syndax Pharmaceuticals and Clementia. In the past he has been a director with multiple companies, including Tobira Therapeutics, Armo Biosciences, NPS Pharmaceuticals, Forest Laboratories, Regado Biosciences, Iroko Pharmaceuticals, Cyclacel Pharmaceuticals, Eckerd Pharmacy and NephroGenex, a biotechnology company specialized in treatment of kidney diseases, where he was CEO from 2012 to 2016. From 2010 to 2012, he served as the Chairman and Chief Executive Officer of Prosidion Ltd., specialized in the treatment of diabetes and obesity. From 2009 to 2010, he served as the Executive Vice President, Chief Financial Officer and Treasurer of OSI Pharmaceuticals. Mr. Legault also served as the President of Eckerd Pharmacies and Executive Vice-President of Rite Aid Corporation. Between 1989 and 2005, he held various roles, such as Chairman and Chief Financial Officer of various companies of the Sanofi-Aventis group. Mr. Legault holds an M.B.A. in Marketing from McGill University (Canada) and a Bachelor's degree from HEC (France). He also studied at Harvard Business School.



#### **Thomas KUHN**

##### *Chief Executive Officer, Director*

Thomas Kuhn began his career with Merck KGaA in 2000 where he held various positions in clinical development, mainly in the therapeutic area of Type 2 diabetes and was responsible, in particular, for forging partnerships with Japanese pharmaceutical laboratories. Between 2004 and 2007, he directed Merck's global R&D projects with two products in Phase 2 clinical trials and all life-cycle management projects, primarily for Glucophage®, the current reference in diabetes treatment.

Following Merck's acquisition of Serono in 2007, Thomas Kuhn was part of the team which refined Merck Serono's strategy for divesting from the diabetes therapeutic area. Thomas Kuhn initiated and concluded the project for the transfer of Merck Serono's assets under development in Diabetes to a new legal entity called Poxel. Since this transfer, Thomas Kuhn has been Poxel's Chief Executive Officer.

Mr. Kuhn holds a pharmacy degree from the University of Lyon I (France) and an M.B.A. from Ashridge University (UK).



**Thierry HERCEND**

*Director*

Thierry Hercend, M.D., Ph.D., has over 30 years of experience in both academia and the pharmaceutical industry, in various therapeutic areas including oncology and inflammatory diseases. Since 2006 Thierry Hercend has been a Venture Partner with Andera Partners. From 2002 to 2005, Thierry Hercend was Vice President in charge of the oncology therapeutic area at Aventis. From 1998 to 2002, he was Vice President of Research, Europe at Vertex Pharmaceuticals. Hercend joined the pharmaceutical industry in 1990 as director of the immunology therapeutic area and then scientific director of the healthcare division at Roussel-Uclaf.

Prior to joining the pharmaceutical industry, Dr. Hercend was Head of the Hemato-Immunology Unit of the Gustave Roussy Cancer Institute, Villejuif, France, Director of Inserm Unit U333 with a focus on tumor immunology, and Professor of Immunology at the Medical Faculty of Paris XI University.

Thierry Hercend has authored more than 120 publications in oncology, autoimmune diseases and transplantation.



**KHOSO BALUCH**

*Independent director*

Khoso Baluch has been a director of the Company since 2012. He retired as a Senior Vice President and President of the Europe Region of UCB, an international biopharmaceutical company, in 2016, after having worked there since 2008. Before joining UCB, Khoso Baluch worked for Eli Lilly & Co. for 24 years, holding international positions spanning Europe, the Middle East and the United States in general management, business development, market access and product leadership. From 2002 to 2008, Khoso Baluch also served as Vice President of the US Diabetes and Family Health Business Unit during his tenure at Lilly. Mr. Baluch also served as a member of the board of the Juvenile Diabetes Research Foundation, Indiana Chapter. Khoso Baluch was also a member of the National Industry Advisory Council of the American Diabetes Association and the Executive Committee of the World Federation of Advertisers (WFA). He holds a Bachelor of Sciences Degree from the City of London University and an MBA from Cranfield University.



**Richard Kender**

*Independent director*

Rich Kender has served as a member of our board of directors since 2015. Mr. Kender joined Merck & Co., Inc. in 1978, and served as Merck's Vice President of Corporate Development from 1996 to 2000. In 2000, he was promoted to Senior Vice President and his responsibilities were expanded to include Corporate Licensing and Worldwide Business

Development, where he managed Merck's Mergers and Acquisitions, Licensing, Financial Evaluation and Analysis and Global Competitive Intelligence departments. Mr. Kender left Merck in September 2013. Mr. Kender is currently a director and member of the audit committees of Seres Therapeutics and of Abide Therapeutics. He holds a Bachelor of Science degree in Accounting from Villanova University and an M.B.A. from Fairleigh Dickinson University.



**Pascale Boissel**

*Independent director*

Pascale Boissel has served as a member of our board of directors since 2015. She is also a Finance and Administration Director of EnyoPharma, a French biotechnology company specialized in the treatment of liver diseases that also studies other therapeutic areas using an original approach inspired by biomimetism. She also assists small biotech companies and Life Science projects in their financial strategy and their operations. These include Novartis, a company developing InSilico models and simulations to speed up the identification and development of new drugs. Before that, she was the Deputy-Chief Executive Officer and Head of Finance and Administration of the BIOASTER institute, a French not-for-profit organization that develops collaborative research programs in the field of infectious diseases and microbiology. She has held this position since 2012. From 2009 to 2012, Ms. Boissel has been the Financial Director of Ipsogen, a molecular diagnostics company. She holds an M.B.A. from HEC (Paris) and is also a certified accountant.



**Janice Bourque**

*Independent director*

Janice Bourque has served as a member of our Board of Directors since January 2016. She has served as the Managing Director, Life Sciences of Hercules Technology Growth Capital Inc., a technology and life science specialty finance company, since 2010. From 2009 to 2010, Ms. Bourque served as a consultant for Commons Capital, where she engaged in fund raising. From 2005 to 2009, she served as the Senior Vice President and Group Head-Life Sciences at Comerica Bank in Boston, Massachusetts. Ms. Bourque also held the position of President and Chief Executive Officer of the Massachusetts Biotechnology Council, the oldest biotechnology trade association in the world, where she was instrumental in its growth from 1992-2004. Ms. Bourque currently serves on the Board of Directors and on the Audit, Governance and Compensation Committees of the Village Bank. Ms. Bourque holds an M.B.A. in Finance and Accounting from the University of New Hampshire and a bachelor's degree in Veterinary Science.



**Kumi Sato**

*Independent director*

Kumi Sato has been a director of Poxel SA since June 2017. For more than 30 years, Kumi Sato has chaired and directed the COSMO Public Relations Corporation, a strategic communication and public relations firm based in Tokyo and specialized in

the health sector through its COSMO Healthcare division. Before becoming chairwoman of the company, in 1987, she founded COSMO International, a strategic consulting firm intended for Japanese companies seeking to penetrate the U.S. market. She has held prestigious roles, such as Chair and founder of Women Japan.com and independent director of Rokko & Associates Inc. In 2010, she founded BioCube, a reflection group on the Japanese health system and other topics related to biotechnology. She is currently a senior advisor for the Global Health Innovative Technology Fund in Tokyo, a lecturer at the Graduate School of Business Breakthrough University and Honorary Chair of the American Chamber of Commerce in Japan. She is also co-chair of the Global Council for the Asia Society, based in New York. She began her career with McKinsey & Co. in New York and obtained a Bachelor of Arts in Oriental Studies from Wellesley College in Massachusetts.

#### **14.2. Conflicts of interest at the level of the administrative bodies and executive management**

The Chairman, Chief Executive Officer and all Directors are direct or indirect shareholders of the Company and/or holders of securities giving access to the Company's share capital (see Sections 15.3 "Share Subscription Warrants, Stock Options and Company Founder Share Subscription Warrants" and Chapter 18 "Principal Shareholders" of this *document de référence*).

There are related-party agreements, as described in Sections 16.2 "Service agreements between Directors and the Company" and 19.3 "Special reports of the Statutory Auditors on regulated agreements" of this *document de référence*.

To the best of the Company's knowledge and subject to personal interests related to the agreements presented in Section 16.2 "Service agreements between Directors and the Company" of this *document de référence*, there is no existing or potential conflict of interest between the duties in respect of the Company and the private interests and/or other duties of the members of the administration and management bodies and the executive management as referred to in Section 14.1 "General information on founders, management and directors" of this *document de référence*.

To the best of the Company's knowledge, there is no other arrangement or agreement entered into with shareholders, customers, suppliers or others pursuant to which one of the Directors or one of the Executives of the Company has been appointed, or providing for a restriction applicable to the persons referred to in Section 14.1 "General information on founders, management and directors" of this *document de référence* concerning any disposal of their interests in the Company's share capital.

## **15. COMPENSATION AND BENEFITS**

### **15.1. Compensation of directors and officers**

The information is prepared by reference to the corporate governance code as published on December 2009 by Middlednext, updated in September 2016 and validated as a reference code by the AMF.

The tables provided for in “AMF Position–Recommendation No. 2009-16” of April 13, 2015 are presented below.

**Table 1: Summary tables of compensation and stock warrants allocated to each executive corporate officer**

Summary table of compensation and Subscription warrants ( <i>BSA</i> ) and Founder warrants ( <i>BSPCE</i> ) granted to each executive corporate officer		
	Financial year 2017	Financial year 2018
<b>Mr. Pierre Legault, Chairman of the Board of Directors</b>		
Fees due for the financial year	140 000 €	125 000 €
Attendance fees	3 000 €	- €
Value of year-on-year variable compensation granted during the financial year		
Value of stock options granted during the financial year (explained in Table 4)	39 353 €	94 737 €
Value of bonus shares awarded (explained in Table 6)		
<b>Total</b>	<b>182 353 €</b>	<b>219 737 €</b>
<b>Mr. Thomas Kuhn, Chief Executive Officer</b>		
Compensation due for the financial year (explained in Table 2)	337 607 €	302 536 €
Value of year-on-year variable compensation granted during the financial year		
Value of stock options granted during the financial year (explained in Table 4)	151 864 €	
Value of bonus shares awarded (explained in Table 6)		130 587 €
<b>Total</b>	<b>489 471 €</b>	<b>433 123 €</b>

**Table 2: Table summarizing the compensation of each executive director**

The following tables show the compensation due to executive directors in respect of the financial years ended December 31, 2017 and 2018 and the compensation they received during these financial years.

	Financial year 2017		As of December 31, 2018	
	amounts	amounts	amounts	amounts
	due <sup>(1)</sup>	paid <sup>(2)</sup>	due <sup>(1)</sup>	paid <sup>(2)</sup>
<b>Mr. Pierre Legault, Chairman of the Board of Directors</b>				
Fixed compensation	€110,000	€99,250	€125,000	€145,750
Variable compensation				

Exceptional compensation	€30,000			
Attendance fees	€3,000			€3,000
Benefits in kind				
<b>TOTAL</b>	<b>€143,000</b>	<b>€99,250</b>	<b>€125,000</b>	<b>€148,750</b>
<b>Mr. Thomas Kuhn, Chief Executive Officer</b>				
Fixed compensation (3)	€191,147	€191,147	€205,883	€205,883
Variable compensation (5)	€90,795	€46,453	€87 500	€90,795
Exceptional compensation	€50,000			
Attendance fees				
Benefits in kind (4)	€5,665	€5,665	€9,153	€9,153
<b>TOTAL</b>	<b>€337,607</b>	<b>€243,265</b>	<b>€302 536</b>	<b>€305,831</b>

- (1) For financial year
- (2) During the financial year
- (3) The compensation of the Chief Executive Officer is provided for under his management contract (see Sections 16.2.1 "Management contract with Thomas Kuhn, Director and Chief Executive Officer") 19.2 "Significant agreements entered into with related parties," and 19.3 "Special report of the statutory auditors on regulated agreements" of this *document de référence*). The bonus of the Chief Executive Officer (variable compensation of a maximum of 50% of fixed compensation) is based on a plan of precise objectives (quantitative and qualitative criteria) corresponding to objectives common to all employees. These objectives are mostly based on the timeliness of the completion of some clinical trials and obtaining dilutive and non-dilutive financing. Variable compensation is paid during the course of Year N+1.
- (4) Benefits in kind correspond to GSC unemployment insurance for corporate officers.
- (5) Variable compensation of the Chief Executive Officer for the 2018 financial year will be paid in one installment, subject to approval of the General Meeting of Shareholders of May 9, 2019.

**Table 3: Table of attendance fees and other compensation received by non-executive directors**

Non-executive corporate officers	Compensation	Amounts paid during financial year 2017 (1)	Amounts paid on December 31, 2018.
<b>Mr. Khoso Baluch</b>	Attendance fees	47 500 €	61 250 €
	Other elements	33 274 €	41 797 €
<b>Ms. Pascale Boissel</b>	Attendance fees	42 629 €	53 250 €
	Other elements	33 274 €	56 443 €
<b>Mr. Rich Kender</b>	Attendance fees	57 035 €	64 250 €
	Other elements	33 274 €	41 797 €
<b>Ms. Janice Bourque</b>	Attendance fees	44 500 €	51 250 €
	Other elements	33 274 €	56 762 €
<b>Ms. Kumi Sato</b>	Attendance fees	9 000 €	42 750 €
	Other elements	66 064 €	72 096 €
<b>Mr. Thierry Hercend</b>	Attendance fees	27 750 €	44 500 €
	Other elements	33 274 €	41 797 €

(1) The General Meeting of Shareholders of June 21, 2018 resolved to award total authorized allocation of attendance fees of 380,000 €. On January 25, 2018, the Board of Directors approved an allocation of attendance fees to the independent



directors and to Mr. Thierry Hercend totaling €35,000 for the 2018 financial year. In addition to this compensation, attendance fees are assigned to directors as a function of their participation in the Board Committees, as follows:

Audit Committee Chairman €15,000, Member €10,000;

Business Development Committee Chairman €15,000, Member €10,000;

Compensation Committee Chairman €12,000, Member €8,000;

Scientific Advisory Committee Chairman €12,000, Member €8,000;

Appointments and Governance Committee Chairman €8,000, Member €5,000;

*Pricing and Strategic Committee*: €1,000 per meeting.

(2) The amounts owed by the Company as "Other compensation" to Pascale Boissel, Janice Bourque, Richard Kender, Thierry Hercend, Khoso Baluch and Kumi Sato for the 2017 and 2018 financial years are linked to the valuation of share warrants that were granted to them during the financial year and which are described in Section 21.1.4.1 "Share warrant plan."

**Table 4: Stock warrants, stock options or founder warrants awarded to each executive director by the Company or any company of its Group during the financial years ended December 31, 2017 and 2018.**

Executive corporate officers	Date of allocation	Nature of the warrants (BSA, SO or BSPCE)	Value of the warrants according to the Black & Scholes method (in euros)	Total warrants allocated	Subscription price per share	Maturity date
Pierre Legault	25-janv-18	Stock options	3,27 €	30 000	6,79 €	30-juin-27
Pierre Legault	27-janv-17	Stock options	3,15 €	12 500	6,76 €	27-janv-27
Thomas Kuhn	30-juin-17	BSPCE	3,04 €	50 000	7,26 €	30-juin-27
<b>TOTAL</b>				<b>92 500</b>		

**Table 5: Stock warrants or Founder warrants exercised by each executive corporate officer during the financial years ended December 31, 2017 and 2018**

None

**Table 6: Bonus shares awarded to each executive director during the financial years ended December 31, 2017 and 2018**

Name of the corporate officer	Plan number and date (1)	Number of bonus shares awarded during the financial year	Value of the shares according to the method used for the consolidated financial statements (2)	Vesting date	Date of availability	Performance conditions
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Thomas Kuhn	2018 Plan, Board meeting of January 25, 2018	33 300	130 587	11,100: January 25, 2019 11,100: January 25, 2020 11,100: January 25, 2021	11,100: January 25, 2020 11,100: January 25, 2020 11,100: January 25, 2021	YES (3)
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(1) Date of allocation of bonus shares (“**Bonus shares**” or “**AGA**” (date of Board of Directors meeting)

(2) Value of shares at the time of their allocation as used in the application of IFRS2, after specifically taking into account any discount related to performance criteria and the probability of the holder’s presence in the company at the end of the vesting period, but before spreading the expense over the vesting period under IFRS 2.

(3) The Bonus shares were allocated to Thomas Kuhn subject to the fulfillment of performance conditions determined by the Board of Directors under a three-year plan.

**Table 7: Bonus shares granted that became available to each executive director during the financial years ended December 31, 2017 and 2018**

None

**Table 8: History of the allocations of stock warrants or founder warrants granted to corporate officers**

See tables in Sections 21.1.4.1 “Share warrant plan” and 21.1.4.2 “Founder Warrant Plan” of this *document de référence*.

**Table 9: Stock warrants or founder warrants granted to the top 10 employees who are not corporate officers and warrants exercised by them**

	2018		2017	
	BSA	BSPCE	BSA	BSPCE
Date of the Board of Directors meeting	N/A	N/A		June 30, 2017 March 31, 2017
Weighted average price				6,53 €
Number of rights granted during each of these financial years to the ten Group employees with the largest number of rights granted as of December 31, 2018	0	0	0	185 000

Number of rights exercised during each of these financial years by the ten Group employees with the largest number of rights exercised as of December 31, 2018	0	0	0	3 200
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**Table 10: Previous allotments of bonus shares.**

Please refer to Section 21.1.4.4 “Bonus share Plan.”

**Table 11**

The following table provides details about the conditions of compensation and other benefits granted to executive corporate officers:

Executive corporate officers	Employment contract		Supplementary pension plan		Compensation or benefits due or likely to be due as a result of termination or change of function		Compensation linked to a non-compete clause	
	Yes	No	Yes	No	Yes	No	Yes	No
<b>Mr. Pierre Legault, Chairman of the Board of Directors</b>		X		X		X		X
	Start date of mandate: General Meeting of Shareholders of January 29, 2016 End date of mandate: General Meeting of Shareholders called to approve the financial statements for the year ended December 31, 2018							
<b>Mr. Thomas Kuhn, Chief Executive Officer and Director</b>		X		X		X		X
	Start date of mandate: General Meeting of Shareholders of June 30, 2017 (renewal) End date of mandate: General Meeting of Shareholders called to approve the financial statements for the year ended December 31, 2019							

\* Thomas Kuhn has a GSC corporate officer insurance policy.

## 15.2. Sums set aside or reported by the Company for the purposes of payment of pensions, retirement or other benefits to directors and managers

The Company did not book any provisions for pensions, retirement payments or any other benefits for corporate officers.

The company did not grant any sign-on or severance bonuses to any corporate officer.

### 15.3. Share Subscription Warrants, Founder Warrants , Stock Options and Bonus shares

Relevant director and executive	BSA Directors	BSA 31 10 2012	BSA 25 07 2014	BSA 16 06 2015	BSA 29 01 2016	BSA 31 03 2016	Stock options 23 11 2016	BSA 27 01 2017	Stock options 27 01 2017	BSPCE 2017-2	BSA 30 06 2017	BSA 2018	Stock options 2018	AGA 2018	Number of shares that may be issued under these rights
<b>Pierre Legault</b> <i>Chairman of the Board of Directors as of April 1, 2016</i>					42 500	42 500	150 000		12 500				30 000		277 500
<b>Thierry Hercend</b> <i>Chairman of the Board of Directors until March 31, 2016</i>	4 500	2 875						12 500				15 000			175 000
<b>Thomas Kuhn</b> <i>Chief Executive Officer</i>										50 000				33 300	83 300
<b>Mohammed Khoso Baluch</b> <i>Independent director</i>		2 125						12 500				15 000			70 000
<b>Richard Kender</b> <i>Independent director</i>			42 500					12 500				15 000			70 000
<b>Pascale Boissel</b> <i>Independent director</i>				42 500				12 500				15 000			70 000
<b>Janice Bourque</b> <i>Independent director</i>					42 500			12 500				15 000			70 000
<b>Kumi Sato</b> <i>Independent director</i>											25 000	15 000			40 000
<b>TOTAL</b>	<b>4 500</b>	<b>5 000</b>	<b>42 500</b>	<b>42 500</b>	<b>85 000</b>	<b>42 500</b>	<b>150 000</b>	<b>62 500</b>	<b>12 500</b>	<b>50 000</b>	<b>25 000</b>	<b>90 000</b>	<b>30 000</b>		<b>855 800</b>

(1) The number of shares that may be issued as a result of these rights is presented after the 20-for-1 stock split, as approved by the General Meeting of Shareholders in March 2014.

See Sections 21.1.4.1 “Share Warrant Plan,” 21.1.4.2 “Founder Warrant Plan,” 21.1.4.3 “Share Subscription Option Plan” and 21.1.4.4 “Bonus share Plan” of this *document de référence* for details of the terms and conditions for exercising the various categories of stock warrants and founder warrants, options and bonus shares.

### 15.4. Elements of compensation and benefits due or likely to be due owing to or after the termination of the duties of executive directors of the Company

None

### 15.5. Loans and guarantees granted to management

None

## 15.6. Principles and components of the compensation and benefits of executive directors in financial year 2019

### 15.6.1. General principles of compensation of the executive directors

The general principles of the compensation policy of the executive directors are decided by the Board of Directors upon the proposal of the Compensation Committee.

The compensation policy takes into account the following principles in accordance with the rules set out in the Middledent Code to which the Company has adhered:

- **Comprehensiveness of the compensation** presented: all compensation components are taken into account in the overall assessment of the compensation; they are clearly substantiated,
- The **principle of balance and consistency**: the Compensation Committee ensures the balance and consistency of the compensation to ensure it is in the company's general interest,
- **Understandability of the rules**: the rules must be simple and transparent; the performance criteria used to establish the variable part of the compensation, or where applicable, for the grant of stock options or bonus shares must be in relation with the company's performance, correspond to its objectives, be exacting, explicable and, as far as possible, of a long-term nature,
- **Proportionality**: the determination of the compensation must ensure a fair balance and take into account both the company's general interest, market practices and the management performance,
- **Transparency**: provision of annual information to the shareholders on the entire amount of compensation and benefits received by the management is carried out transparently in accordance with the applicable regulations,
- The Board of Directors and the Compensation Committee comply with the **principle of comparability** (benchmark). Compensation is assessed in the context of the reference market within the limit of the specificities of the roles, the responsibility assumed, the results obtained and the work carried out by the executive directors.

As of December 31, 2018, the executive directors are:

- Mr. Pierre Legault, Chairman of the Board of Directors; and
- Mr. Thomas Kuhn, Chief Executive Officer.

The structure of the compensation of the executive directors is reviewed every year by the Board of Directors, which sets the various components of said compensation, on the Compensation Committee's recommendations.

At its meeting on January 25, 2018, the Board of Directors resolved to increase the components of compensation of the executive directors, as this structure ensures a link with the company's performance and maintenance of the balance between short-term and medium-term performance. In particular, the Board of Directors resolved to increase the elements of the fixed compensation of the Chairman of the Board of Directors in line with his active role within the Company and a greater contribution from him to the development of the Company's business.

### **Fixed compensation**

The fixed annual compensation of Mr. Pierre Legault and Mr. Thomas Kuhn is determined by the Board of Directors on the Compensation Committee's recommendations.

In this respect, it should be noted that Mr. Pierre Legault, in the capacity of Chairman of the Board of Directors, and Mr. Thomas Kuhn, in the capacity of Chief Executive Officer, receive fixed compensation for financial year 2019 (which will amount to €160,000 for Mr. Legault).

Furthermore, in the event of the appointment of a new Chairman, a new Chief Executive Officer or new Executive Vice-Presidents or several of the above, the principles set out above would be applicable for the determination of their compensation policy, it being specified that the amount could be adapted depending on the profile, experience or the level of responsibility of the new executive director.

### **Variable compensation**

Variable compensation is aimed at associating the executive directors with the Company's short-term performance.

Moreover, the rules for setting this compensation are consistent with the company's strategy. The terms and conditions of the annual variable compensation are understandable for the shareholder and are the subject each year of clear, exhaustive information provided in the annual report.

The indicators taken into account in determining variable compensation and the level of the objectives to be met are set every year by the Board of Directors on the recommendation of the Compensation Committee at the beginning of the reference period to which they apply.

As part of the determination of the variable portion of the compensation for executive corporate officers, the Board of Directors has set financial performance indicators in their objectives and weightings for 2019.

It is specified that any variable compensation to the executive directors may only be paid subject to shareholder approval pursuant to Article L. 225-100 of the French Commercial Code.

#### *Chairman of the Board of Directors – Mr. Pierre Legault*

Mr. Pierre Legault does not receive any variable compensation for 2019 for his term of office as Chairman of the Board of Directors.

#### *Chief Executive Officer – Mr. Thomas Kuhn*

Mr. Thomas Kuhn's target variable annual compensation is subject to performance criteria, for which the targets are set every year. It corresponds to a maximum percentage of the amount of his fixed compensation determined on an annual basis by the Board of Directors on the Compensation Committee's recommendations.

The performance criteria used to determine variable compensation are based on a plan of precise objectives based on quantitative and qualitative criteria, which correspond to objectives common to the company. These objectives are based on the development of the portfolio of products of the Company, the financing of the Company as well as on the performance of various key steps in the field of research and development.

The target level set for each criteria is strategic and economically sensitive information, which cannot be made public.

In the event of the appointment of a new executive director, these same principles will apply, whereby it is specified that in the event of an appointment made during the second half of a financial year, the performance assessment will be made on a discretionary basis by the Board of Directors.

#### **Long-term and exceptional compensation**

##### **Long-term compensation**

For his term of office as Chairman of the Board of Directors, it is specified that for financial years 2018 and 2019, Mr. Pierre Legault received compensation allocated in the form of stock options, in accordance with the recommendations of the Middlednext Code.

In his capacity as Chief Executive Officer, Mr. Thomas Kuhn was awarded bonus share plans for financial years 2018 and 2019.

##### **Exceptional compensation**

At its own discretion, the Board of Directors may award executive directors in office or appointed during the financial year exceptional compensation in certain specific circumstances and in compliance with the principles set out in the Middlednext Code, noting that said compensation may only be paid subject to shareholder approval pursuant to Article L. 225-100 of the French Commercial Code.

##### **Attendance fees**

The Board of Directors has specified that unlike Mr. Thomas Kuhn, Mr. Pierre Legault receives attendance fees in his capacity as Chairman of the Board of Directors.

##### **Compensation or benefits due for termination of the executive directors' office**

Neither executive director is owed compensation during his term of office related to forced departure or a non-compete clause.

##### **Employment contract**

Neither executive director has an employment contract.

##### **Benefits in kind**

In addition, Mr. Thomas Kuhn benefits from GSC unemployment insurance for corporate officers. Mr. Pierre Legault does not benefit from such mandatory social GSC insurance.

##### **Supplementary pension plan**

Neither executive director benefits from a supplementary pension plan for his term of office.

##### **Civil liability insurance coverage for executive directors**

Mr. Pierre Legault and Mr. Thomas Kuhn benefit from civil liability insurance for executive directors.

#### **15.6.2. Structure of the compensation of executive officers for 2018**

In accordance with Article L.225-100 of the French Commercial Code, the General Meeting of Shareholders decides on the fixed, variable and exceptional components of the total compensation and benefits in kind paid or allocated for the previous financial year by separate resolutions for the Chairman of the Board of Directors and the Chief Executive Officer. The General Meeting of Shareholders must explicitly approve the payment of variable or exceptional compensation elements.

It will therefore be proposed at the next General Meeting of Shareholders on May 9, 2019 to decide on the elements of compensation paid or allocated for 2018 to the Chairman of the Board and the Chief Executive Officer, as described below.

For financial year 2018, Mr. Pierre Legault, Chairman of the Board of Directors since March 31, 2016, has received compensation totaling €125,000. On January 25, 2018 the Board of Directors awarded him 30,000 options giving right to subscribe shares, for a subscription price of €6.79 per share. He does not benefit from benefits in kind and has not signed any contract of employment with the Company.

Mr. Thomas Kuhn, Chief Executive Officer, was awarded fixed compensation totaling €205,883 and variable compensation totaling €87,500, corresponding to the partial achievement of the targets set by the Board of Directors. He received benefits in kind during the 2018 financial year totaling €9,153 under a GSC corporate officer insurance policy. On January 25, 2018, the Board of Directors awarded him 33,300 bonus shares subject to performance conditions over the next three years. He has not signed any contract of employment with the Company.



## 16. OPERATION OF ADMINISTRATIVE AND MANAGEMENT BODIES

### 16.1. The Company is a French *société anonyme à Conseil d'administration* (public limited company with a Board of Directors)

By resolution dated June 23, 2010, the Board of Directors decided to separate the duties of Chairman from those of CEO. Pierre Legault has been the Chairman of the Board of Directors since March 31, 2016. Thomas Kuhn represents the Company vis-a-vis third parties in his capacity as Chief Executive Officer.

The detailed composition of the Board of Directors and the expiry dates of the terms of office of the members of the Board of Directors are set out in Section 14.1.1 "Composition of the Board of Directors and Committees" of this *document de référence*.

As the term of office of Richard Kender expires at the end of the General Meeting of Shareholders of June 21, 2018, the Company's General Meeting of June 21, 2018 resolved to renew his term of office as director for a period of three years, i.e., until the end of the General Meeting to be held in 2021 to approve the financial statements for the financial year ending December 31, 2020.

During the financial year ended December 31, 2018 the Board of Directors of the Company met 11 times. The average of the Directors' attendance rate is 95.46%.

### 16.2. Service contracts between the directors and the Company

The Company is linked to some of its Corporate Officers pursuant to the following agreements (see also Section 19.2 "Significant agreements entered into with related parties").

#### 16.2.1. Management agreement with Thomas Kuhn, Director and CEO

This agreement, previously authorized by the Board of Directors on March 28, 2014, was concluded on March 28, 2014. It sets out the conditions for the performance of Thomas Kuhn's office in his capacity as Chief Executive Officer of Poxel, specifically by providing for:

- limitations of powers;
- conditions related to the termination of his duties, including by setting a four-month notice period that may be lifted by the Board of Directors in return for compensation corresponding to the amount he would have received had he worked this notice period; and
- the conditions of his compensation decided by the Board of Directors on the Compensation Committee's recommendation.

The agreement was entered into for the length of Thomas Kuhn's term as CEO, without prejudice to the right of removal vested in the Board. Therefore, the Board will not make any decision with regard to renewal of this agreement as long as Thomas Kuhn remains in office.

Thomas Kuhn received compensation of €305,831 for his services in 2018.

### 16.3. Specialized Committees

The Board of Directors has set up five permanent specialized committees (Audit Committee, Compensation Committee, Scientific Advisory Committee, Governance and Nominations Committee and Business Development Committee), as well as one ad hoc committee (Strategy and Pricing

Committee) to assist the Board of Directors in its work. The role and operating procedures of its Standing Committees are set out in the internal regulations adopted March 12, 2014, as amended on June 30, 2017.

#### **16.3.1. Audit Committee**

##### **16.3.1.1. Objectives – Allocations**

The Audit Committee monitors issues relating to the preparation and the oversight of accounting and financial information and is responsible for making recommendations to the Board of Directors in its permanent assignment of oversight of the management of the Company as required by law and the bylaws of the Company.

Without prejudice to the powers of the Board of Directors, the Audit Committee is specifically responsible for:

- the development process for financial information and where appropriate, formulating recommendations to guarantee this in its entirety;
- the effectiveness of the internal control and risk management systems;
- the statutory audit of the annual and consolidated financial statements by the Statutory Auditors; and
- the process for selecting the Statutory Auditors;
- the independence of the Statutory Auditors.

The Audit Committee is also responsible for approving:

- non-audit services provided by the Statutory Auditors and the level of fees allowed for non-audit services provided by the Statutory Auditors;
- all budgets for statutory audits and other engagements provided by the Statutory Auditors.

The Audit Committee monitors the services provided by the Statutory Auditors in relation to what is permitted by law or regulation.

The Audit Committee is responsible for formulating recommendations on the statutory auditors proposed for nomination by the General Meeting of Shareholders and/or during the renewal of their term and to approve provision of the services referred to in Article L. 822-11-2 of the French Commercial Code. The Chairman of the Audit Committee ensures that the reports of the activities of the Audit Committee to the Board of Directors will permit it to be fully informed, thus facilitating its deliberations.

The annual report will include a presentation on the activity of the Audit Committee during the financial year just elapsed.

If, in the course of its work, the Audit Committee detects a significant risk that did not appear to be adequately addressed, the Chairman of the Audit Committee promptly alerts the Chairman of the Board of Directors.

The role of the Audit Committee is less one of going into the details of the accounts and more about monitoring the processes for their preparation and assessing the validity of the methods chosen for processing significant transactions.

In this context, the Audit Committee may examine the Company's annual financial statements as they are presented to the Board of Directors, hear the opinions of the Statutory Auditors and the Chief Financial Officer and receive information in relation to their analysis work and their conclusions.

Within the scope of their assignments, Committee members have the same rights to information as Directors.

The Audit Committee may use external experts at the expense of the Company, after having informed the Chairman of the Board of Directors or the Audit Committee, and must report on the work by the experts to the Board of Directors.

#### **16.3.1.2. Composition – Compensation**

The Committee is composed of at least two members. Committee members are appointed by the Board of Directors from among the members of the Board, excluding executive directors. They are appointed for a fixed period of time, which may not exceed the length of their terms of office as directors and they may be removed by the Board of Directors at any time and without reason. Their appointments are renewable without limitation.

The Committee may invite any person, internal or external to the Company, to take part in its meetings and its work.

Committee members must be competent in financial or accounting matters and at least one member must be independent in accordance with the provisions of the MiddleNext Code.

The Committee Chairman is appointed by the Board of Directors.

The duties of the Committee members within the Committee may be taken into consideration in determining the allocation of attendance fees.

The Audit Committee met seven times during the 2018 financial year.

#### **16.3.1.3. Operating procedures**

The Committee meets when the Chairman of the Committee of the Board of Directors considers it useful and at least twice per year, particularly before publication of the financial statements. The Committee may be convened by any means at least 24 hours before the meeting by the Committee Chairman or of the Chairman of the Board of Directors, the Chief Executive Officer or any individual to whom one of them shall have delegated the necessary authority.

The Committee meets at the registered office or in any other place mentioned in the meeting notice. It may also meet by video conference or by any means of telecommunication as specified in the internal regulation of the Board of Directors.

Meetings are chaired by the Committee Chairman and, if he/she is absent, by another member designated by the Committee to chair the meeting.

The presence of at least two-thirds of the Committee members in office is necessary for the validity of the deliberations.

A Committee member may be represented by another Committee member.

The Committee's recommendations are adopted by a simple majority and, in the event of a tie in the voting, the Committee Chairman has the deciding vote.

At the end of each meeting, if the members deem it necessary, the minutes of the meeting may be prepared. Minutes are signed by the Chairman of the session and at least one Committee member.

The Committee Chairman reports regularly to the Board of Directors on the Committee's work and shall immediately report any difficulty encountered.

### **16.3.2. Compensation Committee**

#### **16.3.2.1. Objectives – Allocations**

The Committee's role is to make recommendations to the Board of Directors in relation to the appointment and compensation of the executive directors and the operational and functional managers and with regard to appointments and compensation policy and internal profit sharing. In particular, the Compensation Committee:

- a) makes recommendations and proposals to the Board of Directors concerning the appointment, compensation, retirement and provident scheme, supplementary pension benefits, benefits in kind, various financial rights of the Company's managers and executive officers, the allocation of founder warrants, bonus shares, share subscription warrants, share subscription or share purchase options, for the benefit of employees, managers, consultants or other employees of the Company and, where applicable, its subsidiaries, in accordance with legal provisions;
- b) defines the methods for determining the variable portion of the compensation of corporate officers and monitors its application;
- c) proposes a general policy for awarding founder warrants, bonus or performance shares, and options to subscribe or purchase shares, and determines the frequency thereof, depending on the categories of beneficiaries;
- d) examines the system of allocating directors' fees among the members of the Board of Directors, particularly according to their participation in the Company Committees;
- e) expresses its opinion to senior management about the compensation of the principal senior executives.

Within the scope of their assignments, Committee members have the same rights to information as Directors.

#### **16.3.2.2. Composition – Compensation**

The Committee is composed of at least two members. Committee members are appointed by the Board of Directors from among the members of the Board of Directors or third parties. They are appointed for a fixed period of time, which may not exceed, as applicable, the length of their terms of office as directors and they may be removed by the Board of Directors at any time and without reason. Their appointments are renewable without limitation. Executive directors may also be appointed; however, individual executive directors may not take part in deliberations concerning themselves.

The Committee may invite any person, internal or external to the Company, to take part in its meetings and its work.

The Committee Chairman is appointed by the Board of Directors.

The duties of Committee members within the Committee may be taken into consideration in determining the allocation of attendance fees.

The Compensation Committee met five times during the 2018 financial year.

### **16.3.2.3. Operating procedures**

The Committee meets when the Committee Chairman or the Chairman of the Board of Directors considers it useful and at least twice per year, particularly before publication of the financial statements. The Committee may be convened by any means at least 24 hours before the meeting by the Committee Chairman or the Chairman of the Board of Directors or any individual to whom one of them shall have delegated the necessary authority.

The Committee meets at the registered office or in any other place mentioned in the meeting notice. It may also meet by video conference or by any means of telecommunication as specified in the internal regulation of the Board of Directors.

Meetings are chaired by the Committee Chairman and, if he/she is absent, by another member designated by the Committee to chair the meeting.

A Committee member may be represented by another Committee member.

The Committee's recommendations are adopted by a simple majority and, in the event of a tie in the voting, the Committee Chairman has the deciding vote.

At the end of each meeting, if the members deem it necessary, the minutes of the meeting may be prepared. Minutes are signed by the Chairman of the session and at least one Committee member.

The Committee Chairman reports regularly to the Board of Directors on the Committee's work and shall immediately report any difficulty encountered.

### **16.3.3. Business Development Committee**

#### **16.3.3.1. Objectives – Allocations**

The Business Development Committee prepares recommendations for the Board of Directors regarding customer development, in particular:

- a) to make recommendations and proposals to the Board of Directors concerning the main lines of Business Development;
- b) to assist the Chief Executive Officer in implementing this policy;
- c) to analyze the competitive environment, target markets and development opportunities, both in France and abroad;
- d) to analyze the Company's operations and prepares recommendations for their optimization.

Within the scope of their assignments, Committee members have the same rights to information as Directors.

#### **16.3.3.2. Composition – Compensation**

The Committee is composed of at least two members. Committee members are appointed by the Board of Directors from among the members of the Board of Directors or third parties. They are appointed for a fixed period of time, which may not exceed, as applicable, the length of their terms of office as directors and they may be removed by the Board of Directors at any time and without reason. Their appointments are renewable without limitation. Executive directors may also be appointed.

The Committee may invite any person, internal or external to the Company, to take part in its meetings and its work.

The Committee Chairman is appointed by the Board of Directors.

The duties of the Committee members within the Committee may be taken into consideration in determining the allocation of attendance fees.

The Business Development Committee met 10 times during the 2018 financial year.

#### **16.3.3.3. Operating procedures**

The Committee meets when the Chairman of the Committee or of the Board of Directors considers it useful and at least four times per year. The Committee may be convened by any means at least 24 hours before the meeting by the Committee Chairman or the Chairman of the Board of Directors or any individual to whom one of them shall have delegated the necessary authority.

The Committee meets at the registered office or in any other place mentioned in the meeting notice. It may also meet by video conference or by any means of telecommunication as specified in the internal regulation of the Board of Directors.

Meetings are chaired by the Committee Chairman and, if he/she is absent, by another member designated by the Committee to chair the meeting.

A Committee member may be represented by another Committee member.

The Committee's recommendations are adopted by a simple majority and, in the event of a tie in the voting, the Committee Chairman has the deciding vote.

At the end of each meeting, if the members deem it necessary, the minutes of the meeting may be prepared. Minutes are signed by the Chairman of the session and at least one Committee member.

The Committee Chairman reports regularly to the Board of Directors on the Committee's work and shall immediately report any difficulty encountered.

#### **16.3.4. Scientific Advisory Committee**

##### **16.3.4.1. Objectives – Allocations**

The objective of the Scientific Advisory Committee is to prepare strategic advice and recommendations for the Board of Directors regarding research and development programs, in particular:

- a) to make recommendations and proposals to the Board of Directors with regard to current and future R&D projects;
- b) to advise the Board of Directors on the scientific merits of these programs;
- c) to provide general strategic advice on scientific and technological developments.

Within the scope of their assignments, Committee members have the same rights to information as those of Directors.

##### **16.3.4.2. Composition – Compensation**

The Committee is composed of at least two members. Committee members are appointed by the Board of Directors from among the members of the Board of Directors or third parties. They are appointed for a fixed period of time, which may not exceed, as applicable, the length of their terms of office as directors, and they may be removed by the Board of Directors at any time and without reason. Their appointments are renewable without limitation. Executive directors may also be appointed.

The Committee may invite any person, internal or external to the Company, to take part in its meetings and its work.

The Committee Chairman is appointed by the Board of Directors.

The duties of the Committee members within the Committee may be taken into consideration in determining the allocation of attendance fees.

The Scientific Advisory Committee met 12 times during the 2018 financial year.

#### **16.3.4.3. Operating procedures**

The Committee meets when the Committee Chairman or the Chairman of the Board of Directors considers it useful and at least four times per year. The Committee may be convened by any means at least 24 hours before the meeting by the Committee Chairman or the Chairman of the Board of Directors or any individual to whom one of them shall have delegated the necessary authority.

The Committee meets at the registered office or in any other place mentioned in the meeting notice. It may also meet by video conference or by any means of telecommunication as specified in the internal regulation of the Board of Directors.

Meetings are chaired by the Committee Chairman and, if he/she is absent, by another member designated by the Committee to chair the meeting.

A Committee member may be represented by another Committee member.

The Committee's recommendations are adopted by a simple majority and, in the event of a tie in the voting, the Committee Chairman has the deciding vote.

At the end of each meeting, if the members deem it necessary, the minutes of the meeting may be prepared. Minutes are signed by the Chairman of the session and at least one Committee member.

The Committee Chairman reports regularly to the Board of Directors on the Committee's work and shall immediately report any difficulty encountered.

#### **16.3.5. Governance and Nominations Committee**

##### **16.3.5.1. Objectives – Allocations**

The objective of the Governance and Nominations Committee is to assist the Board of Directors on all governance matters and to assist it in the process of appointing new members, and in particular to:

- a) periodically review the diversity of the composition of, especially, the Board of Directors, the organization and functioning of the Board of Directors and its Committees, to formulate recommendations and proposals;
- b) identify and review candidates for appointment as directors or corporate officers or members of a Board Committee;
- c) make recommendations to ensure the succession of the Company's officers and key persons;
- d) make recommendations on all matters relating to the rights and obligations of directors, and in particular in light of conflicts of interest;
- e) ensure the training of directors and the integration of new directors;
- f) discuss the qualification of each director as an independent director at the time of his or her appointment and, if applicable, during the exercise of his or her term;

- g) review the Company's non-financial risk factors;
- h) review and make recommendations on the Board's performance (annual evaluation, self-evaluation);
- i) periodically review the Articles of Association of the Company, the Internal Regulation of the Board of Directors, as well as other internal operating rules of the Board of Directors or the Company (code of conduct, internal regulation of the Company, etc.).

Within the scope of their assignments, Committee members have the same rights to information as Directors.

#### **16.3.5.2. Composition – Compensation**

The Committee is composed of at least two members. Committee members are appointed by the Board of Directors from among the members of the Board of Directors or third parties. They are appointed for a fixed period of time, which may not exceed, as applicable, the length of their terms of office as directors and they may be removed by the Board of Directors at any time and without reason. Their appointments are renewable without limitation. Executive directors may also be appointed.

The Committee may invite any person, internal or external to the Company, to take part in its meetings and its work.

The Committee Chairman is appointed by the Board of Directors.

The duties of the Committee members within the Committee may be taken into consideration in determining the allocation of attendance fees.

The Governance and Nominations Committee met five times during the 2018 financial year.

#### **16.3.5.3. Operating procedures**

The Committee meets when the Committee Chairman or the Chairman of the Board of Directors considers it useful and at least four times per year. The Committee may be convened by any means at least 24 hours before the meeting by the Committee Chairman or the Chairman of the Board of Directors or any individual to whom one of them shall have delegated the necessary authority.

The Committee meets at the registered office or in any other place mentioned in the meeting notice. It may also meet by video conference or by any means of telecommunication as specified in the internal regulation of the Board of Directors.

Meetings are chaired by the Committee Chairman and, if he/she is absent, by another member designated by the Committee to chair the meeting.

A Committee member may be represented by another Committee member.

The Committee's recommendations are adopted by a simple majority and, in the event of a tie in the voting, the Committee Chairman has the deciding vote.

At the end of each meeting, if the members deem it necessary, the minutes of the meeting may be prepared. Minutes are signed by the Chairman of the session and at least one Committee member.

The Committee Chairman reports regularly to the Board of Directors on the Committee's work and shall immediately report any difficulty encountered.



#### 16.3.6. Strategic and Pricing Committee

The permanent Strategic and Pricing Committee was created by a decision by the Board of Directors on June 30, 2017.

This committee has the vocation to meet occasionally to assist the Board of Directors in its work on the discussions with potential partners, as well as in the area of funding.

#### 16.4. Observers

In accordance with the Company's bylaws, the Company has a panel of observers composed of a maximum of five (5) observers, who may be appointed upon a decision by an ordinary general meeting of shareholders, for a term of three (3) years. Their term of appointment ends at the end of the ordinary general meeting of shareholders called to approve the financial statements for the previous financial year and held during the year in which the term expires.

They are dismissed by decision of the Ordinary General Meeting of Shareholders.

Observers are called to attend all meetings of the Company's Board of Directors in the same way as directors. They have the same right to information as the directors.

They take part in meetings of the Board of Directors of the Company in an advisory capacity, and do not have any voting rights.

On the date of this *document de référence*, the Company had the following four observers:

- Mr. Thibaut Roulon, appointed March 28, 2014 for a three-year term;
- Bpifrance Participations (represented by Laurent Higuieret), appointed July 25, 2014 for a three-year term.
- Bpifrance Investissement (represented by Olivier Martinez), appointed June 30, 2017 as observer for a three-year term; and
- Andera Partners (represented by Raphaël Wisniewski), appointed June 30, 2017 as observer for a three-year term.

#### 16.5. Statement related to corporate governance

The Company refers to the Middlednext Code of Corporate Governance as updated in September 2016 and approved as a reference code by the AMF, inasmuch as the principles contained in the Code are compatible with the Company's organization, size, resources and shareholder structure, particularly in relation to the drafting of the corporate governance report, provided for by Article L. 225-37 of the French commercial code.

The Board of Directors consists of eight members, including the Chief Executive Officer. The composition of the Board of Directors is set out in Section 14.1.1 "Composition of the Board of Directors and the Committees" of the *document de référence*.

The Company currently has five independent directors, as defined by the Middlednext Code of Corporate Governance, namely Khoso Baluch, Richard Kender, Pascale Boissel, Janice Bourque and Kumi Sato. These directors are considered independent because they:

- are not employed by nor are executive directors of the Company, nor have they held such a position in the past five years;
- do not have and have not had, over the last two years, significant business relationships with the Company (customers, suppliers, competitors, providers, creditors, bankers, etc.);
- are not reference shareholders of the Company or do not hold a significant percentage of voting rights;
- do not have close ties or family connections with any executive director or reference shareholder;
- have not been auditors of the Company for the last six years.

The table below shows the situation of independent directors in the light of the criteria of independence retained by the Company, in accordance with the Middlednext Code of corporate governance:

Independence criteria	M. Khoso Balush	R. Kender	P. Boissel	J.Bourque	K.Sato	Explanations in case of non-compliance
Not be, or have been within the last 5 years, an employee or executive officer of the Company	Compliant	Compliant	Compliant	Compliant	Compliant	
Not have been in the last 2 years and not be in a significant business relationship with the Company (clients, service providers, creditors, bankers, etc.)	Compliant	Compliant	Compliant	Compliant	Compliant	
Not be a reference shareholder of the Company or hold a significant percentage of voting rights	Compliant	Compliant	Compliant	Compliant	Compliant	
Not having any close family or close ties with a corporate officer or a reference shareholder	Compliant	Compliant	Compliant	Compliant	Compliant	
Not having been an auditor of the Company in the last 6 years	Compliant	Compliant	Conforme	Compliant	Compliant	

The independent directors were awarded share subscription warrants for (i) a subscription price in order to reflect the value of the right represented by these stock warrants based on, where applicable, work carried out by an independent expert, and (ii) an exercise price based on the price of Company shares at the time of the decision of the Board of Directors to issue stock warrants in order to reflect the actual value of the share. Taking into account these elements and the insignificant amounts involved, the Company Board of Directors has found that the allocations of stock warrants to these directors did not undermine their independence.

The internal regulation of the Board of Directors, as well as the specialized Committees it describes, supplement the legal and regulatory provisions, in compliance with the French Commercial Code and the Middlednext Code of Corporate Governance.

The Company has six specialized Committees set up by the Board of Directors: the Audit Committee, the Compensation Committee, the Business Development Committee, the Scientific Advisory Committee, the Governance and Nominations Committee and the Strategic and Pricing Committee, in Section 16.3 “Specialized Committees” of this *document de référence*.

The following table summarizes the Company’s position on each of the recommendations set out in the Middlednext Corporate Governance Code:

Recommendation of the Middlednext Code	Adopted	Will be adopted if applicable	Not adopted
<b>Oversight authority</b>			
R1 - Ethics of board members	X		
R2 - Conflicts of interest	X		
R3 - Composition of the board - Presence of independent members	X		
R4 - Information of the board members	X		
R5 - Organization of the meetings of the board and committees	X		
R6 - Establishment of committees	X		
R7 - Establishment of a board internal regulation	X		
R8 - Choice of each board member	X		
R9 - Duration of the terms of office of board members	X		
R10 - Compensation of board members	X		
R11 - Establishment of an assessment of the board’s work (Note 1)	X		
R12 - Relations with “shareholders”	X		
<b>Executive authority</b>			
R13 - Definition and transparency of the compensation of the company executives	X		
R14 - Preparation of the succession of the “executives”	X		
R15 - Accumulation of work contract and company mandate (Note 2)		X	
R16 - Employee severance benefits (Note 3)		X	
R17 - Supplementary retirement plans (Note 4)		X	
R18 - Stock options and allocation of bonus shares	X		
R19 - Review of the points for monitoring	X		

Note 1: The Company Board of Directors has performed an assessment of its working methods and operation. This action was included in the Board’s work plan for 2018 in the form of a self-assessment in accordance with the internal regulation (Paragraph 1.7). The results were discussed by the Board and will result in an action plan.

Note 2: No executive director of the Company currently has an employment contract. If such a situation were to be put in place, Recommendation 15 would be followed.

Note 3: No executive director of the Company is currently entitled to severance payments. If severance payments of this kind were to be put in place, Recommendation 16 would be followed.

Note 4: Even though no supplementary retirement plan is currently in place, Recommendation 17 to ensure greater transparency for shareholders would be followed where applicable, if the Company were to adopt such plans.

## **16.6. Internal controls**

The Company uses the internal audit system definition set out by the AMF, according to which the internal control procedure is a system that the Company defines and implements under its own responsibility. This system aims to ensure:

- Compliance with laws and regulations;
- Application of the instructions and guidelines set by Senior Management;
- proper functioning of the Company's internal processes;
- Reliability of financial information; and,
- More generally, it helps manage the Company's activities, control the efficiency of its operations and oversee the efficient use of its resources.

The Company continued the implementation during the financial year of an internal control process designed to "internally guarantee the relevance and reliability of the information used and disseminated in the Company's activities."

However, internal control cannot provide an absolute assurance that the Company's objectives will be achieved, or that the risk of error or fraud will be totally controlled or eliminated.

### **Components of internal control**

The internal control system relies on clear coordination of responsibilities, benchmarks, resources and processes. Since its creation, the Company has been in the process of developing a quality assurance system, to compile existing documents and audits, ensure their updating and consistency, and consolidate them when necessary. The processes governing all of the Company's businesses are described in procedures, operating methods, notices and forms. These documents also chart business flows, designate the resources and responsibilities of participants and specify the Company's expertise, while also giving instructions for particular operations.

All of the Company's stakeholders are involved in internal control.

### **Procedures related to the operating processes**

All documents governing quality management are saved on a dedicated intranet allowing for optimized access, as well as continuous changes in business activity (Document Life Cycle Management). The goal is continuous quality improvement in the operating, management and support processes of the Company and the Group.

The quality assurance system covers the following fields:

- Quality assurance, health and safety, risk management;
- Administrative, legal, social and social and financial fields, including internal controls.
- Pharmaceutical, pre-clinical and clinical research and development.

## **Organization of the accounting and financial department**

The financial function is internally managed by the Chief Financial Officer. The accounting function is performed with the assistance of a certified accountant. The Company is committed to maintaining a separation between its activities of production and supervision of the financial statements and hires independent experts for the valuation of complex accounting items (retirement obligations, valuation of share warrants/founder warrants) and/or requiring subjective assumptions.

Payroll and tax audits are carried out by a certified accountant.

The financial statements, prepared in accordance with French standards and IFRS with the assistance of an accounting firm, are subject to an audit by the Company's co-statutory auditors.

The Finance Department reports directly to the Chief Executive Officer.

## **Budget process and "monthly reporting"**

The accounting system implemented by the Company is based on IFRS accounting standards. An annual budget is drawn up by the Company. The Company also draws up a "monthly report," which includes an operating account, balance sheet and cash flow forecasts. These components are presented to the Executive Committee and at each Board of Directors' meeting. The Company monitors the budget precisely.

## **Delegation of authority**

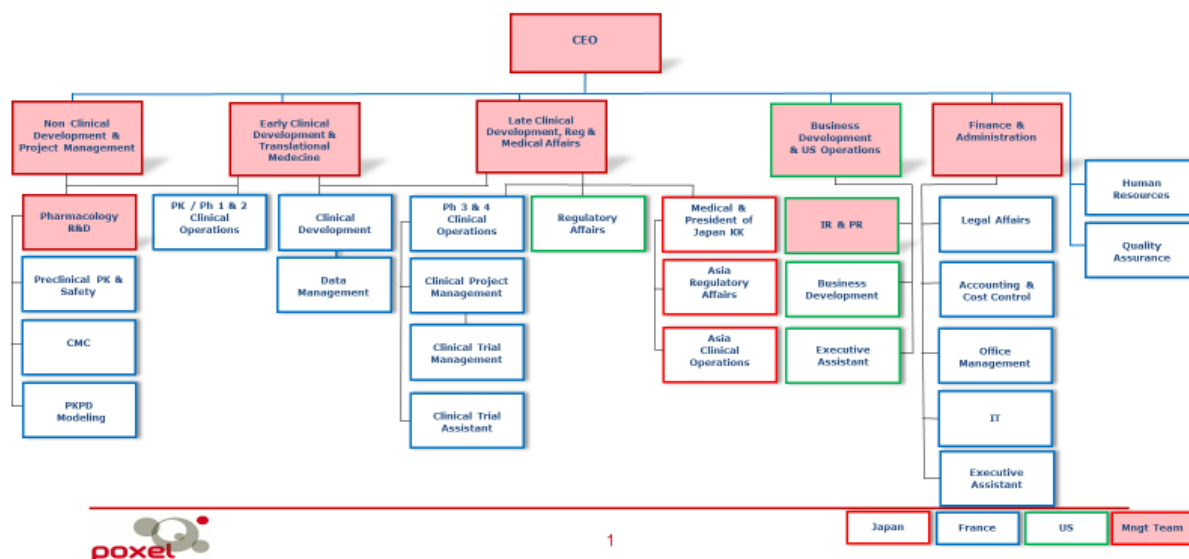
A delegation of authority has been granted to each executive responsible for an activity in order to develop and negotiate purchases of goods or services. The effective order is nevertheless signed by Senior Management (or the Chief Financial Officer, on instructions from Senior Management). Purchase or service requests or pre-clinical or clinical study contracts (which are treated as purchase requests because they are specific to each study) are the subject of requests for expenditure commitments validated by Management Control and Senior Management. Invoices are then reconciled with these commitment requests and delivery notes for the goods, before accounting, approval and payment - these three activities being carried out by different individuals in accordance with the principles of separation of duties.

Most payments are transfers validated by an electronic signature. This system ensures systematic archiving of the transactions and allows for the tracking of the signatories, the bank contact details of the suppliers and a comprehensive ex-post audit if needed.

## 17. EMPLOYEES

### 17.1. Number of employees and breakdown by function

#### 17.1.1. Organizational Structure



The average workforce totaled 33 employees in 2018, as compared to 25 employees in 2017. It is presented in Note 20 to the IFRS financial statements set out in Section 20.1 “IFRS financial statements for the year ended December 31, 2018” of this *document de référence*.

#### 17.1.2. A lean structure, led by an experienced executive committee composed of highly qualified personnel

To ensure development of its products, the Company relies on a dynamic, highly qualified team, with significant experience in large pharmaceutical groups.

As of the date of this document, the Company employs 41 people, including a corporate officer, five contractors, one fixed-term contract employee and 34 employees with permanent contracts. More than 70% of the workforce is assigned to research and development activities, the remaining 30% being assigned to business development operations and to administrative and financial management. The workforce includes four doctors, eight pharmacists, 10 PhDs (some of whom are also doctors or pharmacists) and 10 scientists. The team is composed of 12 men and 29 women.

An executive committee of eight people runs the Company. Members of the executive committee collectively have expertise covering the value chain necessary for development of a new drug. All have held positions of high responsibility in large groups, and for the most part, have key experience working in pharmaceutical companies with widely known diabetes franchises.

	<p><b>Thomas Kuhn, Co-Founder and CEO</b></p> <p>Doctor of Pharmacy (Lyon – France) &amp; MBA (Ashridge – UK)</p> <p>Fifteen years of experience in the pharmaceutical industry (Generics UK and Merck Serono)</p> <p>Has led the strategy and development for diabetes at Merck Serono (products in development and marketed), before directing the divestment of R&amp;D assets, which led to Poxel's creation following completion of a license agreement with Merck Serono.</p>
	<p><b>Pascale FOUQUERAY, Co-Founder and Medical Director responsible for Phase 1 &amp; 2 clinical development and Translational Research</b></p> <p>Doctor of Medicine (Angers-France), Endocrinologist (Paris-France) &amp; Doctor in Sciences (Paris-France)</p> <p>Fourteen years of experience in the pharmaceutical industry (Merck Serono)</p> <p>Responsible for the clinical development of exploratory molecules in diabetes, obesity and gout at Merck Serono, in particular strategies to improve the understanding of action mechanisms and to achieve proof of concept in term of effectiveness.</p>
	<p><b>Sébastien Bolze, Co-Founder and Scientific Director responsible for non-clinical development</b></p> <p>Doctor of Pharmacy (Lyon – France) and doctoral thesis in pharmacokinetics and metabolism</p> <p>Fifteen years of experience in the pharmaceutical industry (Merck Serono; Fournier Pharma; Solvay Pharmaceuticals)</p> <p>Has led several departments: ADME, overall multidisciplinary unit for the selection of candidates (preclinical up to 120 ETP in three countries)</p> <p>Has contributed to many research projects and developments of metabolic disease products (type 2 diabetes, dyslipidemia, atherosclerosis).</p>
	<p><b>Sophie Bozec, Co-Founder and Senior Vice President in charge of Diabetes Pharmacology</b></p> <p>Doctor of Biology (Paris 7 - France)</p> <p>Sixteen years of experience in the pharmaceutical industry (Lipha/Merck Serono)</p> <p>Has led a diabetes research team and managed transversal research projects within Merck Serono before participating in the creation and development of Poxel.</p>
	<p><b>Noah D. Beerman, Executive Vice President in charge of Business Development and President of Operations in the United States</b></p> <p><b>MBA</b></p>

	<p><i>More than 20 years of experience in management and guidance in the biopharmaceutical industry.</i></p> <p>He was the Chairman, CEO and director of RXI Pharmaceuticals (now Galena BioPharma), and until 2013 Executive Vice President and Director of Operations at Coronado Biosciences.</p>
	<p><b>Jonae Barnes - Senior Vice President in charge of Investor Relations / Public Relations</b></p> <p><b>Master's in Finance</b></p> <p>Twenty years of experience with strategic investors and in corporate communications in the pharmaceutical and biotechnology industry</p> <p>She has also held senior roles at Agenus, an immuno-oncology company and at Vision Medicines, an ophthalmology company. She advised private and public biotechnology companies in her practice of Investor Relations</p>
	<p><b>Christophe Arbet-Engels, Medical Director and Executive Vice President responsible for the clinical development of Phase 3 and Medical Affairs</b></p> <p>Doctor of Medicine, Doctor of Pharmacy, PhD (France) and an MBA (USA)</p> <p>More than 25 years of experience in life sciences, acquired at university and in business. He has held positions of responsibility overseeing programs targeting metabolism and diabetes, and directed programs on diabetes, cardiovascular diseases, neurology, orphan diseases and oncology, in international and complex environments.</p>
	<p><b>Anne Renevot, Financial Director</b></p> <p>Twenty-five years of financial experience. Prior to joining Poxel, she was Chief Financial Officer of EOS Imaging, where she contributed to the successful listing of the Company on the Euronext Paris stock exchange, which led to the raising of EUR 39 million. She has conducted significant financing in the framework of private investments, optional line in own funds and bond loans. She was responsible for compliance with the regulation for listed companies, as well as for communication and financial planning. She also played a key role in the Company's acquisitions and partnerships. Previously, Anne Renevot held successive roles as Chief Financial Officer of the Jewelry Manufacturing Division and International Financial Controller at Cartier. Earlier in her career, Anne Renevot was Manager at EY Audit and Management Controller at Legris Industries. Anne Renevot is a graduate of the Audencia Nantes Superior School of Commerce and majored in corporate finance at Ohio State University, in Columbus (Ohio, USA).</p>



This team is surrounded by scientific boards composed of well-known experts in diabetology, clinical development and new formulations, to collect their opinion on the results obtained during development of the Company's products, as well as on the next R&D steps. The composition and role of these scientific boards are detailed in Section 11.1 "Research and Development" of this *document de référence*.

### 17.1.3. Organization of operations

Five departments manage the Company's operations:



- **Scientific Department:** Composed of eight people, the scientific department defines the strategy for non-clinical research and development, defines the design of studies to be performed and then organizes and manages the subcontracting of these studies. The department relies on a network of subcontractors and academic teams for these studies. It continually develops and maintains this network to maintain a close relationship with the teams and good response times. The scientific department also strives to ensure an ad hoc level of quality for the studies conducted (GLPs, GMPs, GCPs, etc.). It has all the necessary skills in chemistry, manufacturing, analytics, packaging, pharmacology, pharmacokinetics and toxicology, either internally or through external consultants. It also uses a network of international experts to challenge its strategy and design its studies. It works closely with the medical department to provide it with the necessary support in the design and completion of pharmacokinetic and/or mechanistic clinical trials, in order also to ensure a smooth transition from preclinical to clinical.
- **Medical Department:** Composed of 18 people, the medical department defines the clinical development strategy in partnership with the scientific and business development departments. The department prepares the design of the studies to be performed, taking into account objectives and constraints while ensuring feasibility. The department selects subcontractors and controls all their activities during the completion of clinical studies, ensuring they are conducted in compliance with good clinical practices. Finally, the medical department analyzes in detail the results, which will then be submitted to a committee of international experts selected by the Company for discussion and validation before any external exploitation.

The Medical Department is made up of two teams: a team carrying out Phase I and II development, and a team carrying out Phase III development, regulatory activities and preparation for commercialization.

- **Business Department:** Consisting of four people, it ensures development of the Company's assets with strategic partners. It establishes the partnership strategy with industrial and biotech companies, academic teams and teaching hospitals. It ensures the smooth operation of these partnering arrangements in relation with the corporate strategy, both for the Company's internal

programs, and also the external opportunities aimed at adding to the Company's portfolio of products. It is also in charge of investor relations and public relations.

- **Administrative and Finance Department:** Consisting of eight people, it manages day-to-day accounting, financial, IT and current legal issues, forecasts and anticipates cash needs by seeking adequate resources for the conduct of projects undertaken by the Company, controls costs and structures administrative procedures to minimize the financial risk factors detailed in Section 4 of this *document de référence*.

## 17.2. Equity and stock options held by members of management

See Section 15 "Compensation and benefits" of this *document de référence*.

## 17.3. Employee share ownership

Some employees own founder warrants that may grant them a 1.50% interest in the capital in case of full exercise (see Sections 21.1.4.1 "Share warrant plan" and 21.1.4.2 "Founder warrant Plan" of this *document de référence*).

## 17.4. Profit sharing and incentive agreements

None.

## 18.MAJOR SHAREHOLDERS

### 18.1. Share capital and voting right distribution

As of the date of this *document de référence*, and in accordance with Article L. 233-13 of the French Commercial Code, as far as the company is aware, the ownership structure and the identity of shareholders directly or indirectly holding more than one twentieth, one tenth, three twentieths, one fifth, one quarter, one third, half, two thirds, eighteen twentieths or nineteen twentieths of the share capital or voting rights at general meetings is as follows:

Shareholders	Total shares	Voting rights	Capital %	Voting rights %
Thomas Kuhn <sup>(1)</sup>	1,506,740	1,506,740	5.82%	5.83%
Other Founders	1,266,806	1,266,806	4.89%	4.90%
<i>Subtotal Founders (2)</i>	<i>2,773,546</i>	<i>2,773,546</i>	<i>10.72%</i>	<i>10.73%</i>
FCPR Innobio	2,174,354	2,174,354	8.40%	8.41%
Bpifrance Participations	2,054,758	2,054,758	7.94%	7.95%
<i>BPIfrance subtotal</i>	<i>4,229,112</i>	<i>4,229,112</i>	<i>16.34%</i>	<i>16.36%</i>
Andera Partners	4,162,716	4,162,716	16.08%	16.11%
Roivant Sciences Ltd	1,431,399	1,431,399	5.53%	5.54%
<i>Subtotal of shareholders holding more than 5% of share capital (2)</i>	<i>11,329,967</i>	<i>11,329,967</i>	<i>43.78%</i>	<i>43.84%</i>
DeuteRx	1,290,000	1,290,000	4.98%	4.99%
Public	11,956,104	11,956,104	46.20%	46.26%
Self-held	38,100	N/A	0.15%	N/A
<b>Total</b>	<b>25,880,977</b>	<b>25,842,876</b>	<b>100.00%</b>	<b>100.00%</b>

(1) Founding individual who is a corporate officer

(2) There is no concerted action between these shareholders, who are presented under the subtotals for purposes of comprehension only.

As far as the Company is aware, there are no other shareholders holding directly or indirectly, alone or in concert, more than 5% of the capital or voting rights at the date of this *document de référence*.

See Section 21.1.4 “Convertible or exchangeable securities or securities with attached warrants” of this *document de référence* for details on the conditions for conversion of the convertible bonds, exercise of subscription or founders’ warrants, and subscription options for bonus shares, and Section 21.1.7.1 “Table showing changes in the capital over the last two financial years” for a detailed presentation of capital increases.

## 18.2. Significant shareholders not represented on the Board of directors

As of the date of this *document de référence*, Roivant Sciences Ltd and DeuteRx LLC are significant shareholders who are not members of the Company Board of Directors as indicated above.

## 18.3. Recent transactions with regard to the share capital of the Company

During financial year 2018, several transactions modified the share capital:

- On February 13, 2018, the Company undertook a capital increase for the benefit of Roivant Sciences Ltd. in the context of entering into a partnership agreement (see Section 22 “Material contracts” in this *document de référence*). The price per share of this transaction was €8.50 and 1,431,399 new shares with a par value of €0.02 were thereby created, with the recording of a capital increase of a nominal amount of €28,627.98, together with a total share premium of €12,138,263.52. Poxel’s share capital amounted to €491,176.54 following this transaction.
- On May 21, 2018 a former employee exercised 400 founders’ warrants corresponding to 8,000 shares, at an exercise price of €2.50, representing a capital increase of €160 together with a share premium of €19,840. Poxel’s share capital amounted to €491,336.54 following this transaction.
- On September 3, 2018, the Company executed a capital increase for the benefit of DeuteRx LLC, as part of the conclusion of a strategic agreement (see Section 22 “Material Contracts” of this *document de référence*). The price per share of this transaction was €6.91 and 1,290,000 new shares with a par value of €0.02 were thereby created, with the recording of a capital increase of a nominal amount of €25,800, together with a total share premium of €8,888,100. Poxel’s share capital amounted to 517,136.54 € following this transaction.

Since the end of the financial year, the Company has increased the share capital of the beneficiaries of the bonus shares allocated by the Board of Directors at its meeting of January 25, 2018, following the recognition by the Board of Directors at its meeting of January 24, 2019 of partial achievement of the performance criteria for certain bonus shares and the end of their vesting period. 24,150 new shares with a nominal value of €0.02 were created with a capital increase in a nominal amount of 483 €. Poxel’s share capital amounted to 517,619.54 € following this transaction.

## 18.4. Transactions in securities carried out by executives and persons mentioned in Article L. 621-18-2 of the French Monetary and Financial Code

During financial year 2018, the executives and persons mentioned in Article L. 621-18-2 of the French Monetary and Financial Code carried out the following securities transactions:

- Acquisition by Bpifrance Participations SA (observer on the Company Board of Directors and legal entity related to Bpifrance Investissement, observer on the Company Board of Directors) of October 24, 2018 of 9,221 Company shares at a unit price of 5.6478 euros;
- Acquisition by Bpifrance Participations SA (observer on the Company Board of Directors and legal entity related to Bpifrance Investissement, observer on the Company Board of Directors) of October 25, 2018 of 22,735 Company shares at a unit price of 5.5748 euros;
- Acquisition by Bpifrance Participations SA (observer on the Company Board of Directors and legal entity related to Bpifrance Investissement, observer on the Company Board of Directors) of October 26, 2018 of 26,900 Company shares at a unit price of 5.4960 euros;
- Acquisition by Bpifrance Participations SA (observer on the Company Board of Directors and legal entity related to Bpifrance Investissement, observer on the Company Board of Directors) of October 29, 2018 of 2,631 Company shares at a unit price of 5.5772 euros;
- Acquisition by Bpifrance Participations SA (observer on the Company Board of Directors and legal entity related to Bpifrance Investissement, observer on the Company Board of Directors) of October 30, 2018 of 10,000 Company shares at a unit price of 5.7665 euros;
- Acquisition by Bpifrance Participations SA (observer on the Company Board of Directors and legal entity related to Bpifrance Investissement, observer on the Company Board of Directors) of October 31, 2018 of 7,000 Company shares at a unit price of 6.1092 euros;
- Acquisition by Bpifrance Participations SA (observer on the Company Board of Directors and legal entity related to Bpifrance Investissement, observer on the Company Board of Directors) of November 5, 2018 of 4,205 Company shares at a unit price of 6.1500 euros;
- Acquisition by Bpifrance Participations SA (observer on the Company Board of Directors and legal entity related to Bpifrance Investissement, observer on the Company Board of Directors) of November 6, 2018 of 8,395 Company shares at a unit price of €6.1376;
- Acquisition by Bpifrance Participations SA (observer on the Company Board of Directors and legal entity related to Bpifrance Investissement, observer on the Company Board of Directors) of November 8, 2018 of 24,697 Company shares at a unit price of €6.3224;
- Acquisition by Bpifrance Participations SA (observer on the Company Board of Directors and legal entity related to Bpifrance Investissement, observer on the Company Board of Directors) of November 9, 2018 of 8,907 Company shares at a unit price of €6.2949; and
- Acquisition by Bpifrance Participations SA (observer on the Company Board of Directors and legal entity related to Bpifrance Investissement, observer on the Company Board of Directors) of November 12, 2018 of 40,906 Company shares at a unit price of €6.4553;

#### 18.5. Voting rights of the main shareholders

As of the date of this *document de référence*, the voting rights of each shareholder are equal to the number of shares held by each of them.

The general meeting of shareholders held on January 8, 2015 resolved to remove the automatic double voting rights as provided for by French law No. 2014-384 of March 29, 2014 aimed at recapturing the real economy.

#### 18.6. Control of the Company

As of the date of this *document de référence*, no shareholder individually holds either control of the Company, or a percentage likely to lead to the presumption of control of the Company within the meaning of the provisions of Article L. 233-3 of the French Commercial Code.

#### 18.7. Agreements that may result in a change of control

No particular provision of the bylaws, any charter or any regulations of the issuer may result in delaying, deferring or preventing a change of control.

#### 18.8. Agreements between the shareholders of which the Company is aware and that may result in restrictions on the transfer of shares and the exercise of voting rights

On February 9, 2018 Roivant Sciences Ltd committed irrevocably to the Company not to sell the shares it holds in the latter, until the lapse of a period of six months, subject to certain customary exceptions. As of August 9, 2018, Roivant Sciences Ltd is no longer bound by this commitment.

On August 29, 2018 Roivant Sciences Ltd irrevocably committed to the Company not to sell the shares it holds in the latter, until the lapse of a period of nine months, subject to certain customary exceptions. An additional 12-month commitment, reduced by 1/12 per month, is also applicable to certain shareholders of DeuteRx.

#### 18.9. Pledges of Company security

As far as the Company is aware, there is no pledge of the Company's securities.

#### 18.10. Crossing of thresholds

On February 14, 2018 Omnes Capital, acting on behalf of funds it manages, declared that on February 12, 2018 it had exceeded the threshold of 5% of the Company's share capital and voting rights and held, on behalf of said funds, 989,293 shares in the Company, representing the same number of voting rights, i.e., 4.03% of the Company's share capital and voting rights.

On February 15, 2018 Roivant Sciences Ltd declared that on February 12, 2018 it had exceeded the threshold of 5% of the Company's share capital and voting rights and held 1,431,399 shares in the

Company, representing the same number of voting rights, i.e., 5.83% of the Company's share capital and voting rights.

On August 6, 2018 Amundi declared that it had exceeded the threshold of 4% of the Company's share capital and voting rights and held 991,108 shares in the Company, representing the same number of voting rights, i.e., 4.03% of the Company's share capital and voting rights.

On September 6, 2018, public industrial and commercial establishment Bpifrance declared that on September 3, 2018 it had indirectly dropped below the threshold of 15% of the capital and voting rights of the Company, through the intermediary of Bpifrance Participations SA and Bpifrance Investissement, and indirectly held 3,871,330 shares in the Company, representing the same number of voting rights, i.e., 14.97% of the share capital and voting rights of the Company.

On September 6, 2018, Caisse des dépôts et consignations declared that on September 3, 2018, it had indirectly dropped below the threshold of 15% of the capital and voting rights of Poxel, through Bpifrance Participations SA and Bpifrance Investissement, and that it held 3,871,330 Poxel shares, representing the same number of voting rights, i.e., 14.97% of the Company's share capital and voting rights.

On October 29, 2018, public industrial and commercial establishment Bpifrance declared that on October 24, 2018 it had indirectly exceeded the threshold of 15% of the share capital and voting rights of the Company, through the intermediary of Bpifrance Participations SA and Bpifrance Investissement, and indirectly held 3,880,551 shares in the Company, representing the same number of voting rights, i.e., 15.01% of the Company's share capital and voting rights.

On October 29, 2018 Caisse des dépôts et consignations declared that on October 24, 2018, through Bpifrance Participations SA and Bpifrance Investissement, it had exceeded the threshold of 15% of the capital and voting rights of Poxel, and that it held 3,880,551 shares in the Company representing the same number of voting rights, namely 15.01% of the Company's capital and voting rights.

On January 8, 2019 Federated Equity Management Company of Pennsylvania and Federated Global Investment Management Corp, acting on behalf of funds they manage, declared that on January 4, 2019 they had exceeded the 2% threshold of the Company's share capital and voting rights and held, on behalf of said funds, 442,420 shares of the Company, representing the same number of voting rights, i.e., 1.711% of the Company's share capital and voting rights.

#### 18.11. Changes in the share price

The Company's shares have been listed on the Euronext Paris regulated market under the symbol "POXEL.PA" since February 6, 2015.

The following table describes the changes in the closing price of the Company's share on Euronext Paris during financial year 2018:

PERIOD	HIGH	LOW
First quarter of 2018	€7.30	€6.06
Second quarter of 2018	€7.65	€5.90
Third quarter of 2018	€7.30	€6.61

Fourth quarter of 2018	€6.47	€4.96
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## 19. RELATED PARTY TRANSACTIONS

### 19.1. Intra-group transactions

During financial year 2018, the Company engaged in intra-group activities with its Japanese subsidiary as described in Section 7.3 “Group financial flows” of this *document de référence*.

### 19.2. Significant agreements concluded with related parties

a) On December 12, 2014 the Company entered into an agreement with Mr. Khoso Baluch to indemnify him for legal costs and convictions he may incur in the event that any liability is imposed against him in his capacity as a Company director. This agreement will remain in force for 10 years following termination of Khoso Baluch’s duties as director and, if necessary, for one year following the termination of any proceedings still ongoing after this 10-year period.

b) The Company entered into a management agreement with Thomas Kuhn, the Company’s CEO. This agreement, previously authorized by the Board of Directors on March 28, 2014, was entered into on March 28, 2014. It sets out the conditions for the performance of Thomas Kuhn’s office in his capacity as CEO of Poxel by providing limitations on the exercise of powers (Article 3) and conditions for the termination of his duties (Article 4), in particular providing for a four-month notice period. This agreement was ratified by the Company’s General Meeting of Shareholders on June 16, 2015 and is included in the special report of the Company’s statutory auditors (see Section 19.3 “Special Report of the statutory auditors on regulated agreements and commitments” of this *document de référence*).

The agreement was entered into for the length of the term of office of Thomas Kuhn as CEO, without prejudice to the right of removal vested in the Board. Therefore, the Board will not make any decision with regard to the renewal of this agreement as long as the term of office of Thomas Kuhn continues. Under this agreement for financial years 2017 and 2018, gross amounts of €337,607 and €338,184, respectively, are included in expenses for the financial year.

c) On December 12, 2014 the Company entered into an agreement with Mr. Richard Kender to indemnify him for the legal costs and convictions he may incur in the event that any liability is imposed against him in his capacity as a Company director. This agreement was entered into following his appointment as a director of Poxel on January 8, 2015. This agreement will remain in force for 10 years following termination of Richard Kender’s duties as director and, if necessary, for one year following the termination of any proceedings still ongoing after this 10-year period.

d) On March 31, 2016, the Company entered into an agreement with Mr. Pierre Legault to indemnify him for the legal costs and convictions he may incur in the event that any liability is imposed against him, in his capacity as a Company director. This agreement was set up in the context of the nomination of Mr. Pierre Legault as a director on March 31, 2016. It aims to offer a guarantee in consideration for duties performed. This agreement will remain in force for 10 years following the termination of his duties as a director and, if necessary, for one year following the termination of any proceedings still ongoing after this 10-year period.

e) On March 31, 2016, the Company entered into an agreement with Ms. Janice Bourque to indemnify her for the legal costs and convictions she may incur in the event that any liability is imposed against her, in her capacity as a Company director. This agreement was set up in the context of the nomination of Ms. Janice Bourque as a director on March 31, 2016. It aims to offer a guarantee in consideration for duties performed. This agreement will remain in force for 10 years following the termination of

her duties as a director and, if necessary, for one year following the termination of any proceedings still ongoing after this 10-year period.

f) On March 16, 2016, the Company entered into an agreement with Ms. Pascale Boissel to indemnify her for the legal costs and convictions she may incur in the event that any liability is imposed against her, in her capacity as a Company director. It aims to offer a guarantee in consideration for duties performed. This agreement will continue in force for 10 years following the termination of her duties as a director and, if necessary, for one year following the termination of any proceedings still ongoing after this 10-year period.

g) On August 1, 2017 the Company entered into an agreement with Ms. Kumi Sato to indemnify her for the legal costs and convictions she may incur in the event that any liability is imposed against her, in her capacity as a Company director. It aims to offer a guarantee in consideration for duties performed. This agreement will remain in force for 10 years following the termination of her duties as a director and, if necessary, for one year following the termination of any proceedings still ongoing after this 10-year period.

h) On June 1, 2018, the Company signed a service agreement with Cosmo Public Relations Corporations, a company chaired and managed by Kumi Sato, member of the Board of Directors, under the terms of which Cosmo Public Relations Corporations is committed to providing communication services to the Company. The members of the Board of Directors have not formally authorized the signature of this service agreement by the Company, although it has been the subject of discussions between the members of the Board of Directors.

### 19.3. Special report of the statutory auditors on regulated agreements and commitments

To the Shareholders,

In our capacity as statutory auditors of your company, we present our report on regulated agreements and commitments.

It is our duty to inform you, on the basis of information provided to us, of the characteristics, the essential terms and the reasons justifying the interest for the company of agreements and commitments of which we have been advised or that we discovered during our engagement, without commenting on their usefulness and appropriateness or identifying such other agreements and commitments as may exist. It is your responsibility, pursuant to Article R. 225-31 of the French commercial code, to assess the interest in concluding these agreements and commitments with a view to their approval.

Furthermore, it is our responsibility, where appropriate, to provide you with the information provided for in Article R. 225-31 of the French commercial code relating to the performance, during the past fiscal year, of agreements and commitments already approved by the general meeting of shareholders.

We applied the procedures that we considered necessary in the light of the professional guidelines of the National Institute of Statutory Auditors relating to this engagement. This consisted in verifying the consistency of the information provided to us with the source documents from which it is derived.

## **AGREEMENTS AND COMMITMENTS SUBJECT TO THE APPROVAL OF THE GENERAL MEETING**

### **Agreements and commitments not authorized and entered into during the past fiscal year**

Pursuant to articles L. 225-42 and L. 823-12 of the French commercial code, we advise you that the following agreements and commitments have not been previously authorized by the board of directors.

We are required to disclose the circumstances explaining which the authorization procedure has not been completed.

- Services agreement with Cosmo Public Relations Corporations, company chaired and managed by Kumi Sato

Person concerned: Kumi Sato, director

Purpose: agreement entered into on June 1<sup>st</sup>, 2018 pursuant to which Cosmo Public Relations Corporations undertakes to provide to the Company services of communication.

Compensation: A gross amount of €56,438.27 has been paid to Cosmo Public Relations Corporations in connection with the contract.

Reason: provide services of communication in Japan to the Company.

The members of the Board of Directors have not formally authorized the signature of this service agreement by the Company, although it has been the subject of discussions between the members of the Board of Directors.

## **AGREEMENTS AND COMMITMENTS ALREADY APPROVED BY THE GENERAL MEETING**

### **Agreements and commitments approved during prior fiscal years and whose performance continued during the past fiscal year**

Pursuant to article L. 225-10 of the French commercial code, we were advised of the following agreements and commitments concluded during the last year that were subject to the prior authorisation of your Board of Directors.

- Indemnification agreement with Ms. Kumi Sato

Person concerned: Kumi Sato, director

Purpose: agreement entered into on 1 August, 2017 with Ms. Kumi Sato to indemnify her for legal costs and convictions she may incur in the event that any liability is imposed on her, in her capacity as a director of the Company.

Reason: this agreement was entered into following the appointment of Ms. Kumi Sato as director. It aims to offer a guarantee in consideration of the functions performed.

- Indemnification agreement with Ms. Janice Bourque

Person concerned: Janice Bourque, director.

Purpose: agreement entered into on 31 March, 2016 with Ms. Janice Bourque to compensate her for judicial costs and convictions that might arise in case of invoking of her responsibility in the framework of her mandate as director of the Company.

Reason: This convention has been put in place in the framework of the appointment of Ms. Janice Bourque as director. It aims to offer a guarantee in consideration of the functions performed.

- Indemnification Agreement of Mr. Pierre Legault

Person concerned: Pierre Legault, director.

Purpose: agreement entered into on 31 March 2016 with Mr. Pierre Legault to compensate him for judicial costs and convictions that might arise in case of invoking of his responsibility in the framework of his mandate as director of the Company.

Reason: This convention has been put in place in the framework of the appointment of Mr. Pierre Legault as director. It aims to offer a guarantee in consideration of the functions performed.

- Indemnification agreement of Mr. Richard Kender

Person concerned: Richard Kender, director.

Purpose: agreement entered into on 12 December, 2014 with Mr. Richard Kender to compensate him for judicial costs and convictions that might arise in case of invoking of his responsibility in the framework of his mandate as director of the Company.

Reason: This convention has been put in place in the framework of the appointment of Mr. Richard Kender as director. It aims to offer a guarantee in consideration of the functions performed.

- Management contract with Mr. Thomas Kuhn

Person concerned: Mr. Thomas Kuhn, Chief Executive Officer.

Subject: management contract with Mr. Thomas Kuhn signed on 28 March, 2014 presenting a mission of management of the company with the limitations of powers which are applicable to him and for a period equivalent to that of his corporate mandate as CEO. This contract also provides the methods used to set his gross earnings.

Compensation: A gross amount of €338,184 has been paid to Mr. Thomas Kuhn in connection with this mission.

- Indemnification agreement of Mr. Mohammed Khoso Baluch

Person concerned: Mohammed Khoso Baluch, director.

Purpose: agreement entered into on 12 December, 2014 with Mr. Mohammed Khoso Baluch to compensate him for judicial costs and convictions that might arise in case of invoking of his responsibility in the framework of his mandate as director of the Company.

Reason: This convention has been put in place in the framework of the appointment of Mr. Mohammed Khoso Baluch as director. The aim of the agreement is to provide a guarantee in consideration for the duties performed.

- Indemnification agreement of Ms. Pascale Boissel

Person concerned: Pascale Boissel, director.

Purpose: agreement entered into on 16 March, 2016 with Ms. Pascale Boissel to compensate her for judicial costs and convictions that might arise in case of invoking of her responsibility in the framework of her mandate as director of the Company.

Reason: This convention has been put in place in the framework of the appointment of Ms. Pascale Boissel as director. The aim of the agreement is to provide a guarantee in consideration for the duties performed.

Signed in Lyon and Courbevoie, on April 8, 2019

Statutory Auditors

MAZARS

Séverine Hervet

PricewaterhouseCoopers Audit

Elisabeth L'Hermite

## 20. FINANCIAL INFORMATION CONCERNING THE ASSETS, FINANCIAL POSITION AND THE RESULTS OF THE COMPANY

### 20.1. Financial statements established using IFRS standards for the financial years ended December 31, 2017 and December 31, 2018

#### 20.1.1. Statement of financial situation

POXEL Statement of financial position		Notes	31/12/2018 K€	31/12/2017 K€
<b>ASSETS</b>				
Intangible assets	6		16 577	
Tangible fixed assets	7		296	143
Other non-current financial assets	8		372	356
Deferred tax assets	22			
<b>Total non-current assets</b>			<b>17 246</b>	<b>500</b>
Trade and other receivables	9		14 262	4 902
Other receivables	9		7 271	7 187
Payable tax assets	22			
Cash and cash equivalents	10		66 737	54 163
<b>Total current assets</b>			<b>88 270</b>	<b>66 253</b>
<b>Total assets</b>			<b>105 516</b>	<b>66 752</b>
<b>LIABILITIES</b>				
<b>Shareholders' equity</b>				
Capital	12		517	463
Share premiums and paid-in capital	12		127 996	106 951
Conversion reserve	12		-5	
Reserves			-86 251	-65 788
Income			13 525	-22 298
<b>Total shareholders' equity</b>			<b>55 782</b>	<b>19 327</b>
<b>Non-current liabilities</b>				
Employee benefits	15		279	230
Non-current financial liabilities	14		359	555
<b>Non-current liabilities</b>			<b>638</b>	<b>785</b>

<b>Current liabilities</b>			
Current financial liabilities	14	13 873	936
Provisions	16	18	84
Trade payables and related accounts	17.1	20 742	9 008
Tax and social security liabilities	17.2	1 129	899
Contract liabilities	17.3	13 334	35 714
<b>Current liabilities</b>		<b>49 096</b>	<b>46 640</b>
<b>Total liabilities</b>			
		<b>105 516</b>	<b>66 752</b>

## 20.1.2. Statement of the overall result

POXEL		Notes	31/12/2018	31/12/2017
Statement of comprehensive income			K€	K€
<b>Revenue</b>	18		<b>74 605</b>	<b>5 290</b>
R&D costs				
R&D costs	19.1		-58 092	-24 096
Subsidy	19.1		3 552	3 122
General and administrative expenses	19.2		-7 527	-6 219
<b>Operating income</b>			<b>12 538</b>	<b>-21 902</b>
Financial expenses	21		-28	-81
Financial income	21		368	64
Foreign exchange gains and losses	21		724	-379
<b>Pre-tax income</b>			<b>13 602</b>	<b>-22 298</b>
Tax expense	22		-77	
<b>Net income</b>			<b>13 525</b>	<b>-22 298</b>
Earnings per share		Notes	31/12/2018	31/12/2017
Weighted average number of shares outstanding			24 833 331	23 033 299
<b>Earnings per share (€/share)</b>	23		<b>0,54</b>	<b>(0,97)</b>
<b>Diluted earnings per share (€/share)</b>	23		<b>0,53</b>	<b>(0,97)</b>

### 20.1.3. Other elements of the Overall Result

POXEL - IFRS Statement of comprehensive income	Notes	31/12/2018 K€	31/12/2017 K€
<b>Net income (loss) for the year</b>		<b>13 525</b>	<b>-22 298</b>
Actuarial gains and losses (not recyclable)	15	5	-70
Consolidation foreign exchange translation differences (recyclable)		-5	
Tax effect related to these items			
<b>Other comprehensive income (net of tax)</b>			<b>-70</b>
<b>Total comprehensive income</b>		<b>13 525</b>	<b>-22 368</b>

### 20.1.4. Variation of own capital

POXEL Change in equity	Capital Number of shares	Capital K€	Premiums linked to capital K€	Reserves and income K€	Other comprehensive income K€	Shareholders' equity K€
<b>At December 31, 2016</b>	<b>22 950 228</b>	<b>459</b>	<b>106 385</b>	<b>-67 463</b>	<b>5</b>	<b>39 385</b>
2017 net income				-22 298		-22 298
Other comprehensive income					-70	-70
<b>Total comprehensive income</b>				<b>-22 298</b>	<b>-70</b>	<b>-22 368</b>
Dividends						
Shares issued (Note 9)	177 200	4	542			546
Issue of warrants (Note 10)			24			24
Share-based payments				1 736		1 736
Treasury shares				3		3
Capital increase expenses						
Other						
<b>At December 31, 2017</b>	<b>23 127 428</b>	<b>463</b>	<b>106 951</b>	<b>-88 021</b>	<b>-65</b>	<b>19 327</b>
2018 net income				13 525		13 525
Other comprehensive income						
<b>Total comprehensive income</b>				<b>13 525</b>		<b>13 525</b>
Dividends						
Shares issued (Note 9)	2 729 399	55	21 046			21 101
Issue of warrants (Note 10)			41			41
Share-based payments				1 881		1 881
Treasury shares				-52		-52
Capital increase expenses			-41			-41
Other						
<b>At December 31, 2018</b>	<b>25 856 827</b>	<b>517</b>	<b>127 996</b>	<b>-72 667</b>	<b>-65</b>	<b>55 782</b>



## 20.1.5. Table of cash flow

POXEL - IFRS Cash flow statement	Notes	31/12/2018 K€	31/12/2017 K€
<b>Cash flows from operating activities</b>			
Net income from continued activities		13 525	-22 298
<b>Net income</b>		13 525	-22 298
(-) Elimination of amortization of intangible assets	6	-2	
(-) Elimination of depreciation of tangible fixed assets	7	-60	-38
(-) Provisions	15-16	-55	-112
(-) Reversals of provisions	16	66	
(-) Expense related to share-based payments	13	-1 881	-1 736
(+) Interest expense			-13
(-) Interest income		368	45
(-) Accretion of the Kreos debt			-33
(-) Subsidy transferred to income	14.2	-28	-33
<b>Cash flow before net finance cost and tax</b>		15 116	-20 377
(-) Change in working capital requirements		19 860	-28 503
<b>Cash flow from operations</b>		<b>-4 744</b>	<b>8 126</b>
<b>Cash flow from investing activities</b>			
Acquisition of intangible assets	6	-7 664	
Acquisition of tangible fixed assets	7	-213	-36
(+) Interests received		337	90
Other investment flows	8	-68	159
<b>Cash flow from investment activities</b>		<b>-7 608</b>	<b>213</b>
<b>Cash flow from financing activities</b>			
Capital increase and share premium net of expenses (1)	12	12 172	546
Subscription of warrants	12	41	24
(-) Interest paid		5	-20
Liabilities - contract Roivant	14.3	13 646	
Repayments of borrowings and conditional advances	14.2/14.3	-188	-1 046
Derivative liability			
<b>Cash flow from financing activities</b>		<b>25 676</b>	<b>-496</b>
Impact of exchange rate fluctuations			
<b>Increase (Decrease in cash)</b>		<b>13 325</b>	<b>7 843</b>
Cash and cash equivalents at beginning of period (including bank facilities)		53 412	45 569
Cash and cash equivalents at end of period (including bank facilities)		66 737	53 412
<b>Increase (Decrease in cash)</b>		<b>13 325</b>	<b>7 843</b>

### Detailed analysis of the variation of the need of rolling funds (BFR)

- (1) In 2018, the capital increase corresponds to:
- the investment in the share capital of Roivant (see Note 4.1) with the creation of 1,431,399 subscribed shares at a price of 8.5 €
  - the exercise by employees of 400 BSPCEs giving the right to subscribe for 8,000 shares at a price of €2.5 per share.
- The issuance of 1.29 million shares under the agreement with DeuteRx (see Note 4.1) did not generate any cash flow. Costs of €41K were recognized as a deduction from the share premium.
- (2) In 2017, the capital increase and share premiums net of expenses (€546,015) corresponds to:
- The exercise by employees of 2,200 BSPCEs giving the right to the issuance of 44,000 shares at a price of €2.5 per share;

- The exercise by employees of 2,000 BSPCEs giving the right to the issuance of 40,000 shares at a price of €3.2 per share;
- The exercise by employees of 4,500 BSPCEs giving the right to the issuance of 90,000 shares at a price of €3.3 per share;
- The exercise by employees of 160 BSPCEs giving the right to the issuance of 3,200 shares at a price of €2.5 per share.

## 20.1.6. Detailed analysis of the change in working capital requirement (WCR)

Breakdown of the change in WCR	31/12/2018	31/12/2017
Trade and other accounts receivable (net of accounts receivable impairment)	9 360	4 866
Other receivables	84	3 190
Trade payables and related accounts	-11 734	-461
Tax and social security liabilities	-230	-440
Other creditors and accrued liabilities	8 733	-35 659
Total changes	6 214	-28 503

## 20.1.7. Notes to the IFRS financial statements

### Note 1: Presentation of the business activities and major events

The information below constitutes the appendix to the consolidated IFRS financial statement, constituting an integral part of the financial statements presented for the years ended December 31, 2017 and December 31, 2018. Each of these years has a duration of twelve months covering the period from 1 January to 31 December.

#### 1.1 Information relating to the Company and to its activity

Incorporated in March 2009 as a result of a spin-off from Merck Serono, Poxel S.A. is a French société anonyme (public limited liability company) with its registered office at 259 Avenue Jean Jaurès, 69007 LYON, registered in the Lyon Trade and Companies Register under number 510 970 817 RCS, further to be referred to as “the Company” or “the Group”, which includes its subsidiary), with the business activity of developing innovative molecules for the treatment of metabolic diseases, of which type 2 diabetes and non-alcoholic steatohepatitis (NASH).

The Company has incurred operating losses every year, except for the financial year of its inception. Such losses result principally from internal and external research and development expenses, related in particular to conducting numerous pre-clinical and clinical trials, primarily as part of the development of Imeglimin. In October 2017, the Company signed an initial contract of strategic partnership with Sumitomo Dainippon Pharma for the development and marketing of Imeglimin, drug candidate for the treatment of type 2 diabetes in Japan, China and eleven other countries in Asia. A second strategic partnership was signed in February 2018 with Roivant Sciences for the development and commercialisation of Imeglimin in the United States, in Europe and in other countries not covered by the agreement with Sumitomo Dainippon Pharma. On August 30, 2018, the Company signed a strategic agreement with DeuteRx for the acquisition of an innovative drug candidate at the clinical development stage for the treatment of NASH, as well as other programs for the treatment of metabolic diseases.

The Company’s future development depends on a combination of several factors, including: (i) the success of its research and development operations; (ii) the continuation of partnership agreements entered into by the Company; (iii) obtaining regulatory approval and market acceptance of the future products proposed by the Company; (iv) obtaining the necessary financing; and (v) the development of competing products by other companies. Consequently, the Company was able, on the

short/medium term, to finance itself through new partnerships for the development and marketing of its drug candidates and through the issuance of new equity instruments.

## **1.2 Closing date**

The financial statements have been prepared under the responsibility of the Company's management and have been approved and authorized to be published by the Board of Directors on March 21, 2019.

## **Note 2: Principles for the preparation of the financial statements**

The financial statements are shown in thousands of euros unless indicated otherwise. Rounding is performed for the calculation of certain financial data and other information contained in these accounts. Accordingly, the figures shown in the form of totals in some tables may not be the exact sum of figures which precede them.

### **Declaration of Conformity**

Poxel has prepared its financial statements, approved by the Board of Directors on March 21, 2019, in accordance with the standards and interpretations issued by the International Accounting Standards Boards (IASB) and adopted by the European Union on the date of preparation of the financial statements, for all periods presented.

This repository, available on the website of the European Commission ([http://ec.europa.eu/internal\\_market/accounting/ias\\_fr.htm](http://ec.europa.eu/internal_market/accounting/ias_fr.htm)), incorporates the International Accounting Standards (IAS and IFRS), the interpretations of the Standing Interpretations Committee - SIC and of the International Financial Interpretations Committee - IFRIC.

The accounting standards and methods and options selected by the Company are described below. In some cases, the IFRS standards leave the choice between the application of a reference treatment or other authorised treatment.

### **Principle of preparation of financial statements**

The Company accounts were prepared according to the principle of historical cost, with the exception of certain categories of assets and liabilities, in accordance with the provisions imposed by the IFRS standards. The categories concerned are mentioned in the following notes.

### **Continuity of Operation**

The going concern assumption has been adopted, taking into account the financial capacity of the Company (available cash) in relation to its financing needs for the 12 months following the closing date.

### **Accounting methods**

The Company has chosen to apply the IFRS 15 "Revenue from ordinary activities derived from contracts concluded with customers" by anticipation on January 1, 2017. The other accounting principles retained are identical to those used for the preparation of the annual IFRS financial statements for the financial year ended December 31, 2017, with the exception of the application of the following new standards, amendments of standards and interpretations adopted by the European Union, with mandatory application for the Company at 1 January, 2018.

**Standards, amendment of standards and interpretations, applicable from the year starting on 1 January, 2018**

- *IFRS 9 - Financial Instruments*
- *IFRS 15 - Revenue from Contracts with Customers*
- *Clarifications to IFRS 15*
- *IFRIC 22 - Transactions in foreign currencies and early consideration*
- *Amendments to IFRS 2 - Classification and measurement of share-based payment transactions*
- *Amendments to IFRS 4 - Application of IFRS 9 with IFRS 4*
- *Amendments to IAS 40 - Transfers of investment property*
- *Improvement of IFRS (2014-2016 cycle).*

These new texts adopted by the European Union have not had a significant impact on the financial statements of the Group.

**Standards, amendments of standards and interpretations not yet adopted by the Group**

***Standards, amendments of standards and interpretations adopted by the European Union but not yet mandatory for the 2018 annual accounts***

- *IFRS 16 - Rentals*
- *Amendments to IFRS 9 - Prepayment features with negative compensation*
- *IFRIC 23 - Uncertainty relating to tax treatment*

***Standards and interpretations issued by the IASB and not yet adopted by the European Union at December 31, 2018***

- *Amendments to IAS 28 - Long-term Interests in Associates and Joint Ventures*
- *Amendments to IAS 19 - Plan amendments, curtailments or settlements*
- *Improvement of IFRS (2015-2017 cycle).*

The Group is currently assessing the impacts following the first application of these new standards and does not anticipate any material impact on its financial statements, with the exception of IFRS 16.

IFRS 16 will be mandatory from January 1, 2019.

IFRS 16 removes the distinction between operational leases and finance leases. Consequently, operational leases will be restated for the application of IFRS 16.

The standard provides for the recognition of all rental contracts in the balance sheet of the lessees, reporting an asset (representing the right of use of the leased asset for the duration of the contract) and a debt (the obligation of payment of rent). The standard will also affect the presentation of the income statement (revenue from operations and financial charges) and cash flow table (flows related to operational activities and flows linked to financing transactions). Regarding the estimate of the duration of lease agreements, the Group will apply the recommendation of the France's national accounting standards body (*Autorité des Normes Comptables*) to the real estate leases agreements in France.

Regarding the procedures for the first-time application of the standard, the Company has decided to opt for the simplified retrospective method. As a result, comparative information will not be restated and the cumulative impact of the first-time adoption of the standard will be recognized in the equity as of January 1, 2019.

On the basis of the contracts in effect at December 31, 2018, the Company estimates preliminary that the future rental liability, determined in accordance with IFRS 16, is in the order of between 1.3 M€ and 1.8 M€.

### **Use of judgments and estimates**

To prepare the financial statements in accordance with IFRS, estimates, judgements and assumptions have been made by the Management of the Company; they could have affected the amounts presented as elements of assets and liabilities, the contingent liabilities at the date of establishment of the financial statements, and the amounts presented as the year's revenue and costs.

These estimates are based on the hypothesis of continuity of operation and are established on the basis of the information available at the time of their establishment. They are evaluated on a continuous basis according to past experience, as well as various other factors deemed reasonable, which constitute the basis of the assessments of the carrying value of assets and liabilities. The estimates may be revised if the circumstances on which they were based evolve or as a result of new information. The actual results could differ significantly from these estimates, depending on different assumptions or conditions.

The main estimates or significant judgements made by the management of the Company include the following elements:

- recognition of revenues (note 18), notably for the estimate of the transaction price and of the choice of the allocation method of the transaction price to the performance obligations;
- allocation of share subscription warrants, stock options, free shares or warrants to employees, executives and external providers (note 13) notably on the evaluation methods of the instruments.

### **Change of the accounting method**

As of January 1, 2018, the Group has applied IFRS 9 "Financial Instruments", which replaces IAS 39 "Financial Instruments: Recognition and Measurement", and deals with the classification and measurement, as well as the impairment and hedge accounting of financial assets and liabilities. The application of the classification and measurement principles provided for in IFRS 9 did not have a material impact on the Group's financial statements.

With the exception of the new text identified above, the Company has not made any other changes in accounting policies in respect of the financial year ended December 31, 2018.

## **Note 3: Accounting policies and methods**

### 3.1 Scope and methods of consolidation

The Group applies IFRS 10 - Consolidated Financial Statements, IFRS 11 - Partnerships, IFRS 12 - Disclosures about interests held in other entities.

IFRS 10 provides a single consolidation model that identifies control as an entity's consolidation criteria. An investor controls an issuing entity if he has power over the entity, is exposed to or entitled to variable returns as a result of his involvement in the entity, and has the ability to use his power over the entity to influence the amount of the return of the investor.

Subsidiaries are entities over which the Group exercises control. They are fully consolidated from the date on which the Group obtains control and are deconsolidated from the date on which the Group ceases to exercise control.

Intra-group balances and transactions are eliminated.

The following entities are included in the scope of the consolidation:

Name	Country	Consolidation method		% Control		% Interest	
		As at December 31		As at December 31		As at December 31	
		2018	2017	2018	2017	2018	2017
POXEL S.A.	France	-	-	-	-	-	-
POXEL JAPAN	Japan	FC	N/A (1)	100%	N/A	100%	N/A

(1) Poxel Japan was established in 2018.

- FC: Full consolidation

### 3.2 Functional currency of presentation

In accordance with IAS 21 - The Effects of Changes in Foreign Exchange Rates - items included in the financial statements of each of the Group's entities are measured in the currency of the primary economic environment in which the entity operates (the "functional currency").

The financial statements of the Company are in euro, which is the reporting currency as well as the functional currency of the Company.

The financial statements of foreign entities whose functional currency is not the euro are converted into euros as follows:

- assets and liabilities are converted at the closing exchange rate at the closing date; and
- income and expenses are converted at the prevailing exchange rate on the transaction date or at the average exchange rate for the period if that rate comes close to the prevailing exchange rate on the transaction date.

Exchange differences resulting from the application of this method are recognized in consolidated shareholders' equity under "other elements of the overall result".

### **3.3 Foreign Currency**

The transactions in foreign currency are converted into the functional currency of the Company by applying the exchange rate in force at the date of the transactions. Monetary assets and liabilities denominated in foreign currency at the date of closure are translated into the functional currency using the exchange rate at this date.

The exchange gains and losses resulting from the conversion of monetary items correspond to the difference between the amortised cost denominated in the functional currency at the opening of the period, adjusted for the impact of the effective interest rate and payments over the period, and the amortised cost expressed in foreign currency converted at the exchange rate at the date of closure.

The non-monetary assets and liabilities denominated in foreign currencies that are measured at fair value are converted into the functional currency using the exchange rate of the date on which the fair value was determined. Exchange differences resulting from these conversions are recorded in the income statement.

The debts and claims denominated in foreign currencies are recorded at the rate of the currency at the time of the original transaction. At the close of the fiscal year, the positions corresponding to assets and liabilities are evaluated at the closure rate.

### **3.4 Intangible assets**

#### **Acquired research and development**

Payments made for the acquisition of a product portfolio are recognized as "Other intangible assets" when they meet the definition of an intangible asset, i.e. when it is a controlled resource, from which the Group expects future economic benefits, and which is identifiable, i.e. separable or resulting from contractual or legal rights.

In accordance with paragraph 25 of IAS 38 "Intangible assets", the first recognition criterion, relating to the probability of future economic benefits generated by the intangible asset, is deemed to be met for research and development work when they vest separately.

In this context, amounts paid to third parties in the form of initial payments or milestone payments relating to proprietary medicinal products that have not yet received marketing authorization, are recognized as assets. These rights are amortized on a linear basis over their useful life from the time the marketing authorization is obtained. Unamortized rights (before marketing authorization) are subject to impairment tests in accordance with the procedures defined in Note 3.6.

#### **Internally generated research and development costs**

In accordance with IAS 38 - Intangible Assets, research costs are recognized in the consolidated financial statements as expenses in the period in which they are incurred.

Development costs are recognized as intangible assets only if all of the following criteria are met:

- Technical feasibility necessary for the completion of the development project;

- Intention of the Company to complete the project;
- ability of the latter to use this intangible asset;
- Demonstration of the probability of future economic benefits attached to the asset;
- Availability of technical, financial and other resources in order to complete the project;
- Reliable assessment of development expenditure.

The expenditures are activated only from the date, on which the conditions for activation of the intangible asset are met. The expenditures cease to be registered as assets when the intangible asset is ready to be used. The costs of development reported as assets are amortised over their useful life.

Due to the risks and uncertainties related to regulatory approvals and the research and development process, the Group believes that the six criteria set out in IAS 38 have not been met to date and that the application of this principle has resulted in the recognition as an expense of all development costs incurred in all periods presented.

### **Other Intangible Assets**

Other intangible assets mainly consist of acquired software. Costs related to the acquisition of software licenses are recognized based on the costs incurred to acquire and install the corresponding software. Software is amortized on a linear basis over a period of one to three years depending on their period of use.

### **3.5 Tangible assets**

In accordance with IAS 16 - Property, Plant and Equipment, tangible assets are recognized at their acquisition cost (purchase price and directly attributable costs) or at their production cost by the Group, as appropriate.

Tangible assets are amortized on a linear basis over their estimated useful lives.

The depreciation periods and methods used are primarily the following:

Elements	Depreciation periods
Facilities and fixtures	5 to 10 years - Linear
Computer hardware	1 to 3 years - Linear
Furniture	5 years - Linear

The useful life of tangible assets and any residual values are reviewed at the end of each financial year and, in the event of a material change, result in a prospective revision of the amortization table.



The amortisation of tangible assets is recognised in the income statement in the category of administrative costs in the light of the nature of assets held.

### **Lease contract**

The lease contracts, for which substantially all of the risks and benefits are retained by the lessor, are classified as operating leases. Payments for these operating leases, net of any incentive, are recognized as an expense in the income statement on a straight-line basis over the duration of the contract.

The properties financed by financial lease agreements within the meaning of the standard IAS 17, which essentially transfer the risks and benefits inherent to the property to the Company, are recorded on the asset side of the balance sheet. The corresponding debt is recorded as a liability in the "Financial Liabilities".

### **3.6 Recoverable amount of non-current assets**

In accordance with IAS 36, assets having an indefinite useful life are not amortized or depreciated and are subject to an annual impairment test. The depreciated assets are subject to an impairment test whenever there is an internal or external index showing that an asset could have lost its value.

The impairment test consists of comparing the net book value of the tested asset to its recoverable amount. The test is carried out at the level of the cash-generating unit ("UGT"), which is the smallest group of assets that includes the asset, and the continued use of which generates cash inflows that are largely independent of those from other assets or groups of assets.

An impairment is recognized up to a maximum of the excess of the carrying value on the recoverable value of the asset. The recoverable value of an asset corresponds to its fair value minus costs of assignment or its useful value, if the latter is higher.

Impairment tests are performed at the closing date of the financial year for unamortized assets (whether or not there is an indication of impairment), based on forecast cash flows determined by management. The estimates used to calculate the recoverable amount are sensitive and depend on assumptions specific to the nature of the Group's business with respect to:

- Estimates of development costs, sales and cost of sales over the term of patent protection,
- the discount rate: the discount rates are determined on the basis of a base rate calculated for the Company, adjusted where necessary by a specific risk premium.
- Long-term sales forecasts;
- Actions of competitors;
- The results of R&D activities (effectiveness of compounds, results of clinical trials, etc.);
- The probability of obtaining regulatory approval;
- The amount and timing of the costs expected to develop intellectual property into commercially viable products.

The fair value minus the disposal costs is the amount, which can be obtained from the sale of an asset during a transaction in conditions of normal competition between well informed and willing parties, decreased by the costs of disposal.

The value in use is the present value of estimated future cash flows expected to arise from the continued use of an asset and from its disposal at the end of its useful life. The value in use is determined on the basis of estimated cash flows based on the development plan for the assets and the resulting expected sales, and are discounted using long-term after-tax market rates that reflect market estimates of the time value of money and the specific risks of the assets.

As of December 31, 2018:

- The Group has no intangible assets with an indefinite life.
- As explained in Note 3.4, the Group has an amortizable intangible asset related to the acquired R&D, which amortization will start as from the obtention of the marketing authorization. This asset has been subject of a depreciation test (as mentioned in note 6);
- No non-current asset present an internal or external index of loss of value.

### **3.7 Financial Assets**

Since January 1, 2018, and in accordance with IFRS 9 - Financial Instruments, the Group's financial assets are classified into two categories according to their nature and management's intention:

- Financial assets at fair value in the income statement;
- Financial assets at amortized cost.

All purchases and sales of financial assets are recorded at the settlement date.

#### **Financial assets at fair value in the income statement**

This category includes investment securities. They represent the assets held for the purposes of transaction, i.e. the assets acquired by the Company with the objective of transfer in the short term. They are valued at their fair value and the changes in fair value are recorded in the income statement.

#### **Financial assets at amortized cost**

This category includes other financial assets (non-current), trade receivables (current) and other receivables and associated accounts (current). The other non-current financial assets include advances and guarantee deposits issued to third parties, as well as term deposits that are not considered to be cash equivalents.

Financial assets at amortized cost mainly include deposits and guarantees, restricted cash, trade receivables, other receivables, conditional advances and loans. These are non-derivative financial assets with fixed or determinable payments that are not listed on an active market. They are initially recognized at fair value plus transaction costs directly attributable to the acquisition or issue of the financial asset, except for trade receivables initially recognized at the transaction price as defined in IFRS 15.

After initial recognition, these financial assets are measured at amortized cost using the effective interest rate method when the following two conditions are met:

- (a) the financial asset is held in a business model whose objective is to hold financial assets in order to collect contractual cash flows; and
- (b) The contractual terms of the financial asset give rise, at specified dates, to cash flows consisting solely of payments of principal and interest on the remaining principal due.

Gains and losses are recognized in the consolidated statement of income when they are derecognized, subject to a change in contractual cash flows and/or an impairment loss.

IFRS 9 - Financial Instruments requires an entity to recognize a provision for expected credit losses on a financial asset at amortized cost at each balance sheet closing date. The amount of the provision for expected credit losses is equal to: (i) the expected credit losses over 12 months, or (ii) the expected credit losses over the entire lifetime. The latter applies if the credit risk has increased significantly since the initial recognition of the financial instrument. An impairment loss is recognized, where appropriate, on a case-by-case basis to take into account recovery difficulties that may arise based on information available at the time the financial statements are prepared.

Contested receivables are derecognized when the Company does not reasonably expect to recover the financial asset in whole or in part. The provision for existing credit losses is then reversed.

### **Cash, cash equivalents and financial instruments**

Cash and short-term deposits recorded in the balance sheet include banking availability, the availability of cash and short-term deposits very liquid having initial maturity term less or equal to three months and which are not subject to a material risk of changes of the fair value.

Cash equivalents are comprised of securities (UCITS). Cash equivalents are held for the purposes of transaction, readily convertible to a known amount of cash and are subject to an insignificant risk of changes in value. They are valued at their fair value and the changes in value are recorded in the income statement.

For the purposes of the cash flow table, in accordance with IAS 7, net cash includes cash and cash equivalents, net of bank overdrafts.

### **Fair value of financial instruments**

The securities of qualified investment of cash equivalents at the end of the year are recorded at fair value, their fair value being based on their market value.

The financial loans and debt are recorded at amortised cost, calculated using the effective interest rate (TIE) or optionally at fair value in the income statement.

The fair value of client receivables and supplier debts is assimilated to their value at the balance sheet, in view of very short deadlines for payment of these claims. It is the same for the other current receivables and other current debts.

The Company has distinguished between three categories of financial instruments, depending on the consequences of their characteristics on their mode of valuation and relies on this classification to present some of the information requested by the IFRS 7 standard:

- Category of level 1: Financial instruments that are the subject of quotations on an active market;
- Category of level 2: Financial instruments, whose assessment involves valuation techniques based on observable parameters;
- Level 3 category: Financial instruments whose valuation involves valuation techniques based fully or partially on unobservable parameters; an unobservable parameter is defined as a parameter whose value is the result of assumptions or correlations that are based neither on prices of transactions observable on the markets, for the same instrument at the date of valuation, nor on available market data observable at the same date.

The instruments recognized at fair value through profit or loss held by the Company are cash equivalents, falling within the category of level 1 and term deposits in level 2.

### **3.8 Capital**

The classification as equity depends on the specific analysis of the characteristics of each instrument issued. Based on this analysis, when the entity that has issued the financial instrument is not under a contractual obligation to deliver cash or another financial asset to the holder, the financial instrument is an equity instrument. Therefore, if the holder of an equity instrument is entitled to a proportional share of dividends, the issuer has no contractual obligation to make such distribution, as this is the only decision of the shareholders at the annual general meeting.

Own shares held are deducted from equity.

Ancillary costs directly attributable to the issuance of shares or options on shares are recorded as a deduction from equity. Furthermore, in the absence of clarification of the IAS 32 standard, the company has made the choice to count these costs as a deduction from equity before the completion of the operation in the case where an annual closure would intervene between the date of service and the operation. In the hypothesis where the operation would not take place, these costs would then be registered as charges in the next fiscal year.

### **3.9 Payments in shares**

Since its creation, the Company has put in place several compensation plans that may be settled in equity instruments in the form of "share warrants" ("BSA") or "founders' warrants" ("BSPCE"), stock options or free shares, granted to employees, managers, consultants and members of the Board of Directors.

In accordance with IFRS 2, the cost of transactions settled in equity instruments is recognized is measured at fair value at the grant date and recognized as an expense over the period in which the rights to benefit from the equity instruments vest, in consideration of an increase in equity capital.

The Company has applied the IFRS 2 standard to all equity instruments granted, from the origin of the Company, to employees, members of the Board of Directors or to physical persons providing services, such as consultants.

Fair value is calculated using the most appropriate formula for the terms and settlement of each plan (see Note 13).

### **3.10 Borrowings**

As of January 1, 2018, and in accordance with IFRS 9 - Financial Instruments, financial liabilities are measured at amortized cost or fair value through net income. Financial liabilities due within one year are presented as "Current financial liabilities" in the consolidated statement of financial position.

Financial liabilities are classified as financial liabilities recorded at amortised cost or financial liabilities recorded at the fair value in the income statement.

#### **Financial liabilities recorded at amortised cost**

Borrowings and other financial liabilities, such as conditional advances, are recorded at amortized cost calculated using the effective interest rate. The fraction of less than one year of financial liabilities is presented in "current financial liabilities".

#### **Financial liabilities recorded at the fair value in the income statement**

If applicable, particularly if the existence of a hybrid instrument is found, a financial liability may be accounted for at fair value in the income statement.

#### **Conditional advances**

Funds received from Bpifrance Financement, the French public investment bank (formerly Oséo) as conditional advances, are recognized as financial liabilities, whereby the Company has the contractual obligation to repay these conditional advances in cash on the basis of a repayment schedule. Each allocation of an advance is made to help finance a specific development milestone. The details of the conditional advances are provided in Note 14.2. Receipts or repayments of conditional advances are presented in the "Financing" section of the cash flow statement.

The Company receives conditional interest-free advances to finance research and development projects. The difference between the present value of the advance at the market rate (i.e. the capital repaid at maturity without interest and discounted at market rate) and the amount received in cash from Bpifrance Financement constitutes a grant within the meaning of the IAS 20 standard. This benefit is determined by applying a discount rate equal to the market interest rate.

The implicit interest rate resulting from taking into account all repayments, plus the additional payments due in the event of commercial success described in Note 14.2, is used to determine the amount recognized annually as a financial expense, based on observable rates of comparable companies.

In the event of a change in the repayment schedule, the Company recalculates the net carrying amount of the debt resulting from the discounting of expected new future cash flows at the initial

effective interest rate. The resulting adjustment is recognized in the income statement in the period in which the change is recognized.

Subsidies are shown separately in the consolidated income statement. The Company has opted for a classification as a deduction from “research and development costs”, as they correspond to support for innovation and the financing of research activities in accordance with IAS 20.

In the consolidated statement of financial position these advances are recognized under “Financial liabilities” as either current or non-current depending on their maturity. If the Company does not achieve a particular milestone that could trigger the repayment of the conditional advance, the remaining liability is recognized as a subsidy.

### **Subsidies**

Subsidies received are non-refundable receipts recognized as revenue when there is reasonable assurance that the Company will meet the conditions attached to them, and that they will be received. Subsidies that are upfront payments are recognized as revenue up to the expenses incurred in the research program to which the grant relates.

### **Research tax credit**

The Company is entitled to the provisions of Articles 244c and 49f of the French General Tax Code relating to the French research tax credit (“Crédit d'Impôt Recherche” or “CIR”). The CIR is authorized by the French tax authorities to encourage companies to perform technical and scientific research. Companies that show that they have expenses that meet the requisite criteria (research expenses made in France or, since January 1, 2005, in the European Union or in another State party to the Agreement on the European Economic Area that has entered into a tax treaty with France containing an administrative assistance clause) are entitled to a tax credit, which may be used to pay the corporate tax due for the financial year in which the expenses were incurred and the following three years, or as the case may be, can be reimbursed in cash. Expenses taken into account for the calculation of the CIR only pertain to research and development expenses.

The Company has been entitled to the CIR since its inception and received cash refunds the year following the date of its registration as a tax credit in the Group's financial statements, in accordance with Community tax rules applicable to small and medium-sized companies.

The CIR is recognized in the consolidated statement of net income under “other operating income” because it meets the definition of a government subsidy as defined in IAS 20 - Accounting for Government Grants and Disclosure of Government Assistance.

### **3.11 Social Commitments**

The French employees of the Company benefit of pensions provided by the law in France:

- Obtaining a retirement severance pay, paid by the company, upon their retirement (defined benefit plan);
- Payment of retirement pensions by the social security organisations, which are funded by the contributions of businesses and employees (defined contribution plan).

In accordance with IAS 19 - Employee Benefits, the liability for defined benefit plans is estimated using the projected unit credit method.

Under this method, the cost of the pension benefit is recognized in the consolidated statement of income to ensure that it is spread evenly over the employees' lifetime service. Pension obligations are measured at the present value of estimated future payments, discounted at market rates for high quality corporate bonds with terms corresponding to the estimated term of the compensation payments. The difference between the amount of the provision at the beginning of a period and at the closing date of the period is recognized in profit or loss for the portion representing current service cost and net interest cost, and through other comprehensive income for the portion representing actuarial gains and losses.

The Group's payments under the defined contribution plan are recognized as expenses in the consolidated statement of income in the period in which they become payable.

### **3.12 Provisions**

The provisions correspond to the commitments resulting from disputes and various risks, whose due date and the amount are uncertain, which the Company may be facing in the framework of its activities.

Under IAS 37, a provision is recognized when the Company has an obligation towards a third party as a result of a past event, which it is likely to cause an outflow of resources to the benefit of this third party, without expected consideration at least equivalent of the latter, and that the future outputs of liquidity can be estimated reliably. The amount recognised as a provision is the estimate of the expenditure required for the extinction of the obligation, updated if necessary at the closing date.

### **3.13 Corporate income taxes**

Income tax assets and liabilities payable for the financial year and prior financial years are recognized for the amount that is expected to be recovered from or paid to the tax authorities in accordance with IAS 12 - Income Taxes. The tax rates and tax regulations used to determine these amounts are those which have been adopted or quasi adopted at the closing date.

The deferred taxes are recorded using the balance sheet method and the variable deferral, for all temporary differences existing at the date of closing between the tax base of assets and liabilities and their book value in the balance sheet, as well as on the reportable deficits. Temporary differences are related to tax losses carried forward.

A deferred tax asset is recognized for deductible temporary differences, unused tax losses and unused tax credits to the extent that it is probable that taxable profits will be available and that the deductible temporary differences will be utilised in excess of the amount of the deferred tax liability existing within the same tax jurisdiction and taxable entity. The assessment of the amount of deferred tax assets may require management to make estimates regarding the period in which tax loss carryforwards must be used, as well as of the level of future taxable income.

### **3.14 Revenue**

The turnover of the Company comes from the sale of licenses and research and development services. The turnover is shown net of tax on the value added and discounts.

- Sale of licenses

The licenses granted by the Company correspond to rights of use. Therefore, the income from these licenses is recognised immediately from the date when the customer can begin to use the license. The consideration received can be fixed or variable. Variable consideration is only recognized if it is highly probable that a significant reversal will not take place.

When the compensation of a license is done in the form of royalties, based on the future sales carried out by the customer, the company applies the exception provided by the IFRS 15 to the general rule for the assessment of variable payments. Royalties are thus found in business figures when customer's sales take place.

- Services

The Company provides research and development services to clients. These services are made in the context of obtaining a future Marketing Authorisation (MA). The turnover in respect of these services is recognized according to the progress, and the customer receives the service as the company performs the work. The progress is measured by the costs.

- Cooperation Agreements

The Company may conclude cooperation agreements, which provide for both the sale of a license and research and development services. For these contracts, the Company estimates the amount to which it is entitled in exchange of the elements promised to customers. The amount that is highly probable (non-refundable advances, guaranteed payments and estimation of research and development expenses incurred) is allocated to the various elements of the contract in proportion to their specific sales prices.

When the specific sales price of a license is highly variable or uncertain, the company applies the residual method to evaluate it. This method is to determine the specific sales price by the difference between the overall price of the contract and the sum of the prices of specific sale (observable or estimable) of other goods and services promised in the contract.

The contracts may provide for staggered payments, whose perception depends on the achievement of certain development, regulatory or commercial objectives. Milestone payments are recognized when it is highly probable that the criteria are met and the risk of reversal of recognized revenue is low.

### 3.15 Financial income (expense)

The financial result includes all:

- changes in fair value of the debts recorded at fair value through profit or loss;
- expenses related to the financing of the Company;
- income related to the perceived interests.



- foreign exchange gains or losses

### **3.16 Earnings per share**

In accordance with IAS 33, basic loss per share is calculated by dividing the income attributable to shareholders of the Company by the weighted average number of outstanding common shares for the period.

Diluted loss per share is measured by adjusting the income attributable to the holders of ordinary shares and the weighted average number of outstanding ordinary shares for the effects all the dilutive potential ordinary shares.

If, in the calculation of diluted loss per share, instruments giving deferred rights to capital such as stock options or warrants (BSAs) do not generate an dilutive effect, these instruments are not taken into account.

## **Note 4: Significant events**

### **4.1: Significant events in the 2018 financial year**

#### **License agreement with DeuteRx**

On August 30, 2018, the Company announced the signing of a strategic agreement with DeuteRx for the acquisition of DRX-065, an innovative drug candidate at the clinical development stage for the treatment of NASH, as well as other programs for the treatment of metabolic diseases. The Company thus acquired the exclusive worldwide ownership of DRX-065 (R-pioglitazone stabilized by deuterium substitution), a clinical development program for the treatment of NASH. It has also acquired other programs, including deuterated drug candidates for the treatment of rare and specialized metabolic diseases.

This agreement resulted in an initial payment of €6.8 M (\$8 M) and the issuance for the benefit of DeuteRx of 1.29 million new ordinary shares of Poxel at the price of €6.91 per share, representing 4.99% of the capital of Poxel.

An intangible asset of €16.572 K was recognized as of December 31, 2018 under this contract.

#### **Licence contract with Roivant Sciences GmbH**

On 9 February, 2018 we signed an exclusive contract with Roivant Sciences GmbH ("Roivant") for development and commercialisation of Imeglimin, oral drug candidate developed by us from treatment of type 2 diabetes, in the United States, in Europe and in other countries not covered by the partnership existing in Eastern and South-Eastern Asia between us and Dainippon Pharma.

The agreement includes an initial payment of \$35 million (approximately EUR 28 million) to the benefit of the Company. Payments linked to attainment of the objectives of regulatory development and sales, up to a maximum of 600 million dollars (approximately 486 million euros), are also planned. The contract includes the payment of two-digit royalties on net sales made by Roivant, the percentage of which is growing according to the level of sales.

Roivant will take in charge the costs of development and marketing of the Imeglimin, and the Company will participate in the financing of the program for the development of up to \$25 million

(approximately EUR 20 million) under an unconditional commitment, to be paid over two years from the date of signature of the license agreement.

In addition, Roivant has invested \$15 million (approximately 12 million euros) in the capital of Poxel, by subscription of 1,431,399 new common shares of the Company at a price of 8.50 € per share.

The accounting treatment of this contract is presented in Note 18.

### **Increases in capital**

Several capital increases took place in the 2018 financial year:

- As part of the agreement signed in February 2018, discussed above, the Company issued 1,431,399 new common shares to Roivant Sciences at a price of 8.50 € per share, representing a capital increase of 29 K€ and an issue premium of 12,138 K€.
- on May 21, 2018 an employee exercised 400 founders' warrants, giving right to subscribe to 8,000 common shares at a price of 2.5€, representing a capital increase of 0.2 K€, together with a share premium of 20 K€.
- In August 2018, in the context of the agreement with DeuteRx (see above), the Company issued 1.29 million new ordinary shares of Poxel at the price of €6.91 per share.

Accordingly, the share capital is €517,136.84 as of December 31, 2018, divided in 25,856,827 shares of €0.02 of nominal value.

### **Establishing a subsidiary in Japan**

In March 2018, the Company established a subsidiary in Japan, ("POXEL JAPAN KK"), registered in Tokyo. This subsidiary is fully owned by POXEL SA. Its share capital is 20 million yen.

### **4.2: Post-balance-sheet date events**

None

### **Note 5: Segment information**

The Group operates in one single segment: the development of innovative molecules for the treatment of metabolic diseases, in particular diabetes type 2 diabetes and non-alcoholic steatohepatitis (NASH).

Poxel SA maintains a subsidiary in Japan since 2018, which did not have any significant activities at the closing date. Most of the assets and operating income presented are therefore located in France. The Group's performance is currently recorded at the consolidated level.

In 2018, the Group's revenues are divided among two customers: Sumitomo Dainippon Pharma for 89%, and Roivant Science GMBH for 11%.

In 2017, Sumitomo Dainippon Pharma represented almost 100% of the Group's revenue.

### **Note 6: Intangible assets**

<b>GROSS VALUES OF INTANGIBLE ASSETS</b> <b>(Amounts in thousands of euros)</b>	<b>Software</b>	<b>Product portfolio</b>	<b>Total</b>
<b>Statement of financial position at December 31, 2016</b>	<b>2</b>		<b>2</b>
Capitalization/acquisition of development costs			
Acquisition			
Retirement			
Transfer			
<b>Statement of financial position at December 31, 2017</b>	<b>2</b>		<b>2</b>
Capitalization/acquisition of development costs	6	16 572	<b>16 578</b>
Acquisition	6	16 572	<b>16 758</b>
Retirement			
Transfer			
<b>Statement of financial position at December 31, 2018</b>	<b>9</b>	<b>16 572</b>	<b>16 580</b>

#### **AMORTIZATION/DEPRECIATION**

<b>Statement of financial position at December 31, 2016</b>	<b>2</b>		<b>2</b>
Increase			
Decrease			
<b>Statement of financial position at December 31, 2017</b>	<b>2</b>		<b>2</b>
Increase	2		<b>2</b>
Decrease			
<b>Statement of financial position at December 31, 2018</b>	<b>4</b>		<b>4</b>

#### **CARRYING AMOUNT**

<b>At December 31, 2017</b>			
<b>At December 31, 2018</b>	<b>5</b>	<b>16 572</b>	<b>16 577</b>

In 2018, under the contract signed with DeuteRx (see Note 4.1), the Company acquired an innovative drug candidate under clinical development for the treatment of NASH (DRX-065), as well as other programs for the treatment of metabolic diseases for a non-refundable sum of 15,780 K€, of which 8,914 K€ paid in shares and \$8 million (6,866 K€) paid in cash, as well as additional variable payments (see Note 25.5). This acquisition is recognized as an intangible asset for an amount of €16,572 K, which includes €791 K of acquisition costs.

The implementation of the depreciation tests described in note 3.6 revealed no depreciation on the presented financial years. In the context of the sensibility tests, the Company has not identified any variation of the key assumptions likely to lead to a depreciation, the actualized value of the flows related to the activated project being very superior to the book value of the assets related to the project. The principal retained assumptions are:

- Discount rate : 11 %
- Projected cash flow of 15 years.

The amortization of intangible assets related to the license will start when the marketing authorization is obtained.

Because of the risks and uncertainties related to the process of research and development, the six criteria of capital property are not deemed to be met for any of development projects in progress. Consequently, all internal costs incurred by the Company are recognized as expenses.

## Note 7: Tangible fixed assets

GROSS VALUES OF TANGIBLE ASSETS (Amounts in K€)	Fixtures and Fittings	IT equipment	Furniture	Total
<b>Statement of financial position at December 31, 2016</b>	<b>111</b>	<b>62</b>	<b>46</b>	<b>220</b>
Acquisition		31	5	36
Retirement		-1		-1
Transfer				
<b>Statement of financial position at December 31, 2017</b>	<b>111</b>	<b>92</b>	<b>51</b>	<b>254</b>
Acquisition	128	33	52	213
Retirement				
Transfer				
<b>Statement of financial position at December 31, 2018</b>	<b>239</b>	<b>125</b>	<b>103</b>	<b>467</b>

AMORTIZATION/DEPRECIATION				
<b>Statement of financial position at December 31, 2016</b>	<b>14</b>	<b>35</b>	<b>25</b>	<b>74</b>
Increase	12	19	6	38
Decrease		-1		-1
<b>Statement of financial position at December 31, 2017</b>	<b>27</b>	<b>53</b>	<b>31</b>	<b>111</b>
Increase	20	27	12	60
Decrease				
<b>Statement of financial position at December 31, 2018</b>	<b>47</b>	<b>81</b>	<b>43</b>	<b>170</b>

CARRYING AMOUNT				
<b>At December 31, 2017</b>	<b>84</b>	<b>38</b>	<b>21</b>	<b>143</b>
<b>At December 31, 2018</b>	<b>192</b>	<b>44</b>	<b>60</b>	<b>296</b>

The Company does not hold any financial lease contracts.

There were no impairment findings in the application of IAS 36.

## Note 8: Other non-current financial assets

OTHER NON-CURRENT ASSETS (Amounts in K€)	31/12/2018	31/12/2017
Cash portion of liquidity agreement	78	130
Deposits relating to operating leases	93	67
Other deposits	201	159
<b>Total</b>	<b>372</b>	<b>356</b>

The non-current financial assets consist of guarantee deposits paid in the framework of:

- the cash portion of the liquidity agreement signed with Oddo Corporate Finance (78 K€ in 2018 versus 130 K€ in 2017);
- sureties concerning contracts for the simple rental of premises for the financial years ended December 31, 2017 and 2018;
- Deposits relating to salary portage contracts.

## Note 9: Customers and other receivables

At 14,262 K€ in 2018 and 4,902 K€ in 2017, receivables correspond to the chargeback to Sumitomo Dainippon Pharma of 14,216 in 2018 and 4,877 K€ in 2017 for research expenses incurred under the Imeglimin phase 3 TIMES program in Japan. The amount of these receivables is recognized according to the advances of the costs of the program.

Other receivables can be broken down in the following manner:

<b>OTHER RECEIVABLES (Amounts in K€)</b>	<b>31/12/2018</b>	<b>31/12/2017</b>
Research tax credit	3 539	3 122
Value added tax	937	2 006
Receivables from suppliers	1 219	1 318
Prepaid expenses	1 081	552
Other tax receivable	382	
Accrued holdings	81	178
Other	32	9
<b>Total other receivables</b>	<b>7 271</b>	<b>7 187</b>

## Research Tax Credit ("CIR")

The company benefits from the provisions of articles 244 quater B and 49 septies F of the General Tax Code relating to the tax credit research. In accordance with the principles described in Note 3.10, the research tax credit is recognized as a reduction of research cost during the year, to which eligible research expenditures relate. It is presented as a grant in the category of "research and development expenses".

In the absence of a taxable result, and of corporate taxes at least equal to the amount of the debt to the State relating to the research tax credit ("CIR"), the amount not imputed to the IS debt is refundable in the year following the year of its finding, when the Company has the status of SMES in the European sense.

## Value added tax

VAT receivables primarily relate to input VAT as well as to the requested refund of VAT.

## Supplier debtors

In 2017 and 2018, the debtor suppliers correspond, for 1.3 M€, to advances paid to subcontractors in the framework of the Phase 3 study of Imeglimin, re-charged to Sumitomo Dainippon Pharma, and for which consideration is located in advances received for the same amount (see note 17.2).

## Other taxable receivables and payables

Other tax receivables correspond to a payment made by the Company following a tax notification contested by the Company. The analysis carried out by the Company and its counsels makes it possible to consider its right to recover the paid sums as reasonable. As a result, no provision is recognized in this respect.

## Note 10: Cash and cash equivalents

The position of cash and cash equivalents is as follows:

<b>CASH AND CASH EQUIVALENTS</b> <b>(Amounts in K€)</b>	<b>31/12/2018</b>	<b>31/12/2017</b>
Bank accounts	7 292	4 120
Term deposits	59 445	50 044
<b>Total cash and cash equivalents</b>	<b>66 737</b>	<b>54 163</b>

The cash and cash equivalents net of the financial liabilities (see note 14) is equal to €52 506 k as of December 31, 2018 and € 52 672k as of December 31, 2017.

## Note 11: Financial assets and liabilities

The assets and liabilities of the Company are assessed in the following manner for each year:

<b>(Amounts in K€)</b>  <b>Balance sheet headings</b>	<b>31/12/2018</b>		<b>Value - statement of financial position according to IFRS 9</b>		
	<b>Value Statement of financial position</b>	<b>Fair value (3)</b>	<b>Fair value in the income statement</b>	<b>Loans and Receivables (2)</b>	<b>Debts at amortized cost (1)</b>
Non-current financial assets	372	372		372	
Trade and other receivables	14 262	14 262		14 262	
Other receivables	6 334	6 334		6 334	
Cash and cash equivalents	66 737	66 737	66 737		
<b>Total assets</b>	<b>87 705</b>	<b>87 705</b>	<b>66 737</b>	<b>20 968</b>	
Current financial liabilities	13 873	13 873			13 873
Non-current financial liabilities	359	359			359
Trade payables and related accounts	20 742	20 742			20 742
<b>Total liabilities</b>	<b>34 973</b>	<b>34 973</b>			<b>34 973</b>

(Amounts in K€)	31/12/2017		Value - statement of financial position according to IFRS 9		
	Value Statement of financial position	Fair value (3)	Fair value in the income statement	Loans and Receivables (2)	Debts at amortized cost (1)
Non-current financial assets	356	356		356	
Trade and other receivables	4 902	4 902		4 902	
Other receivables	5 180	5 180		5 180	
Cash and cash equivalents	54 163	54 163	50 044	4 120	
<b>Total assets</b>	<b>64 602</b>	<b>64 602</b>	<b>50 044</b>	<b>14 559</b>	
Current financial liabilities	936	936			936
Non-current financial liabilities	555	555			555
Trade payables and related accounts	9 008	9 008			9 008
<b>Total liabilities</b>	<b>10 499</b>	<b>10 499</b>			<b>10 499</b>

(1) The book value of debts at amortized cost has been considered as a reasonable estimate of the fair value.

(2) The fair value of loans and receivables corresponds to the value presented in the balance sheet (value at the date of the transaction, which is the subject of an impairment test at each closing).

(3) The fair value of financial assets recorded at fair value in the income statement (such as the SICAV) is determined on the basis of the level 1 of the fair value assessment and corresponds to a market value.

## Note 12: Capital

### Issued Capital

The capital at December 31, 2018 amounted to 517,136,84€, divided into 25,856,827 common shares of 0.02 € of nominal value each, fully paid, after taking into account the various capital increases occurred in 2018 and recalled below.

This number is defined outside share subscription warrants ("BSA"), stock options, free shares and founders' warrants ("BSPCE"), granted to certain natural persons, employed or not employed by the Company and not yet exercised.

COMPOSITION OF SHARE CAPITAL	31/12/2018	31/12/2017
Capital (in euros)	517 137	462 549
Number of shares	25 856 827	23 127 428
of which ordinary shares	25 856 827	23 127 428
of which preferred shares	0	0
Nominal value (in €)	0,02 €	0,02 €

During the 2018 financial year, several transactions modifying the capital took place, shown in Note 4.1.

### Table of the evolution of the share capital

Date	Nature of operations	Number of shares constituting the capital	Capital movement in K€	Share premium in K€
<b>At December 31, 2016</b>		<b>22 950 228</b>	<b>459</b>	<b>106 385</b>
January 2017	Exercise of employee founder's warrant	44 000	1	109
May 2017	Exercise of employee founder's warrant	40 000	1	127
June 2017	Exercise of warrants	90 000	2	298
Oct 2017	Exercise of employee founder's warrant	3 200		8
Nov 2017	Subscription of warrants/founder's warrant			24
<b>At December 31, 2017</b>		<b>23 127 428</b>	<b>463</b>	<b>106 951</b>
February 2018	Roivant capital increase	1 431 399	29	12 138
May 2018	Exercise of employee founder's warrant	8 000		20
August 2018	DeuteRx capital increase	1 290 000	26	8 888
	Capital increase expenses			-41
	Subscription of warrants/founder's warrant			41
<b>At December 31, 2018</b>		<b>25 856 827</b>	<b>517</b>	<b>127 996</b>

## Distribution of dividends

The Company did not distribute any dividends during the fiscal years ended December 31, 2017 and 2018.

The results of the previous financial years are fully allocated to the reserves.

## Note 13: Share subscription warrants, founder warrants, stock options and free shares

### Share subscription warrants ("BSA")

The table below summarizes the data relating to option plans issued, as well as the assumptions used for the valuation according to IFRS2:

							Assumptions used - calculation of fair value according to IFRS 2							
Date of allotment	Type	Number of warrants issued	Number of lapsed stock options	Number of options exercised	Number of outstanding stock options	Maximum of shares to be issued*	Underlying fair value *	Fair value of the warrant*	Maturity	Exercise price in €*	Duration of exercise	Volatility	Risk-free rate	Total valuation IFRS2 (Black&Scholes)
Board Meeting of July 5, 2010	Warrants for directors	4 500	0	4 500	0	0	3,33 €	1,50 €	5 years	3,33 €	10 years	45%	3,5%	135 125 €
At December 31, 2010		4 500	0	4 500	0	0								
At December 31, 2011		4 500	0	4 500	0	0								
At December 31, 2012		4 500	0	4 500	0	0								
Board Meeting of February 20, 2012	Warrants 10/31/2012	2 500	0	0	2 500	50 000	4,23 €	2,04 €	5 years	4,00 €	10 years	52%	2,2%	71 843 €
At December 31, 2013		7 000	0	4 500	2 500	50 000								
Board Meeting of March 12, 2013	Warrants 10/31/2012	2 500	0	0	2 500	50 000	8,00 €	5,16 €	4,5 years	4,00 €	10 years	55%	1,8%	227 848 €
At December 31, 2014		9 500	0	4 500	5 000	100 000								
Board Meeting of January 8, 2015	Warrants 07-25-2014	42 500	0	0	42 500	42 500	8,20 €	5,16 €	6 years	4,00 €	10 years	57%	0,0%	219 468 €
Board Meeting of April 29, 2015	Warrants 06-16-2015	42 500	0	0	42 500	42 500	13,57 €	6,77 €	6 years	9,37 €	10 years	57%	0,0%	287 591 €
Board Meeting of May 7, 2015	Warrants 06-16-2015	240 000	0	0	240 000	240 000	13,57 €	6,46 €	6 years	9,62 €	10 years	57%	0,1%	1 550 959 €
At December 31, 2015		334 500	0	4 500	330 000	425 000								
Board Meeting of January 29, 2016	Warrants 01-29-2016	42 500	0	0	42 500	42 500	9,07 €	2,84 €	6 years	9,05 €	10 years	53%	0,2%	120 779 €
Board Meeting of January 29, 2016	Warrants 01-29-2016	42 500	0	0	42 500	42 500	9,07 €	2,84 €	6 years	9,05 €	10 years	53%	0,2%	120 779 €
Board Meeting of March 31, 2016	Warrants 01-29-2016	42 500	0	0	42 500	42 500	12,23 €	5,19 €	6 years	9,26 €	10 years	53%	0,0%	220 461 €
At December 31, 2016		462 000	0	4 500	457 500	552 500								
Board Meeting of January 27, 2017	Warrants 01-27-2017	62 500	0	0	62 500	62 500	6,76 €	2,66 €	5,5 years	7,17 €	10 years	53%	0,0%	166 369 €
Board Meeting of June 30, 2017	Warrants 06-30-2017	25 000	0	0	25 000	25 000	6,61 €	2,64 €	5,5 years	6,90 €	10 years	53%	0,0%	66 064 €
At December 31, 2017		549 500	0	4 500	545 000	640 000								
Board Meeting of January 25, 2018	Warrants 2018	90 000	0	0	90 000	90 000	6,74 €	2,84 €	5,5 years	6,60 €	10 years	53%	0,1%	255 625 €
At December 31, 2018		639 500	0	4 500	635 000	730 000								

The warrants issued before the division of the nominal value by 20, effective in March 2014, are convertible to 20 common shares. Consequently, the underlying fair value, the fair value of the warrant and the exercise price have been adjusted in order to take this into account.



The exercise price for the rights attributed after the listing on the stock market is based on the mean share price during 20 days before the award.

Exercise rights for each of the plans vest as follows:

- the rights to exercise "Director BSA" vest annually by one-third at each anniversary date of the award.
- The rights to exercise BSA "31/10/2012" vest immediately on the date of award by the General Meeting.
- The rights to exercise "07/25/2014 BSAs" vest annually by one-third at each anniversary date of the award.
- The rights to exercise the warrants issued in 2016 vest one year after the date of award.
- In 2017, the rights to exercise BSA vest annually in full at each anniversary date of the award.
- The rights to exercise BSA issued in January 2018 vest in full at each anniversary date of the award.

The exercise of issued warrants is not subject to a condition of performance. On the other hand, it is subject to a condition of presence.

These plans are qualified as "equity settled". The Company does not commit to repurchase these instruments from employees in the event of departure or in the case of non-occurrence of a particular event.

## Stock-options

The table below summarizes the data relating to option plans issued, as well as the assumptions used for the valuation according to IFRS2:

Date of allotment	Type	Number of warrants issued	Number of lapsed stock options	Number of options exercised	Number of outstanding stock options	Maximum number of shares to be issued	Assumptions used - calculation of fair value according to IFRS 2						
							Underlying fair value	Fair value of the warrant	Maturity	Exercise price in €	Duration of exercise	Volatility	Risk-free rate
Board Meeting of March 31, 2016	Stock options	80 000	0	0	80 000	80 000	12,55 €	5,88 €	5.5 years	12,55 €	10 years	53%	0,0%
Board Meeting of November 23, 2016	Stock options	150 000	0	0	150 000	150 000	6,47 €	3,15 €	6 years	6,47 €	10 years	53%	0,0%
<b>At December 31, 2016</b>		<b>230 000</b>	<b>0</b>	<b>0</b>	<b>230 000</b>	<b>230 000</b>							
Board Meeting of January 27, 2017	Stock options	12 500	0	0	12 500	12 500	6,76 €	3,15 €	5.5 years	6,76 €	10 years	53%	0,0%
Board Meeting of January 27, 2017	Stock options	185 000	0	0	185 000	185 000	6,76 €	3,27 €	6 years	6,76 €	10 years	53%	0,0%
Board Meeting of June 30, 2017	Stock options	97 500	5 000	0	92 500	92 500	6,61 €	3,20 €	6 years	6,61 €	10 years	53%	0,0%
<b>At December 31, 2017</b>		<b>525 000</b>	<b>5 000</b>	<b>0</b>	<b>520 000</b>	<b>520 000</b>							
Board Meeting of January 25, 2018	Stock options	215 000	7 500	0	207 500	207 500	6,74 €	3,27 €	6 years	6,79 €	10 years	53%	0,2%
Board Meeting of September 27, 2018	Stock options 2018-2	130 000	0	0	130 000	130 000	6,82 €	3,31 €	6 years	6,82 €	10 years	53%	0,1%
<b>At December 31, 2018</b>		<b>870 000</b>	<b>12 500</b>	<b>0</b>	<b>857 500</b>	<b>857 500</b>							

The rights to exercise stock options vest:

- annually by one-third for stock options allocated in 2016;
- for the stock options allocated in 2017:
  - o one year after the allocation date for the 12,500 stock options allocated by the Board of Directors of January 27;
  - o annually by one-third for the 185,000 stock options allocated by the Board of Directors of January 27;
  - o annually by one-third for the 97,500 stock options allocated by the Board of Directors June 30;
- annually by one-third for stock options allocated in 2018;

The exercise of issued warrants is not subject to a condition of performance. On the other hand, it is subject to a condition of presence.

These plans are qualified as "equity settled". The Company does not commit to repurchase these instruments from employees in the event of departure or in the case of non-occurrence of a particular event.

### Founders' warrants ("BSPCE")

The table below summarizes the data relating to option plans issued, as well as the assumptions used for the valuation according to IFRS2:

Date of allotment	Type	Number of warrants issued	Number of lapsed stock options	Number of options exercised	Number of outstanding stock options	Maximum of shares to be issued*	Assumptions used - calculation of fair value according to IFRS 2						
							Underlying fair value *	Fair value of the warrant*	Maturity	Exercise price in €*	Duration of exercise	Volatility	Risk-free rate
Board Meeting of June 20, 2010	BCE 06-10-2010-1	5 000	2 750	560	1 690	33 800	3,33 €	1,77 €	5 years	2,50 €	10 years	45%	3,5%
Board Meeting of December 17, 2	BCE 06-10-2010-2	3 000	0	3 000	0	0	3,33 €	1,72 €	4.5 years	2,50 €	10 years	45%	3,7%
<b>At December 31, 2010</b>		<b>8 000</b>	<b>2 750</b>	<b>3 560</b>	<b>1 690</b>	<b>33 800</b>							
Board Meeting of September 20, 2	BCE 06-10-2010-2	1 500	0	0	1 500	30 000	3,74 €	2,00 €	3.5 years	2,50 €	10 years	50%	4,0%
<b>At December 31, 2011</b>		<b>9 500</b>	<b>2 750</b>	<b>3 560</b>	<b>3 190</b>	<b>63 800</b>							
<b>At December 31, 2012</b>		<b>9 500</b>	<b>2 750</b>	<b>3 560</b>	<b>3 190</b>	<b>63 800</b>							
<b>At December 31, 2013</b>		<b>9 500</b>	<b>2 750</b>	<b>3 560</b>	<b>3 190</b>	<b>63 800</b>							
Board Meeting of March 12, 201	BCE 10-31-2012	5 000	0	2 300	2 700	54 000	8,00 €	5,58 €	4.5 years	3,20 €	10 years	55%	1,80%
<b>At December 31, 2014</b>		<b>14 500</b>	<b>2 750</b>	<b>5 860</b>	<b>5 890</b>	<b>117 800</b>							
<b>At December 31, 2015</b>		<b>14 500</b>	<b>2 750</b>	<b>5 860</b>	<b>5 890</b>	<b>117 800</b>							
Board Meeting of July 29, 2016	BSPCE 07-29-2016	45 000	45 000	0	0	0	7,53 €	3,30 €	5.5 years	8,45 €	10 years	53%	0,00%
<b>At December 31, 2016</b>		<b>59 500</b>	<b>47 750</b>	<b>5 860</b>	<b>5 890</b>	<b>117 800</b>							
Board Meeting of March 31, 201	BSPCE 03-31-2017	100 000	0	0	100 000	100 000	6,76 €	2,63 €	6 years	5,91 €	10 years	53%	0,00%
Board Meeting of June 30, 2017	BSPCE 2017-2	177 500	15 000	0	162 500	162 500	6,61 €	3,04 €	6 years	7,26 €	10 years	53%	0,00%
Board Meeting of September 21,	BSPCE 2017-3	15 000	0	0	15 000	15 000	5,76 €	2,72 €	6 years	6,01 €	10 years	53%	0,0%
<b>At December 31, 2017 and 2018</b>		<b>352 000</b>	<b>62 750</b>	<b>5 860</b>	<b>283 390</b>	<b>395 300</b>							

\* After splitting of the stock by 20

The warrants issued before the division of the nominal value by 20, effective in March 2014, are convertible to 20 common shares. Consequently, the underlying fair value, the fair value of the warrant and the exercise price have been adjusted in order to take this into account.

The exercise price for the rights attributed after the listing on the stock market is based on the mean share price during 20 days before the award.

The rights to exercise all BSPCE vest annually by one-third at each anniversary date of the award.

The exercise of warrants is not subject to a condition of performance. On the other hand, it is subject to a condition of presence.

These plans are qualified as "equity settled". The Company does not commit to repurchase these instruments from employees in the event of departure or in the case of non-occurrence of a particular event.

### Valuation methods of the warrant, stock-options and BSPCE

The fair value of the options was determined using the Black & Scholes evaluation model. The modalities of the assessment used in estimating the fair value of the options are specified below:

- For the rights attributed before listing on the stock exchange, the share price used is equal to the price of subscription of investors or by reference to internal valuations; for the rights attributed after listing on the stock exchange, the share price used is equal to the share price on the date of award;
- The risk free rate is determined from the average life of instruments;

- The volatility has been determined on the basis of a sample of listed companies in the biotechnology sector, on the date of subscription of the instruments and on a period equivalent to the duration of the life of the option.

### Performance bonus shares

Date of allotment	Type	Number of free shares issued	Number of free shares lapsed	Number of free shares vested	Number of free shares outstanding	Maximum number of shares to be issued
Board Meeting of January 25, 2018	Free shares	126 500	5 750	0	120 750	120 750
At December 31, 2018		126 500	5 750	0	120 750	120 750

On 25 January 2018, the Board of Directors allocated 126,500 performance bonus shares to employees.

The final allocation of free shares is defined and carried out annually, by one-third on each anniversary date of the allocation. Each annual tranche is subject to a presence condition and three performance conditions, each of which determines the achievement of one-third of the annual tranche:

- two annual performance conditions not linked to market conditions, so that the total number of delivered shares will depend on the level of achievement of the conditions for the years 2018, 2019 and 2020. For each of these conditions, the probability of achieving the objective is estimated by management. The expense recognized in this respect as at December 31, 2018 is based on the number of performance bonus shares that the Company expects to allocate. This number is defined on the basis of management's estimate.
- an annual performance condition linked to market conditions and reflected in the assessment of the fair value.

The fair value of options subject to market condition was determined using the Monte Carlo model. The modalities of the assessment used in estimating the fair value of the performance bonus shares are specified below:

- the share price used is equal to the share price on the allocation date;
- The risk free rate is determined from the average life of instruments;
- The volatility has been determined on the basis of a sample of listed companies in the biotechnology sector, on the date of subscription of the instruments and on a period equivalent to the duration of the life of the option.

These plans are qualified as "equity settled". The Company does not commit to repurchase these instruments from employees in the event of departure or in the case of non-occurrence of a particular event.

### Detail of the expense recorded according to IFRS 2 in respect of fiscal years 2017 and 2018:

Type	Date granted	Number of outstanding stock options	IFRS 2 cost of the plan	Cumulative expense as at 1/1/2017	2017 expense	Cumulative expense as at 12/31/2017	2018 expense	Cumulative expense as at 12/31/2018
Warrants for directors	Board Meeting of July 5, 2012	0	135	135		135		135
Warrants 10/31/2012	Board Meeting of February 2, 2013	2 500	72	72		72		72
Warrants 10/31/2012	Board Meeting of March 12, 2013	2 500	228	228		228		228
Warrants 07-25-2014	Board Meeting of January 8, 2015	42 500	219	203	17	219		219
Warrants 06-16-2015	Board Meeting of April 29, 2016	42 500	288	219	54	273	15	288
Warrants 06-16-2015	Board Meeting of May 7, 2016	240 000	1 551	1 432	118	1 551		1 551
Warrants 01-29-2016	Board Meeting of January 2, 2017	42 500	121	68	37	105	15	120
Warrants 01-29-2016	Board Meeting of January 2, 2017	42 500	121	68	37	105	15	120
Warrants 01-29-2016	Board Meeting of March 31, 2017	42 500	220	102	79	181	33	214
Warrants 01-27-2017	Board Meeting of January 2, 2018	62 500	166		154	154	12	166
Warrants 06-30-2017	Board Meeting of June 30, 2018	25 000	66		33	33	33	66
Warrants 2018	Board Meeting of January 2, 2019	90 000	256				236	236
<b>Total - warrants</b>		<b>635 000</b>	<b>3 443</b>	<b>2 527</b>	<b>529</b>	<b>3 056</b>	<b>359</b>	<b>3 415</b>

Type	Date granted	Number of outstanding stock options	IFRS 2 cost of the plan	Cumulative expense as at 1/1/2017	2017 expense	Cumulative expense as at 12/31/2017	2018 expense	Cumulative expense as at 12/31/2018
BCE 06-10-2010-1	Board Meeting of June 20, 2011	1 690	177	177		177		177
BCE 06-10-2010-2	Board Meeting of December 1, 2011	0	103	103		103		103
BCE 06-10-2010-2	Board Meeting of September 1, 2012	1 500	60	60		60		60
BCE 10-31-2012	Board Meeting of March 12, 2013	2 700	558	558		558		558
BSPCE 07-29-2016	Board Meeting of July 29, 2017	0	99	80	54	134	-35	99
BSPCE 03-31-2017	Board Meeting of March 31, 2018	100 000	263		122	122	94	216
BSPCE 2017-2	Board Meeting of June 30, 2018	162 500	532		161	161	233	393
BSPCE 2017-3	Board Meeting of September 1, 2018	15 000	41		7	7	21	28
<b>Total - Founders' warrants (BSPCE)</b>		<b>283 390</b>	<b>1 832</b>	<b>978</b>	<b>343</b>	<b>1 321</b>	<b>313</b>	<b>1 634</b>

Type	Date granted	Number of outstanding stock options	IFRS 2 cost of the plan	Cumulative expense as at 1/1/2017	2017 expense	Cumulative expense as at 12/31/2017	2018 expense	Cumulative expense as at 12/31/2018
Stock options	Board Meeting of March 31, 2017	80 000	471	334	117	451	19	471
Stock options	Board Meeting of November 1, 2017	150 000	472	29	273	302	123	425
Stock options	Board Meeting of January 2, 2018	12 500	39		36	36	3	39
Stock options	Board Meeting of January 2, 2018	185 000	605		342	342	183	525
Stock options	Board Meeting of June 30, 2018	92 500	312		96	96	138	234
Stock options	Board Meeting of January 2, 2019	207 500	679				383	383
Stock options 2018-2	Board Meeting of September 1, 2018	130 000	430				68	68
<b>Total - Stock Options</b>		<b>857 500</b>	<b>3 008</b>	<b>363</b>	<b>865</b>	<b>1 228</b>	<b>918</b>	<b>2 146</b>

Type	Date granted	Number of free shares outstanding	IFRS 2 cost of the plan	Cumulative expense as at 1/1/2017	2017 expense	Cumulative expense as at 12/31/2017	2018 expense	Cumulative expense as at 12/31/2018
Free shares	Board Meeting of January 2, 2019	120 750	474				291	291
<b>Total - Free shares</b>		<b>120 750</b>	<b>474</b>				<b>291</b>	<b>291</b>

	Number of outstanding instruments	IFRS 2 cost of the plan	Cumulative expense at opening	2017 expense	Cumulative expense as at 12/31/2017	2018 expense	Cumulative expense as at 12/31/2018
<b>Grand total</b>	<b>1 941 640</b>	<b>8 757</b>	<b>3 869</b>	<b>1 736</b>	<b>5 605</b>	<b>1 881</b>	<b>7 487</b>

The total charge related to BSA, stock options, AGA and BSPCE is 1,881 K€ (including 686 K€ in research and development costs and 1,195 K€ in general and administrative expenses) for the year ended December 31, 2018 and 1,736 K€ (including 546 K€ research and development costs and 1,190 K€ in general and administrative expenses) for the year ended December 31, 2017.

## Note 14: Loans and financial debt

CURRENT AND NON-CURRENT FINANCIAL DEBTS (Amounts in K€)	31/12/2018	
	31/12/2018	31/12/2017
Repayable advances	359	555
<b>Non-current financial liabilities</b>	<b>359</b>	<b>555</b>
Repayable advance	218	181
Bank facilities		751
Roivant agreement	13646	
Overdraft charges	8	4
<b>Current financial liabilities</b>	<b>13 873</b>	<b>936</b>
<b>Total financial debt</b>	<b>14 231</b>	<b>1 491</b>

### Breakdown of financial debts by maturity

The maturities of financial debts are broken down as follows during the years presented:

CURRENT AND NON-CURRENT FINANCIAL DEBTS (Amounts in K€)	31/12/2018			
	Gross amount	Portion less than one year	1 - 5 years	More than 5 years
Repayable advances	577	218	359	
Roivant agreement	13 646	13 646		
Overdraft charges	8	8		
<b>Total financial debt</b>	<b>14 231</b>	<b>13 873</b>	<b>359</b>	

CURRENT AND NON-CURRENT FINANCIAL DEBTS (Amounts in K€)	31/12/2017			
	Gross amount	Portion less than one year	1 - 5 years	More than 5 years
Repayable advances	736	181	555	
Overdraft charges	4	4		
Bank facilities	751	751		
<b>Total financial debt</b>	<b>1 491</b>	<b>936</b>	<b>555</b>	

### 14.1 Debts to credit institutions

The Company has not contracted bank loans in the years 2017 and 2018. It has had recourse to a bank overdraft as of the end of 2017, for an amount of €751 K, reimbursed in January 2018.

### 14.2 Repayable advances

The table below shows the evolution of repayable advances:

	PXL770	Imeglimin (New Formulation)	Total
<b>At December 31, 2016</b>	<b>111</b>	<b>733</b>	<b>845</b>
(+) Collection of funds			
(-) Refund of expenses	-73	-69	-142
Subsidies			
Financial expenses	5	28	33
<b>At December 31, 2017</b>	<b>43</b>	<b>692</b>	<b>736</b>
(+) Collection of funds			
(-) Refund of expenses	-45	-143	-188
Subsidies			
Financial expenses	2	27	28
<b>At December 31, 2018</b>		<b>577</b>	<b>577</b>

#### Breakdown of repayable advances by due date

	Repayable advances		Total
	PXL770	Imeglimin (New Formulation)	
<b>At December 31, 2018</b>		<b>577</b>	<b>577</b>
Portion less than one year		218	218
Portion one to five years		359	359
Portion more than five years			

	Repayable advances		Total
	PXL770	Imeglimin (New Formulation)	
<b>At December 31, 2017</b>	<b>43</b>	<b>692</b>	<b>736</b>
Portion less than one year	43	137	181
Portion one to five years		555	555
Portion more than five years			

#### Advance repayable Bpifrance Financement / ERDF - PXL770

On August 31, 2011, the Company obtained a repayable, interest-free grant from Bpifrance Financement as part of the European Regional Development Fund, or ERDF fund, for a maximum amount of 250 K€ in the context of the “development and selection of a new AMPK activator drug for the treatment of diabetes.”

Following the technical success of the project, the repayment of this innovation assistance was made according to a schedule that began in 2013 and was completed in the 2018 financial year.

#### Repayable advance from Bpifrance Financement Innovation - Imeglimin (New Formulation)

In October 2011, the Company obtained refundable assistance for innovation on the part of Bpifrance Financement for 950 K€, not bearing interest, for the "development of a new formulation of Imeglimin for the treatment of diabetes".

Payments from Bpifrance Financement were made in instalments between the signature date of the contract and the end of the project, the main stages of which were as follows:

- first installment of €700 K on January 16, 2012;
- the balance, limited to €150 K on September 2, 2016.

Following the technical success of the project, the repayment of this innovation subsidy began in 2013 and continues as follows:

- €12 K for the last two quarters of 2016;
- €12 K for the first two quarters of 2017 and €23 K for the following two quarters;
- €22 K for the first two quarters of 2018 and €49 K for the following two quarters;
- €49 K for the first two quarters of 2019 and €71 K for the following two quarters;
- €71 K for the first two quarters of 2020 and €83 K for the following two quarters;
- the balance in 2021.

The fair value of this advance has been determined on the basis of a market interest rate estimated at 3.84% per year. The difference between the amount of the advance at the historic cost and that of the advance updated at the market rate is recognised in revenue as a subsidy received from the State.

#### **14.3 Obligation to participate in the financing of the Roivant's development program**

As regards the Roivant Sciences' contract, the Company received an initial payment of \$35 million and has also committed to contribute \$25 million to the financing of the development of Imeglimin in the United States and Europe. The portion of the initial payment that is counterpart to the obligation to participate in the financing of Roivant's development program has been treated as a debt. The remaining balance to be paid at the closure, amounting to 13,646 k€, is fully classified as current financial debts.

This agreement provides that, until the Company has fully paid its obligation to participate in the financing of Roivant's development plan, and in the event that the Company's immediately available cash, less expected disbursements within 30 days, is less than 3 times the amount of such residual obligation, for at least 10 consecutive days, then, the Company would be required to establish an irrevocable letter of credit with a leading bank for the benefit of Roivant, for the residual amount of such obligation calculated on such date. Roivant may return this letter of credit for collection if the Company defaults in the repayment of its obligation, or in the event of termination of the contract at Roivant's initiative and under certain conditions. If the Company is unable to obtain a letter of credit, or if it is cancelled, then, the amounts due to Roivant by the Company on that date will be immediately payable.

At the closure date, the Company is in compliance with the terms of the contract on the basis of its available cash balances amounting to 66,737k€.

## Note 15: Commitments toward personnel

### 15.1 Defined benefit plan

The commitments toward the staff are composed of the retirement indemnity, evaluated on the basis of the provisions laid down by the applicable collective agreement, namely, the collective agreement the pharmaceutical industry.

These commitments are not covered by plan assets.

This commitment concerns only the employees under French law. The main actuarial assumptions used for the evaluation of severance benefits at retirement are the following:

ACTUARIAL ASSUMPTIONS	31/12/2018	31/12/2017
Retirement age	Voluntary retirement at 65/67 years	
Collective bargaining agreements	Pharmaceutical industry	
Discount rate (IBOXX Corporates AA )	1,83%	1,68%
Mortality table	INSEE 2017	INSEE 2017
Rate of salary revaluation	2%	2%
Turnover rate	Low	Low
Social security expenses rate	50%	50%

The provision for commitment of retirement has evolved in the following way:

EMPLOYEE BENEFITS (Amounts in K€)	Retirement benefits
<b>At December 31, 2016</b>	<b>131</b>
Cost of past services	24
Financial costs	5
Actuarial gains or losses	70
<b>At December 31, 2017</b>	<b>230</b>
Cost of past services	51
Financial costs	4
Actuarial gains or losses	-5
<b>At December 31, 2018</b>	<b>279</b>

### 15.2 Defined contribution plans

The Group's payments under the defined contribution plan are recognized as expenses in the consolidated statement of income in the period in which they become payable. They amounted respectively to 197 K€ and 252 K€ in respect of the years 2017 and 2018.



## Note 16: Provisions

The Company may be involved in judicial, administrative or regulatory procedures in the normal course of its activity. A provision is recorded by the Company as soon as there is a sufficient likelihood that such disputes will entail costs for the Company.

In 2017, the Company established a provision of 83 K€ for social and tax risks. In 2018 this provision was reversed to the amount of 65 K€, corresponding to a tax administration adjustment not contested by the Company.

No additional provision has been considered necessary for the fiscal year ended December 31, 2018.

## Note 17: Suppliers and other current liabilities

### 17.1. Suppliers and related accounts

No discount has been practised on the suppliers and accounts attached to the extent where the amounts were not of maturity greater than one year at the end of each fiscal year concerned.

<b>TRADE PAYABLES AND RELATED ACCOUNTS (Amounts in K€)</b>	<b>31/12/2018</b>	<b>31/12/2017</b>
Trade payables	8 651	3 249
Invoices not received	12 091	5 758
<b>Total trade payables and related accounts</b>	<b>20 742</b>	<b>9 008</b>

The increase in trade payables and related accounts is mainly due to the increase in costs incurred in the Phase 3 TIMES program for Imeglimin in Japan in 2018.

### 17.2 Tax and social security liabilities

The tax and social debts are broken down as follows:

<b>TAX AND SOCIAL SECURITY PAYABLES (Amounts in K€)</b>	<b>31/12/2018</b>	<b>31/12/2017</b>
Employees and related accounts	510	465
Social security and other social bodies	394	390
Other taxes and duties	225	44
<b>Total tax and social security liabilities</b>	<b>1 129</b>	<b>899</b>

### 17.3 Other current liabilities

Other liabilities are broken down as follows:

<b>OTHER CURRENT LIABILITIES</b> <b>(Amounts in K€)</b>	<b>31/12/2018</b>	<b>31/12/2017</b>
Deferred income - Initial payment of Sumitomo contr	12 077	34 301
Advances from clients	1 257	1 317
Other		95
<b>Total other current liabilities</b>	<b>13 334</b>	<b>35 714</b>

Deferred income relates to the initial payment received under the Sumitomo Dainippon Pharma contract, which is recognized as an advance on the costs of the TIMES Phase 3 program for Imeglimin in Japan (see Note 18).

Under the Roivant Sciences contract, the Company is committed to contributing to the financing of the development of Imeglimin in the United States and in Europe for 25 million dollar. This commitment is recognized under other current liabilities (see Note 18).

The instalments received correspond to the re-charging of advances paid by the Company to a CRO in the framework of the TIMES program of phase 3 for the Imeglimin in Japan.

### **Note 18: Turnover**

<b>REVENUE</b> <b>(Amounts in K€)</b>	<b>31/12/2018</b>	<b>31/12/2017</b>
Sumitomo Contract	66 412	5 290
Roivant Contract	8 192	
<b>Total revenue</b>	<b>74 604</b>	<b>5 290</b>

In 2018, revenue reflected the contract signed with Sumitomo Dainippon Pharma in October 2017 and the contract signed with Roivant Sciences GmbH in February 2018(see significant events in the financial year in Note 4.1).

At December 31, 2017, the recognized turnover is linked to the Sumitomo contract.

#### **Accounting treatment of the Roivant Sciences GmbH contract:**

On February 9, 2018 the Company signed an exclusive contract with Roivant Sciences GmbH ("Roivant") for the development and marketing of Imeglimin, an oral drug candidate developed by the Company for treatment of type 2 diabetes, in the United States, in Europe and in other countries not covered by the existing partnership in Eastern and South-Eastern Asia between the Company and Dainippon Pharma (see Note 4.1).

This contract is analyzed as the assignment to Roivant of an exclusive license for Imeglimin. No other performance obligation has been identified.

The contract price on the transaction date was valued at \$10 million. This price is made up of a non-refundable fixed payment of \$35 million, less \$25 million granted by the Company in the form of a firm commitment to take part in financing Roivant's development program.

This amount was recognized in full as revenue on the date the license was granted for a value of \$10 million net.

The part of the initial payment having for counterpart the undertaking to participate to the financing of the research program of Roivant have been treated as a current liability. The remaining amount to be paid at the closure being equal to 13 646k€ is entirely classified as a current liability (see note 14.3).

The license agreement also provides for the payment by Roivant of development, regulatory and marketing milestone payments as well as fees based on Imeglimin sales in the areas covered by the license. These payments fall within the category of variable consideration to which the Company is entitled for transferring the license to Roivant.

- Since milestone payments based on development and regulatory milestones were not considered as highly probable as of December 31, 2018, no revenue was recognized in this respect in 2018. These payments will be considered as highly probable when the development of Imeglimin is advanced sufficiently to achieve the technical and regulatory milestones defined.
- Milestone payments based a level of sales and fees from Imeglimin sales benefit from the exception provided by IFRS 15 relating to intellectual property license rights. Payments and fees will be recognized as revenue as and when they become due, depending on the sales recorded by Roivant.

#### **Accounting treatment of the Sumitomo contract:**

In October 2017, the Company signed a partnership contract with the Sumitomo Company, under which the two companies will co-develop Imeglimin for the treatment of type 2 diabetes in Japan. Sumitomo Dainippon Pharma will fund the costs of phase 3 and marketing.

This Contract provides:

- that the Company is entitled to an initial payment of 36,031 K€, which pays for the license and the exclusive rights granted to Sumitomo Dainippon Pharma as well as for the co-development. It was redeemed in December 2017 and is non-refundable;
- That the Company receive the reimbursement of costs of external development engaged in the framework of the Phase 3 and under the conditions laid down in the contract.

The Company analyses the license granted and the co-development for Japan as two separate performance obligations:

- The obligation of performance is satisfied immediately for the license, as this is a case of a static license.
- The obligation of performance is satisfied continuously for the co-development. The nature of the services related to the co-development corresponds to the research work. At December 31, 2018 the remaining performance obligations amount to 36,190 K€, as opposed to 104,882 K€ at December 31, 2017.

The contract price is composed of fixed payments and of variable considerations considered as highly likely, that is to say the initial payment and reimbursement of direct costs estimated at each closure. Therefore, the corresponding income incorporates the initial payment and refunds.

The price of the transaction has been allocated to the two obligations of performance following the residual method, because the price of the license is highly variable and uncertain. The price of the specific obligation of co-development has been established on the basis of the estimated costs for the satisfaction of the obligation of performance plus a margin in line with the practices of the market. This has led to allocation of the full price of the transaction to the obligation of performance of co-development. This allocation reflects the savings of the contract since the highly probable payments aim to ensure a reasonable margin on the research and development work, the license being essentially paid via the future amounts, not highly probable at year-end.

The income allocated to the service of research and development is recognized according to the progress on the basis of the estimate of the direct costs, internal and external, for any phase of co-development. This is a method that best represents the progress of the work. The Company expects to achieve a positive margin on this contract.

The contract also provides for regulatory and commercial milestone payments.

These milestone payments fall into the category of variable consideration.

Their payment is not highly probable at December 31, 2018. They are therefore not recognized on that date.

The contract also provides for the payment of royalties based on sales of Imeglimin in the licensed territories. No sales were made by Sumitomo under the license granted by Poxel, and no amount was therefore recognized as of that date

## Note 19 Details of expenses and income by function

### 19.1 Research and Development

RESEARCH AND DEVELOPMENT (Amounts in K€)	31/12/2018	31/12/2017
Subcontracting, studies and research	52 195	18 951
Personnel expenses	3 617	3 273
Share-based payments	686	546
Travel, Missions and Receptions	589	459
Intellectual property fees	256	340
Compensation Temporary workers Fees	661	481
Other Charges	88	46
<b>R&amp;D costs</b>	<b>58 092</b>	<b>24 096</b>
Research tax credit	3 552	3 122
<b>Subsidies</b>	<b>3 552</b>	<b>3 122</b>

The research and development costs reflect mainly the studies on the Imeglimin and PXL770 projects. The Company is performing its studies through its network of sub-contracted service providers. The remuneration of these contracts constitutes the essential part of its operating expenses in the field of research.

The major part of the increase in subcontracting costs is related to the TIMES program for which €46 million expenses were exposed in 2018, and most of which are not eligible for the research tax credit. This amount also includes the fees to be paid to Merck Serono under the contract signed with Roivant Sciences GmbH (see Note 25.2).

The change in personnel expenses is primarily linked to the reinforcement of the clinical research teams.

The change in fees related to R&D activities is mainly due to the support of DeuteRx with the integration of the new potential medicine DRX-065.

## 19.2 General and Administrative Expenses

<b>GENERAL AND ADMINISTRATIVE EXPENSES (Amounts in K€)</b>	<b>31/12/2018</b>	<b>31/12/2017</b>
Compensation Temporary workers Fees	2 388	2 103
Personnel expenses	1 845	1 579
Share-based payments	1 195	1 190
Travel, Missions and Receptions	688	445
Other Charges	1 410	902
<b>General and Administrative expenses</b>	<b>7 527</b>	<b>6 219</b>

In 2018, the change in fees was primarily due to market studies conducted. As elaborated in Note 6, depending on their destination, fees that are directly related to the acquisition of the portfolio of products under development from DeuteRx, are recognized either as assets or deducted from the issue premium for the share directly linked to the capital increase.

The change in personnel costs and travel expenses is related to the strengthening of the administrative team.

The increase in other expenses is primarily correlated to the change in personnel: leasing of premises and additional equipment, maintenance expenses and related insurance policies (up €0.3 million), acquisition of new software licenses (up €0.1 million), increase in the CFE business tax (up €0.1 million).

The CICE is not significant.

## Note 20: Number of Employees

The Group's mean workforce during the last two financial years is as follows:

<b>WORKFORCE</b>	<b>FY 2018</b>	<b>FY 2017</b>
Managerial staff	32	24
Non-managerial staff	1	1
<b>Total workforce</b>	<b>33</b>	<b>25</b>

In 2017 the mean workforce integrates the portage staff of the Tokyo and Boston offices at 3 and 4, respectively.

Following the creation of the Japanese subsidiary, the 5 employees in the Boston offices are now integrated into the average 2018 workforce.

## Note 21: Financial income and charges, net

<b>FINANCIAL INCOME (EXPENSES)</b> <b>(Amounts in K€)</b>	<b>31/12/2018</b>	<b>31/12/2017</b>
Kreos interest		-47
Other financial expenses	-28	-34
Financial income	368	64
Foreign exchange (losses) and gains	724	-379
<b>Total financial income (expenses)</b>	<b>1 064</b>	<b>-396</b>

The financial results as of December 31, 2017 and 2018 mainly consists of:

- foreign exchange gains and losses, related to the evolution of the Yen and Dollar exchange rates;
- proceeds from financial investments;
- other financial expenses, which correspond to the effect of discounting repayable advances.

The Kreos debt has been repaid in full in 2017.

## Note 22: Income taxes

The amount of Company's fiscal deficits indefinitely carried over at December 31, 2018 was 105,991 K€.

In 2018, the Company charged €1,508 K of prior tax loss carryforwards against revenues generated by partnership contracts signed during the year, which constitute non-recurring revenues.

The tax rate applicable to the Company for its profits excluding long-term capital gains, is the applicable rate in France, i.e., 33.33%. The tax rate voted for subsequent years is 31% in 2019, 28% in 2020, 26.5% in 2021 and 25% as from 2022.

The tax rate applicable to the Company for its long-term capital gains related to intellectual property is the applicable rate in France, i.e. 15% in 2017 and 2018.

The Company believes that to date, the likelihood of generating taxable profits does not allow it to recognize all or part of the balance of its loss carryforwards as assets.

Under the principles described in Note 3.13, no deferred tax asset is recorded in the books of the Company beyond the deferred tax liabilities.

## Reconciliation between theoretical tax and effective tax

<b>Tax proof</b>	<b>31/12/2018</b>	<b>31/12/2017</b>
Net income	13 525	-22 298
Consolidated tax	-77	
<b>Pre-tax income</b>	<b>13 602</b>	<b>-22 298</b>
Current tax rate in France	33,33%	33,33%
<b>Theoretical tax at current rate in France</b>	<b>4 534</b>	<b>-7 433</b>
Permanent differences	-1 258	-922
Share-based payment	627	579
Prior year losses used	-503	
Non-capitalized tax loss adjusted by deferred tax	-3324	7 776
<b>Group tax income/expense</b>	<b>77</b>	
<i>Effective tax rate</i>	<i>0,6%</i>	<i>0,0%</i>

Permanent differences include the impact of the research tax credit (operational revenue not taxable fiscally).

#### Nature of deferred taxes

<b>NATURE OF DEFERRED TAXES (Amounts in euros)</b>	<b>31/12/2018</b>	<b>31/12/2017</b>
Other temporary differences	93	77
Temporary differences related to the Sumitomo contract	1 589	2 802
Loss carryforwards	35 330	35 833
<b>Total items of a deferred tax asset nature</b>	<b>37 013</b>	<b>38 711</b>
Temporary differences on contracts	2 137	
Temporary differences on repayable advances	13	22
Other temporary differences	21	
<b>Total items of a deferred tax liabilities nature</b>	<b>2 171</b>	<b>22</b>
<b>Net total items of a deferred tax nature</b>	<b>34 841</b>	<b>38 689</b>
Unrecognized deferred taxes	-34 841	-38 689
<b>Total net of deferred taxes</b>		

Deferred taxes 2018 shown based on a tax rate of 25% (rate applicable as of 2022).

#### Note 23: Earnings per share

<b>EARNINGS PER SHARE</b>	<b>31/12/2018</b>	<b>31/12/2017</b>
Weighted average number of shares outstanding	24 833 331	23 033 299
Net income for the year (in K€)	13 525	-22 298
<b>Basic earnings per share (€/share)</b>	<b>0,54</b>	<b>(0,97)</b>
<b>Diluted earnings per share (€/share)</b>	<b>0,53</b>	<b>(0,97)</b>

### Basic earnings

The base result per share is calculated by dividing the net result attributable to the shareholders of the Company by the weighted average number of common shares outstanding during the financial year.

### Diluted earnings

Diluted earnings per share are calculated on the same basis as net income, by taking into account the conversion of all instruments in the average number of shares outstanding potentially dilutive comprising warrants (226 336 shares), BSPCE (232 800 shares), stock options (247 500 shares) and free shares (24 150 shares).

In 2017, the set of instruments giving right to the capital in a deferred way (BSA, BSPCE and stock options) are regarded as non-dilutive because they induce a reduction in the loss per share. This way, diluted loss per share is identical to the base loss per share.

### Note 24: Related parties

No advantage posterior to the employment is granted to members of the Board of Directors.

Compensation paid to executives (Chairman and members of the Board of Directors) is broken down as follows (in euros):

<b>Compensation of corporate officers</b>	<b>31/12/2018</b>	<b>31/12/2017</b>
Fixed compensation due	331	191
Variable compensation due	123	46
Benefits in kind	9	6
Employer's contributions	120	96
Attendance fees	333	362
Share-based payments	693	745
Consultancy fees		
<b>TOTAL</b>	<b>1 610</b>	<b>1 446</b>

The terms of the allocation of the variable parts are established on the basis of qualitative and quantitative objectives set at 100% on the respect of goals at the level of the Company, common to all of the employees.

The modalities of assessment of the benefit relative to payments based on shares are presented in note 13.



## Note 25: Off-balance sheet commitments

### 25.1 Commercial Leases

#### Real estate leases

In 2015, in relation with its activities, the Company moved its headquarters and entered into a commercial lease in Lyon with an effective date of July 1, 2015. Its term is nine complete and consecutive years, until June 30, 2024. The Company has the possibility to provide notice to terminate only every three years.

In November 2017, the Company entered into a commercial lease enabling it to enlarge the office space at its headquarters, effective from April 1, 2018. Its term is nine complete and consecutive years, until March 31, 2027. The Company has the possibility to provide notice to terminate only every three years.

The Group has also subleased an office in Paris for a 12-month term that is renewable annually, effective January 1, 2013.

In Japan the Company entered into a lease for its offices in Japan as of January 15, 2018, for a period of 2 years.

In December 2018, the Company entered into a five-year lease agreement for its offices in the United States.

#### Contractual obligations and commitments

The following table summarizes the Company's commitments as at December 31, 2018:

Financial commitments	Commitment until the next renewal period				Total
	1 year maximum (excluding indexation)	1 to 3 years (excluding indexation)	3 to 5 years (excluding indexation)	> 5 years	
Rentals	353	559	130		1 042

### 25.2 Obligations under the contract signed with Merck Serono during the creation of the Company

The Company entered into a transfer and license agreement with Merck Serono on March 19, 2009 amended on July 30, 2009, June 22, 2010, May 23, 2014 and then November 28, 2014 (the "MS Agreement"), which falls within the scope of the spin-off of Merck Serono's research and development activities in the cardiometabolic field.

Pursuant to the terms of the MS Agreement, Merck Serono transferred certain patents and granted a license for other patents and know-how to the Company for research and development, and the marketing of pharmaceutical products. This license is exclusive for a list of 25 molecules, by program, selected by the Company.

In consideration of the rights that have been granted in the framework of the MS Contract, the Company must pay to Merck Serono:

- Royalties on net sales of products covered by the patents assigned or licensed in license by Merck Serono at a high single digit rate for the Imeglimin, and at a low single digit rate for other projects;
- a percentage of the income from any partnership agreement relating to the drug candidates covered by the patents granted or licensed, at a low double digit rate. For other products, if the Company enters into a partnership agreement, it would have to pay a percentage of the income from the partnership for the products covered by the patents transferred or licensed from Merck Serono, at a rate depending on the product and its stage of development at the time of the partnership.

As part of the application of this contract to the partnership agreement signed with Roivant in February 2018, the company and Merck Serono have a different interpretation of Poxel's revenue base to be subject to royalties. The Company considers, with its advisors, that its interpretation is justified by well-founded legal arguments and that the probability of an outflow of resources beyond the amount recorded is remote. Consequently, this discrepancy, applied to payments already received from Roivant on 31 December 2018 has not been the subject of a provision but constitutes a contingent liability for the company.

### **25.3 Obligation under the DeuteRx contract**

On August 29, 2018 the Company entered into a purchase contract with DeuteRx for DRX-065, a potential medication under clinical development for the treatment of non-alcoholic steatohepatitis (NASH), a portfolio of other potential specialty medications for the treatment of rare metabolic diseases, and all related industrial and intellectual property rights of DeuteRx.

This agreement specifies, for the entire product portfolio, the issue of up to 4 million shares in the Company in favor of DeuteRx, and milestone payments linked to the attainment of development, regulatory and sales targets, amounting to a maximum of \$545 million, part of which may be paid through the issue of shares in the Company. It also provides for the payment of royalties at a low-range figure on sales. The first milestone payment corresponds to the Company's decision to commence the phase 3 clinical development program for the drug candidates covered under that agreement, and will be made exclusively through the issue of shares in the Company.

### **22.4 Obligation under other agreements**

In the framework of its activities, the Company regularly uses subcontractors and concludes research and partnership agreements with various organizations, or CRO, which perform preclinical trials and clinical studies in relationship with the drug candidates, mainly Imeglimin and to a lesser extent, PXL 770. The cost of the services rendered by the CROs is counted as an operating cost when it is engaged, or, depending on the nature, for their result at the date of the financial statements.

## **Note 26: Management and assessment of financial risks**

The principal financial assets held by the Company are cash and cash equivalents held to finance the business activities and development of the Company and the client receivables in the context of the partnership contracts. The Company may be exposed to different types of financial risks: market risk, credit risk and liquidity risk. When appropriate, the Company uses simple ways proportionate to its size in order to minimize potentially adverse effect of these risks on financial performance. It is not the Company's policy to invest in financial instruments for speculative purposes.

### **Interest rate risk**

The Company has a very low exposure to interest rate risk, considering that:

- its liquid assets include fixed term deposits;
- the repayable advances are not subject to interest rate risk;
- no debt has been entered into at a variable interest rate.

### **Credit risk**

The credit risk is associated with the deposits with banks and financial institutions. For its cash investments, the Company uses first-rate financial institutions and does not bear any significant credit risk with regard to its cash.

### **Foreign currency risk**

The Company is exposed to foreign exchange risk taking into account the volume of transactions that it carries out in yen in the framework of the contract signed with Sumitomo Dainippon Pharma. However, it covers this risk in application of the principle provided in the contract, according to which the Company re-invoices Sumitomo in the same currency as the currency in which it was charged for its purchases.

The Company is also exposed to the foreign currency risk due to 13.6m€ liability towards Roivant (in USD). In any case, the Company has covered the major part of the risk by having subscribed to currency term accounts for an amount of 11.4m€ as of December 31, 2018.

At this stage, the Company has not adopted any other recurring mechanism of coverage to protect its activity against currency fluctuations. From time to time, the Company may nevertheless subscribe currency term accounts in order to cover a commitment in currency as described above.

In the future, with the growth of its activity, which could expose the Company to the exchange risk in a more significant manner, it will consider using a suitable policy to cover these risks.

### **Shares risk**

The Company does not hold any equity investments or marketable securities traded on a regulated market.

### **Liquidity risk**

The Company is not exposed in the short term to liquidity risk, taking into account the fact that the cash available on December 31, 2018, which amounts to 66,737 K€, is sufficient to finance the development of the Company in the course of the next twelve months.

### **Note 27: Statutory auditors' fees**

	Exercice 2018			Exercice 2017		
	PwC	Mazars	Total	PwC	Mazars	Total
Commissariat aux comptes	60	60	120	39	39	78
Services Autres que la Certification des Comptes	12	12	24	23	19	42
<i>Requis par les textes</i>	12	12	24	23	19	42
<i>Autres SACC</i>	0	0	0	0	0	0
Total des honoraires	72	72	144	62	58	120

## 20.2. Verification of Annual Historical Financial Information

### Auditors' report on the consolidated financial statements

To the attention of the General Meeting of Shareholders

#### Poxel

Immeuble Le Sunway  
259 avenue Jean Jaurès  
69007 Lyon

### Opinion

In accordance with the assignment entrusted to us by Poxel's General Meeting of Shareholders, we have audited the consolidated financial statements of Poxel for the year ended December 31, 2018, as attached to this report.

Considering the IFRS standards as adopted by the European Union, we certify that the consolidated financial statements give a true and fair view of the results of operations occurred during the year ended and of the financial position and assets and liabilities, at the end of the financial year, of the group of persons and entities included in the consolidation.

The opinion expressed above is consistent with the content of our report to the audit committee.

### Basis of opinion

#### Audit standards

We conducted our audit in compliance with the professional standards applicable in France. We consider that the materials we have collected are sufficient and appropriate to provide a basis for our opinion.

Our liability under these standards is described in the section « Liability of the auditors for the audit of the consolidated financial statements » of this report.

### Independence

We conducted our audit in compliance with the independence rules applicable to us, for the period from January 1, 2018 to the date of issue of our report, and in particular we did not provide services prohibited by the article 5(1) of Regulation (EU) No. 537/2014 or by the Code of Ethics for Auditors.

### Observation

Without qualifying our opinion, we draw your attention to the point set out in Note 2 “Principles for the preparation of financial statements” from the schedule to consolidated financial statements in regards to the consequences related to the application of IFRS standard 9 “Financial instruments”.

### **Justification of the assessments - Key points of the audit**

As required by articles L. 823-9 and R.823-7 of the French Commercial Code related to the justification of the assessments, we bring to your attention the key points of the audit related to the risks of material misstatements which, in our professional judgment, were the most significant for the audit of the consolidated financial statements for the year ended, as well as the responses we have provided to those risks.

These assessments were made in the context of the audit of the consolidated financial statements taken as a whole and of the formation of our opinion expressed above. We do not express an opinion on items within the consolidated financial statements considered alone.

### **Recognition of revenue from collaborative agreements, licenses and services agreements**

*(Note 4.1 «Significant events », notes 3.14 et 18 « Revenues »)*

#### *Risk identified*

Poxel generated revenue from collaborative agreements and licenses agreements for its drug-candidates and its own technologies with biopharmaceutical and pharmaceutical companies for a total amount of € 74.6 million as at December 31, 2018.

These agreements provide for various types of payment: upfront payments, payments for the achievement of clinical and regulatory objectives, payments for research and development services, payments based on sales objectives and royalties which amounts are determined on the basis of sales of marketed products.

The method for accounting such products depends in particular of the kind of services provided by Poxel and its subsidiary to its partners. A wrong interpretation of the agreements executed by the partners may lead to inadequate recognition of the related incomes in regards to the IFRS standard 15. The agreements may provide for services for which the income is to be taken under account on the basis of costs incurred. In this eventuality, the management must estimate costs on completion and monitor the costs incurred for these services.

The acknowledgement of incomes is a key element of the audit due to the several contractual provisions which determine the accounting method and the required estimates in order to define the income to be acknowledged.

#### **Our response**

We have reviewed the license and partnership agreements entered into with Sumitomo Dainippon Pharma and Roivant Sciences GmbH and have carried out an analysis of these elements, in particular the requirements of the parties, services to be provided and the compensation components.

We obtained the analysis and estimates made by the management in order to determine the amount of incomes related to these agreements.

We assessed the relevance of the methods used and the consistency of the assessments carried out by the management to determine the services included in the agreements, the transaction price, how the

transaction price is allocated to the various services performed by Poxel and the acknowledgement of the incomes related to the agreements.

With the help of our specialists, we examined the compliance of the Company's accounting treatments with standard IFRS 15 as adopted by the European Union.

In relation with income recognized in advance, we corroborated, on a test basis, the assumptions and data used by the management to determine the costs at completion with internal and external justifications (including contracts with subcontractors) and justifications for costs incurred.

Finally, we checked that an appropriate information was provided in the notes of consolidated financial statements.

#### **Accounting treatment and valuation of the products portfolio acquired from DeuteRx**

*(Note 4.1 « Significant events », notes 3.4 et 6 « Intangible assets », note 25.3 « Requirements under agreement with DeuteRx »)*

##### *Risk identified*

In August 2018, Poxel acquired, through a strategic agreement concluded with the company DeuteRx, the drug-candidate DRX-065 in clinical development for the treatment of Non-Alcoholic Steatohepatitis (« NASH ») and other programs including drug-candidates deuterated for the treatment of rare and specialized metabolic disorders.

Poxel has paid to DeuteRx an upfront payment composed of an amount of € 6.9 million (\$ 8 million) and of an amount of 1.29 million new ordinary shares of Poxel at a price of € 6.91 per share, representing 4.99% of the share capital (either € 8.9 million at the time of the transaction). As mentioned in the note 25.3, this agreement also provides:

- Payments by Poxel to DeuteRx related to the achievement of some clinical and regulatory objectives and products sales objectives (in cash or shares of Poxel, as the case may be)
- Payment of royalties on sales.

This transaction appears to be significant and non-recurring for Poxel, this led the Company to question itself about the relevant accounting treatment for this transaction.

On December 31, 2018, Poxel has accounted an intangible asset for € 16.6 corresponding to the upfront payment of € 15.8 million and of € 0.8 million of acquisition fees.

We considered the accounting treatment of this agreement as a key element of the audit because this transaction appears material and non-recurring for the Company.

##### *Our response*

We obtained the agreement entered into with DeuteRx and have reviewed it by examining the terms of payment and of transfer of intellectual property.

With the help of our specialists, we examined the compliance of the accounting treatment in regards to the IFRS standards as adopted by the European Union.

Finally, we checked that an appropriate information was provided in the note of the consolidated financial standards.

#### **Accounting and valuation of royalties paid under the sale and license agreement executed with Merck Serono**

*(Notes 19 “Details of expenses and income by function” and 25.2 “Requirements under agreement executed with Merck Serono when the company was created”)*

*Risk identified*

Poxel entered into with Merck Serono a sale and license agreement dated March 19, 2009 and amended on July 30, 2009, June 22, 2010, May 23, 2014 then November 28, 2014. This agreement provides in particular that the Company must pay to Merck Serono, as royalties, a percentage of the incomes received from any partnership agreement relating to drug-candidates included by the patents sold or licensed, and especially the Imeglimin.

As mentioned by the note 4.1 to schedules of consolidated financial statements, the Company has concluded, in February 2018, with Roivant Sciences GmbH an exclusive agreement for development and marketing of Imeglimin, in the United States, in Europe and in other countries.

A percentage of the income related to this agreement must be paid to Merck Serono as royalties. As indicated in the note 25.2, Merck Serono has a different interpretation of the basis for calculating the royalties to be paid.

We considered the recognition and valuation of these royalties as a key point of the audit, the estimation of the expense recorded in the accounts in this respect required the management judgment in particular to determine the basis for calculating the royalties.

*Our response*

We took under consideration the agreement and its amendments executed by Merck Serono and the agreement executed with Roivant.

We have consulted the arguments exchanged between Poxel and Merck Serono. We asked for an external confirmation to the advisors of Poxel and analyzed the response to this request in the context of this divergence of interpretation. We examined the merits of the arguments put forward by Poxel and its advisors to determine the elements to be included or excluded from the basis for calculating royalties.

We assessed the relevance of the methods used to calculate these fees on the basis of the analysis conducted by management and its advisors.

Finally, we checked that an appropriate information was provided in the schedule to the consolidated financial statements.

**Specific verifications**

In accordance with the professional standards applicable in France, we have also performed the specific verifications as required by law and regulations of the information relating to the group, given in the management report.

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

**Information resulting from other legal and regulatory requirements**

***Appointment of the auditors***

We have been appointed as auditors of the Company Poxel by your General Meeting of Shareholders dated January 29, 2016 for Mazars and January 31, 2014 for PricewaterhouseCoopers Audit.

On December 31, 2018, PricewaterhouseCoopers Audit was in the fifth year of the achievement of its assignment without interrupting and Mazars in the fourth year, considering that Mazars Lyon, as member of the Mazars network, was Poxel's auditor from 2009 to 2014. The PricewaterhouseCoopers Audit and Mazars networks are in their fourth year of their assignment without interruption since the Company's shares were admitted to trading on a regulated market.

### **Liability of the management and persons involving in the corporate governance in regards to the consolidated financial statements**

It is the management responsibility to establish consolidated financial statements which present a true and fair view in compliance with IFRS standards as adopted in the European Union, and to set up internal control that it believes is necessary for the preparation of consolidated financial statements without any material misstatement, whether due to fraud or error.

By preparing the consolidated financial statements, the management is in charge of evaluating the Company's ability to continue its business, presenting in these financial statements, if any, all information related to the business continuity and applying business accounting policy, unless it is intended to winding up the Company or to cease its business.

The audit committee is responsible for monitoring the process of preparing financial information and for monitoring the effectiveness of internal control and risk management systems, as well as, if applicable, internal audit, with respect to procedures related to the preparation and processing of accounting and financial information.

The consolidated financial statements have been approved by the Board of Directors.

### **Liability of the auditors in regard to the audit of consolidated financial statements**

#### *Audit objective and approach*

It is our responsibility to prepare a report related to the consolidated financial statements. Our objective is to obtain reasonable assurance that the consolidated financial statements taken as a whole are free from material misstatement. The reasonable assurance is a high level of assurance, but does not guaranty that an audit conducted in accordance with professional standards of practice permits automatically to identify any material misstatement. Misstatements may result from fraud or error and are considered material when it can reasonably be expected that they could, individually or in aggregate, influence the economic decisions that users of the accounts make based on them.

As provided by the article L.823-10-1 of the French Commercial Code, our mission of certification of accounts does not consist in guaranteeing the viability or quality of the management of the Company.

As part of an audit conducted in compliance with professional standards applicable in France, the auditor exercises his professional judgment throughout the audit.

In addition:

- It identifies and evaluates the risks of material misstatement of the consolidated financial statements, whether due to fraud or error, defines and performs audit procedures to address these risks, and obtains information that it considers sufficient and appropriate to reach an opinion. The risk of not detecting a material misstatement due to fraud is higher than the one



related to a material misstatement due to error, as fraud may involve collusion, falsification, willful misrepresentation, misrepresentation or bypass of internal control;

- it reviews the relevant internal control for the audit in order to design audit procedures that are appropriate under the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the internal control;
- it evaluates the adequacy of the accounting policies used and the reasonableness of the accounting valuations made by management, as well as the information relating to them provided in the consolidated financial statements;
- it evaluates the appropriateness of management's use of the going concern accounting policy and, depending on the information collected, whether or not there is a material uncertainty related to events or circumstances that could affect the Company's ability to continue as a going concern. This evaluation is based on the information collected up to the date of its report, it being recalled, however, that subsequent circumstances or events could jeopardize the continuity of operations. If it concludes that a material uncertainty exists, it draws the attention of the readers of its report to the information provided in the consolidated financial statements about that uncertainty or, if these information are not provided or are not relevant, it issues a qualifying certification or a refusal to certify;
- it evaluates the overall presentation of the consolidated financial statements and evaluates whether the consolidated financial statements reflect the underlying transactions and events in such a way as to give a true and fair view.
- In regards to the financial information of the persons or entities included within the scope of consolidation, it collects information that is considers sufficient and appropriate to express an opinion on the consolidated financial statements. He is responsible for the management, supervision and audit of the consolidated financial statements and for the opinion expressed on them.

#### *Report to the Audit Committee*

We deliver to the Audit Committee a report that includes the scope of the audit work and the work program implemented, as well as the conclusions arising from our works. We also report to it, where applicable, the material weaknesses in internal control that we have identified with respect to the procedures relating to the preparation and processing of accounting and financial information.

Among the elements communicated in the report to the Audit Committee, there are the risks of material misstatements, which we consider to have been the most important for the audit of the consolidated financial statements for the year ended and which therefore constitute the key audit issues, which we are required to describe in this report.

We also provide the Audit Committee with the declaration provided for in article 6 of Regulation (EU) No. 537-2014 confirming our independence, within the meaning of the rules applicable in France as defined in particular by articles L. 822-10 to L. 822-14 of the French Commercial Code and in the Code of Ethics for the Auditors. If necessary, we discuss with the Audit Committee the risks to our independence and the safeguards applied.

Signed in Lyon and Courbevoie on April 8, 2019

## The Auditors

MAZARS

Séverine Hervet

PricewaterhouseCoopers Audit

Elisabeth L'Hermite

### 20.3. Table of the Company results of the last 5 years

Amounts in K€	Dec. 31, 2014	Dec. 31, 2015	Dec. 31, 2016	Dec. 31, 2017	Dec. 31, 2018
<b>CAPITAL AT YEAR END</b>					
Share Capital	250	390	459	463	517
Number of existing ordinary shares	12 508 156	19 482 394	22 950 228	23 127 428	25 856 827
<b>OPERATIONS AND RESULTS</b>					
Revenue exclusive of VAT	0	60	70	8 579	74 599
Earnings before tax, employee profit-sharing, and allocations to depreciation, amortization and provisions	(8 405,64)	(17 261,45)	(26 079,70)	(15 052,97)	9 558,07
Income taxes	(1 977,12)	(1 918,07)	(3 042,90)	(3 122,19)	(3 475,69)
Earnings after tax, employee profit-sharing, and allocations to depreciation, amortization and provisions	(6 440,86)	(15 366,36)	(23 068,82)	(12 054,41)	11 400,32
<b>EARNINGS PER SHARE</b>					
Earnings before tax, employee profit-sharing, and allocations to depreciation, amortization and provisions	(0,67)	(0,89)	(1,14)	(0,65)	0,37
Earnings after tax, employee profit-sharing, and allocations to depreciation, amortization and provisions	(0,51)	(0,79)	(1,01)	(0,52)	0,44
<b>EMPLOYEES</b>					
Average number of employees during the financial year	11	15	17	20	27
Total payroll for the financial year	1 123	1 147	1 658	2 090	2 421
Cost of social benefits paid during the financial year	284	365	538	937	1 164

### 20.4. Date of the latest financial information

The date of the latest financial information is December 31, 2018.

### 20.5. Policy of distribution of dividends

**20.5.1.** Dividends and reserves distributed by the Company in the course of the last two financial years

None

**20.5.2.** Distribution Policy

It is not intended to initiate a policy of payment of dividends in the short term in view of the stage of development of the Company.

#### **20.6. Proposal for allocation of the profit for financial year 2018**

It is proposed to allocate the profit for the financial year ended December 31, 2018 in full to the carry-forward account.

#### **20.7. Expenses not deductible for tax purposes**

In accordance with the provisions of Article 223 quater of the French General Tax Code, we inform you that the financial statements for the year under review include a sum of €7,372 corresponding to non-tax-deductible expenses as specified in Article 39-4 of the French General Tax Code and that there is therefore no tax to be paid.

#### **20.8. Legal and arbitration proceedings**

At the date of this *document de référence*, for a period covering the last twelve months, there are no governmental, judicial or arbitration procedures, which could have or have recently had a material impact on the financial position or the profitability of the Company.

## 20.9. Information on the time limits for payment of suppliers

Invoices received and issued unpaid at the end of the financial year for which the term has expired (see table under I of Article D. 441-4)													
	Article D. 441 I.(1): Invoices <u>received</u> unpaid at the end of the financial year, for which the term has expired						Article D. 441 I.(2): Invoices <u>issued</u> unpaid at the end of the financial year, for which the term has expired						
	0 days <i>(indicative)</i>	1 - 30 days	31 - 60 days	61 - 90 days	91 days and over	Total (1 day and over)	0 days <i>(indicative)</i>	1 - 30 days	31 - 60 days	61 - 90 days	91 days and over	Total (1 day and over)	
(A) Late payment tranches													
Number of invoices involved	119					25	6					0	
Total amount of invoices involved excluding tax	4 941 354	3 821 685	6 140	0	123 020	3 950 845	8 598 648	0	0	0	0	0	
Percentage of total purchases excluding tax for the financial year	8,73%	6,75%	0,01%	0,00%	0,22%	6,98%							
Percentage of revenue excluding tax for the financial year							20,92%	0,00%	0,00%	0,00%	0,00%	0,00%	
(B) Invoices excluded from (A) relating to disputed or unrecognized debts and receivables													
Number of excluded invoices													
Total amount of excluded invoices													
(C) Reference payment terms used (contractual or statutory period - Article L. 441-6 or the French Commercial Code) <span>Article L. 443(1) of</span>													
Payment periods used to calculate late payments	<input type="checkbox"/> Contractual terms: (To be specified)						<input type="checkbox"/> Contractual terms: (To be specified)						
	<input type="checkbox"/> Statutory terms: (To be specified)						<input type="checkbox"/> Statutory terms: (To be specified)						

## 20.10. Material change in the financial or business position

To the knowledge of the company, there have been no material change in the financial or business position of the Company since December 31, 2018.

## 20.11. Statutory auditors' fees

	Exercice 2018			Exercice 2017		
	PwC	Mazars	Total	PwC	Mazars	Total
Commissariat aux comptes	60	60	120	39	39	78
Services Autres que la Certification des Comptes	12	12	24	23	19	42
<i>Requis par les textes</i>	12	12	24	23	19	42
<i>Autres SACC</i>	0	0	0	0	0	0
<b>Total des honoraires</b>	<b>72</b>	<b>72</b>	<b>144</b>	<b>62</b>	<b>58</b>	<b>120</b>

## 21.ADDITIONAL INFORMATION

### 21.1.1. Amount of share capital

As of the date of this *document de référence*, the share capital amounted to €517,619.54, divided into 25,880,977 fully paid-up shares with a nominal value of €0.02 each.

At the date of the opening of the financial year ended December 31, 2018 the capital amounted to €460,684.56, divided into 23,034,228 fully paid-up shares with a nominal value of €0.02 each.

### 21.1.2. Non-equity securities

None

### 21.1.3. Number, book value and nominal value of the shares held by the Company or for the Company

The Company's General Meeting of Shareholders of June 21, 2018 authorized the Board of Directors, for a period of eighteen months from the date of the Meeting, to implement a share buyback program within the framework of the provisions of Article L. 225-209 of the French Commercial Code and in accordance with the general regulation of the AMF under the conditions described below:

**Maximum number of shares that may be purchased:** 10% of the total number of shares constituting its share capital at the date of the repurchase of the shares. When the shares are acquired for the purpose of promoting the trading and the liquidity of the shares, the number of shares taken into account for the calculation of the limit of 10% provided above corresponds to the number of shares purchased, after deduction of the number of shares resold during the duration of the authorization.

#### Objectives of the buyback of shares:

- promote the trading and the liquidity of the Company shares in the framework of a liquidity contract to be agreed with an independent investment services provider, in conformity with the Charter of Ethics of the AMAFI dated March 8, 2011 recognized by the decision dated March 21, 2011 of the AMF; and/or
- enable it to honor obligations related to the stock option programs, allocation of free shares, employee savings plans or other free share allocations to employees of the Company or affiliates, including (i) the implementation of all Company stock option plans pursuant to the provisions of Articles L. 225-177 *et seq.* of the French Commercial Code, (ii) the allocation of shares to employees under profit-sharing schemes and the implementation of all company savings plan under the conditions provided by the law, including Articles L. 3332-1 to L. 3332-8 *et seq.* of the French Labor Code, or (iii) the allocation of free shares pursuant to the provisions of Articles L. 225-197-1 *et seq.* of the French Commercial Code; and/or
- remit the shares on the occasion of the exercise of the rights attached to the securities giving access to capital by reimbursement, conversion, exchange, presentation of a warrant or in any other way, in the respect of the regulations in force; and/or
- buy shares for holding and subsequent remittance in exchange for or as payment in the framework of the possible operations of the merger, de-merger, contribution or of external growth; and/or
- the cancellation of all or part of the bought-back shares.

**The maximum purchase price:** €20 (excluding acquisition costs), subject to adjustments intended to take into account the impact of new transactions involving the Company's capital, including a change of the nominal value of the share, capital increase by capitalization of reserves, the allocation of free shares, stock split or consolidation, distribution of reserves or any other assets, amortization of capital, or any other operation involving equity.

**Maximum amount of funds that can be assigned to buyback:** €10,000,000

It is stated that the number of shares acquired by the Company in view of their holding and subsequent surrender in payment or in exchange as part of a merger, de-merger or contribution may not exceed 5% of its capital.

The shares thus bought may be canceled.

It is specified that the establishing of the share repurchase program and its implementation will be the subject of communications in accordance with the legal and regulatory provisions.

Moreover, on the basis of the resolution at the General Meeting of Shareholders of April 15, 2014, the Company signed a liquidity agreement on March 16, 2015 with Banque Oddo and Cie. An amount of €250,000 was initially allocated to this liquidity agreement.

As of December 31, 2018, 38,100 shares were included in the liquidity account for a remaining cash balance of €78,080.26.

#### **21.1.4. Convertible or exchangeable securities or securities accompanied by warrants**

At the date of this *document de référence*, the securities giving access to capital are the following:

##### **21.1.4.1. Stock subscription warrant plan**

	Warrant 06.23.2010 <sup>1</sup>	Warrant 10.31.2012 <sup>2</sup>		Warrant 07.25.2014 <sup>3</sup>	Warrant 6.16.2015 <sup>5</sup>		Warrant 1.29.2016			Warrant 6.30.2017		Warrants 6.21.2018
Date of General Meeting of Shareholders	06/23/2010	10/31/2012		07/25/2014	06/16/2015		01/29/2016			06/30/2017		06/21/2018
Date of attribution by the Board of Directors	7/05/2010	2/20/2013	03/12/2014	1/08/2015	4/29/2015	5/07/2015	1/29/2016	3/31/2016	1/27/2017	6/30/2017	1/25/2018	1/24/2019
Total amount of authorized warrants	6,200	5,000		(4)	(4)		(4)			(4)		(6)
Total amount of attributed warrants	4,500	2,500	2,500	42,500	42,500	240,000	85,000	42,500	62,500	25,000	90,000	120,000
Executive or corporate officer beneficiaries:												
- Thierry Hercend	4,500	1,000	1,875						12,500		15,000	20,000

	Warrant 06.23.2010 <sup>1</sup>	Warrant 10.31.2012 <sup>2</sup>		Warrant 07.25.2014 <sup>3</sup>	Warrant 6.16.2015 <sup>5</sup>		Warrant 1.29.2016			Warrant 6.30.2017		Warrants 6.21.2018
- Khoso Baluch (8)		1,500	625						12,500		15,000	20,000
- Richard Kender (8)				42,500					12,500		15,000	20,000
- Pascale Boissel (8)					42,500				12,500		15,000	20,000
- Janice Bourque (8)							42,500		12,500		15,000	20,000
- Pierre Legault							42,500	42,500				
- Kumi Sato (8)										25,000	15,000	20,000
Other beneficiaries						240,000						
Effective date of exercise of warrants	6/23/2011	2/20/2013	3/12/2014	7/25/2015	6/16/2016	5/07/2015	1/29/2017	3/31/2017	1/27/2018	6/30/2018	1/25/2019	1/24/2020
Warrant expiration date	06/23/2020	10/31/2022		7/25/2024	6/16/2025		1/29/2026	3/31/2026	1/27/2027	6/30/2027	1/25/2028	1/24/2029
Warrant Subscription price	€0	€12		€0.63	€1.41	€1.45	€1.60	€1.63	€0.38	€0.36	€0.35	€2.66 (7)
Warrant exercise price	€66.67	€80.00		€4.00	€9.37	€9.62	€9.05	€9.26	€7.17	€6.90	€6.60	€5.20 (7)
Number of shares subscribed	4,500	0	0	0	0	0	0	0	0	0	0	0
Total number of warrants canceled or voided	0	0	0	0	0	0	0	0	0	0	0	0
Total amount of remaining warrants	0	2,500	2,500	42,500	42,500	240,000	85,000	42,500	62,500	25,000	90,000	120,000
Maximum number of shares that can be subscribed	0	50,000	50,000	42,500	42,500	240,000	85,000	42,500	62,500	25,000	90,000	120,000

<sup>1</sup>. Each 06.23.2010 warrant entitles the holder to subscribe in cash for twenty (20) new shares at a price of €3.3335.

<sup>2</sup>. Each 10.31.2012 warrant entitles the holder to subscribe in cash for twenty (20) new shares at a price of €4.00.

<sup>3</sup>. Each 25.07.2014 warrant entitles the holder to subscribe in cash for one (1) new ordinary share at a price of €4.00.

<sup>4</sup> The total number of warrants authorized had been set by the General Meeting of Shareholders as a percentage of capital under a delegation that had expired due to an identical resolution during the General Meeting of Shareholders of June 21, 2018 (see Note 9).



<sup>5</sup>. The 06.16.2015 warrants were issued on the condition precedent of voting by the General Meeting of Shareholders of June 16, 2015 on a delegation of authority in favor of the Board of Directors. This delegation of authority was given by the General Meeting of Shareholders in its 18<sup>th</sup> resolution.

<sup>6</sup>. By virtue of the delegation voted by the General Meeting of Shareholders on June 21, 2018 under its 5<sup>th</sup> resolution, the maximum nominal amount of capital increases that may be carried out immediately or in the future pursuant to the delegation of authority relating to the warrants will be (i) €15,000 and (ii) may not exceed, with the securities that may be issued through the exercise of founder warrants, stock options and free shares that may be granted, 5% of share capital on a fully diluted basis recognized at the date of the decision to award the warrants; it being specified that the maximum amounts referred to in (i) and (ii) above will be increased by the securities issued to protect the rights of holders of securities giving access to capital pursuant to the provisions of the French Commercial Code.

<sup>7</sup>. The subscription price and the exercise price of the 6.21.2018 warrants were determined after valuation by an independent expert.

8. The attribution of warrants to independent directors does not undermine their independent character.

#### 21.1.4.2. Founder warrant (BSPCE) plan

	BSPCE 6.10.2010 <sup>1</sup>	BSPCE 6.10.2010-2 <sup>1</sup>		BSPCE 10.31.2012 <sup>2</sup>	BSPCE 2016 <sup>3</sup>	BSPCE 2017		
						2017-01	2017-02	2017-03
Date of General Meeting of Shareholders	6/10/2010	6/10/2010		10/31/2012	1/29/2016	6/30/2017		
Date of attribution by the Board of Directors	N/A	12/17/2010	9/20/2011	3/12/2014	7/29/2016 <sup>3</sup>	3/31/2017	6/30/2017	9/21/2017
Total amount of BSPCE authorized	5,000	5,200		5,000	(4)	(5)		
Total amount of attributed founders' warrants	5,000	3,000	1,500	5,000	45,000	100,000	177,500	15,000
Including executive or corporate officer beneficiaries: - Thomas Kuhn							50,000	
Effective date of exercise of BSPCE	6/10/2011	6/10/2011	6/10/2012	3/12/2014	7/29/2016	3/31/2018	6/30/2018	9/21/2018
BSPCE expiration date	6/10/2020	6/10/2020		10/31/2022	7/29/2026	03/31/2027	06/30/2027	09/21/2027
BSPCE exercise price	€2.50	€2.50		€3.20	€8.45	€5.91	€7.26	€6.01

	BSPCE 6.10.2010 <sup>1</sup>	BSPCE 6.10.2010-2 <sup>1</sup>		BSPCE 10.31.2012 <sup>2</sup>	BSPCE 2016 <sup>3</sup>	BSPCE 2017		
						2017-01	2017-02	2017-03
Number of shares subscribed	3,200	60,000	0	46,000	0	0	0	0
Total number of BSPCE canceled or voided	2,750	0	0	0	45,000	0	15,000	0
Total amount of exercised BSPCE	560	3,000	0	2,300	0	0	0	0
Total amount of remaining BSPCE	1,690	0	1,500	2,700	0	100,000	162,500	15,000
Maximum number of shares that can be subscribed	33,800	0	30,000	54,000	0	277,500		

<sup>1</sup>. Each BSPCE 06.10.2010 entitles the holder to subscribe for twenty (20) ordinary shares at a price of €2.50. Every year as of June 10, 2011, one third of the BSPCE 06.10.2010 can be exercised on condition that the holders are employees or executives subject to the employee tax regime on the exercise date.

<sup>2</sup>. Each BSPCE 10.31.2012 entitles the holder to subscribe for twenty (20) ordinary shares at the price of €3.20. BSPCEs 10.31.2012 may be exercised at any time, on condition that the holder is an employee or an executive subject to the employee tax regime at the exercise date.

<sup>3</sup>. Each BSPCE 2016 entitles the holder to subscribe for one (1) ordinary share at a price of €8.45. BSPCEs 2016 may be exercised, on condition that the holder is an employee or an executive subject to the employee tax regime on the exercise date, as from the subscription thereof by increments of one third every year as from the signature of the Term and Conditions for the BSPCE 2016.

<sup>4</sup> The total number of BSPCE authorized had been set by the General Meeting of Shareholders as a percentage of capital under a delegation that had expired as a result of an identical resolution during the General Meeting of Shareholders of June 30, 2017 (see Note 5).

<sup>5</sup>. The maximum nominal amount of the capital increases that may be carried out immediately or in future pursuant to the delegation of authority and the delegations of authority relating to the issue of BSPCE, stock options and free shares, will be (i) €15,000 and (ii) may not exceed, with the securities that may be issued through the exercise of BSPCE, stock options and free shares that may be granted, 7.5% of share capital on a fully diluted basis recognized at the date of the decision to award the warrants; it being specified that the maximum amounts referred to in (i) and (ii) above will be increased by the securities issued to protect the rights of holders of securities giving access to capital pursuant to the provisions of the French Commercial Code.

### 21.1.4.3. Stock option plan

	SO 1.29.2016			SO 6.30.2017		SO 6.21.2018	
Date of General Meeting of Shareholders	1/29/2016			6/30/2017		6/21/2018	
Date of attribution by the Board of Directors	3/31/2016	11/23/2016	1/27/2017	6/30/2017	1/25/2018	9/27/2018	1/24/2019
Total amount of stock options authorized	(1)	(1)	(1)	(1)	(1)	(1)	(2)
Total amount of attributed SO	80,000	150,000	197,500	97,500	215,000	130,000	40,000
Including executive or corporate officer beneficiaries: - Pierre Legault	0	150,000	12,500	0	30,000	0	40,000
Effective date of progressive exercise of stock options	3/31/2016	11/23/2017	1/27/2018	6/30/2018	1/25/2019	9/27/2019	1/24/2020
SO expiration date	3/31/2026	11/23/2026	1/27/2027	6/30/2027	6/30/2027	9/27/2028	1/24/2029
SO exercise price	€12.55	€6.47	€6.76	€6.61	€6.79	€6.82	€5.16
Number of shares subscribed	0	0	0	0	0	0	0
Total number of SO canceled or voided	0	0	0	5,000	7,500	0	0
Total amount of remaining SO	80,000	150,000	197,500	92,500	207,500	130,000	40,000
Maximum number of shares that can be subscribed	80,000	150,000	197,500	92,500	207,500	130,000	40,000

<sup>1</sup> The total number of stock options authorized had been set by the General Meeting of Shareholders as a percentage of capital under a delegation that had expired as a result of an identical resolution during the General Meeting of Shareholders of June 21, 2018 (see Note 2).

<sup>2</sup> The maximum nominal amount of capital increases that may be carried out immediately or in the future pursuant to the delegation of authority relative to options will be (i) €15,000 and (ii) may not exceed, with the

*securities that may be issued through the exercise of BSPCE, warrants, and free shares that may be granted, 5% of capital on a fully diluted basis recognized at the date of the decision to award the options; it being specified that the maximum amounts referred to in (i) and (ii) above will be increased by the securities issued to protect the rights of holders of securities giving access to capital pursuant to the provisions of the French Commercial Code.*

#### **21.1.4.4. Free share plan**

	June 30, 2017 free share allocation	June 21, 2018 free share allocation
Date of General Meeting of Shareholders	6/30/2017	6/21/2018
Date of attribution by the Board of Directors	1/25/2018	1/24/2019
Total number of free shares authorized	(1)	(2)
Total number of free shares attributed	126,500	240,000
Including executive or corporate officer beneficiaries: - Thomas Kuhn	33,300	40,000
Vesting date	(3)	(4)
Date of end of holding period	(3)	(4)
Number of vested shares	24,150	0
Total number of shares canceled or voided	21,840	0
Number of shares for which the vesting and holding period have ended	0	0
Potential shares at the time of writing this report	80,490	240,000

<sup>1</sup>. *The total number of free shares granted had been set by the General Meeting of Shareholders as a percentage of capital under a delegation that had expired as a result of an identical resolution during the General Meeting of Shareholders of June 21, 2018 (see Note 2).*

<sup>2</sup>. *The maximum nominal amount of capital increases that may be carried out immediately or in the future pursuant to the delegation of authority relative to free shares will be (i) €15,000 and (ii) may not exceed 10% of the number of shares constituting the share capital at the date of decision to attribute free shares and (iii) may not exceed, with the securities that may be issued through the exercise of BSPCA, warrants and share subscription options that may be granted, 5% of capital on a fully diluted basis recognized at the date of the decision to award the options; it being specified that the maximum amounts referred to in (i) and (ii) above will be increased by the securities issued to protect the rights of holders of securities giving access to capital pursuant to the provisions of the French Commercial Code.*

<sup>3</sup> The free shares allocated on June 30, 2017 are subject to the condition of presence of beneficiaries on the vesting date and to performance conditions assessed by the Board of Directors according to a three-year plan.

The first third of the free shares allocated on June 30, 2017 for which the performance conditions were assessed by the Board of Directors on January 24, 2019 will be subject to an additional holding period of one year.

The second third of the free shares allocated on June 30, 2017 for which the performance conditions will be assessed by the Board of Directors at its first meeting in 2020, will not be subject to an additional holding period.

The final third of the free shares allocated on June 30, 2017 for which the performance conditions will be assessed by the Board of Directors at its first meeting in 2021, will not be subject to an additional holding period.

<sup>4</sup> The free shares allocated on June 21, 2018 are subject to the condition of presence of beneficiaries on the vesting date and to performance conditions assessed by the Board of Directors according to a three-year plan.

The first third of the free shares allocated on June 21, 2018 for which the performance conditions will be assessed by the Board of Directors at its first meeting in 2021, will not be subject to an additional holding period (two-year vesting period).

The second third of the free shares allocated on June 21, 2018 for which the performance conditions will be assessed by the Board of Directors at its first meeting in 2021, will not be subject to an additional holding period.

The final third of the free shares allocated on June 21, 2018 for which the performance conditions will be assessed by the Board of Directors at its first meeting in 2022, will not be subject to an additional holding period.

#### **21.1.4.5. Summary of dilutive instruments**

The table below presents the summary of dilutive instruments as of the date of this *document de référence*:

	<b>Warrants</b>	<b>BSPCE</b>	<b>SO</b>	<b>FSA</b>
Total number of attributed warrants/BSPCE/SO/FSA	759,500	352,000	910,000	366,500
Potential total number of shares that may be subscribed or bought based on the warrants/BSPCE/SO/FSA attributed	940,000*	627,500*	910,000	366,500
Total number of warrants/BSPCE/SO/FSA canceled or voided	0	62,750	12,500	21,860
Total number of warrants/BSPCE/SO/FSA exercised	4,500	5,860	0	24,150
Total number of remaining warrants/BSPCE/SO/FSA	755,000	283,390	897,500	320,490

	Warrants	BSPCE	SO	FSA
Total number of shares that may be subscribed or bought based on the remaining warrants/BSPCE/SO/FSA	850,000*	395,300*	897,500	320,490

*\* After taking into consideration the conversion ratio of 20 shares for 1 BSPCE decided by the Company's Board of Directors on March 28, 2014.*

The total dilution that may arise as a result of the exercise of all of the financial instruments conferring access to the share capital or the exercise of all the warrants, BSPCE, stock options and free shares entitling access to 2,463,290 of the Company's shares corresponds to a potential dilution of 8.69% on a fully diluted basis, or a total of 28,344,267 shares.

#### **21.1.5. Acquisition rights and/or obligations attached to the capital issued but not paid-in and capital increase commitment**

The following table summarizes the delegations in the course of validity granted by the General Meeting of Shareholders in the area of capital increases and the use of these delegations in the last year.

Date of the General Meeting of Shareholders	Subject of the delegation	Duration of validity	Ceiling (in nominal value when it is expressed in euros)	Date and terms of use by the Board of Directors
June 21, 2018	Authorization to be given to the Board with a view to the purchase by Company of its own shares (10 <sup>th</sup> resolution)	18 months	10% of the total number of shares making up the share capital on the date of the repurchase by the Company	N/A
June 21, 2018	Authorization to the Board of Directors to reduce share capital by canceling treasury shares (11 <sup>th</sup> resolution)	18 months	10% of the total number of shares making up the share capital per 24-month period.	N/A
June 21, 2018	Delegation of authority to the Board of Directors to carry out a capital increase by issuing shares, equity securities conferring access to other equity securities or conferring the right to an allotment of debt securities and/or securities conferring access to equity securities, maintaining preferred subscription rights (12 <sup>th</sup> resolution)	26 months	€190,000 <sup>1</sup> ,  €270,147 <sup>4</sup> , and €100,000,000 <sup>5</sup>	N/A
June 21, 2018	Delegation of authority to the Board of Directors to carry out a capital increase by issuing shares, equity securities conferring access	26 months	€200,000 <sup>1</sup> , €270,147 <sup>4</sup> ,	N/A

Date of the General Meeting of Shareholders	Subject of the delegation	Duration of validity	Ceiling (in nominal value when it is expressed in euros)	Date and terms of use by the Board of Directors
	to other equity securities or conferring the right to an allotment of debt securities and/or securities conferring access to equity securities, canceling preferred subscription rights, by making a public offering and the option conferring a priority right (13 <sup>th</sup> resolution) <sup>6</sup>		and €100,000,000 <sup>5</sup>	
June 21, 2018	Delegation of authority to the Board of Directors to increase capital by capitalizing premiums, reserves, profits or other items (14 <sup>th</sup> resolution)	26 months	€148,000 <sup>1 and 4</sup>	N/A
June 21, 2018	Delegation of authority to the Board of Directors to carry out a capital increase by issuing shares, equity securities conferring access to other equity securities or conferring the right to an allotment of debt securities and/or securities conferring access to equity securities, canceling preferred subscription rights in favor of a specific category of persons (defined as:  (1) natural persons or legal entities or French or foreign UCITS, investing, on a principal basis, or having invested over one million euros during the 24 months preceding the capital increase considered, (a) in the pharmaceutical sector, or (b) in growth stocks listed on a regulated market or a multilateral trading system (such as Euronext Growth) considered as "Community SMEs" within the meaning of Appendix I to Regulation (EC) No 651/2014 of the European Commission of June 17, 2014; and/or  (2) one or more strategic partners of the company, located in France or abroad, having concluded or about to conclude one or more partnership agreements (development, co-development, distribution, manufacturing, etc.) or trade agreements with the company (or a subsidiary) and/or the companies they control, that control them or that are controlled by the same person or the same persons, directly or indirectly, within the meaning of Article L.	18 months	€200,000 <sup>1</sup> , €270,147 <sup>4</sup> , and €100,000,000 <sup>5</sup>	<b>Board of August 29, 2018</b>  Use of the delegation to carry out a capital increase of 1,290,000 shares for a nominal amount of €25,800 in favor of a designated person.

Date of the General Meeting of Shareholders	Subject of the delegation	Duration of validity	Ceiling (in nominal value when it is expressed in euros)	Date and terms of use by the Board of Directors
	<p>233-3 of the French Commercial Code; and/or</p> <p>(3) all credit institutions or investment services providers with a license to provide the investment service mentioned in Article L. 321-1(6) of the French Monetary and Financial Code, acting under a program to increase capital by exercise of stock options or a related transaction.</p> <p>(15<sup>th</sup> resolution)<sup>2</sup></p>			
June 21, 2018	<p>Delegation of authority to the Board of Directors to carry out a capital increase, within the limit of 20% of the share capital per year, by issuing shares, equity securities conferring access to other equity securities or conferring the right to an allotment of debt securities and/or securities conferring access to equity securities, canceling preferred subscription rights, by making an offer to qualified investors or a restricted group of investors, within the meaning of Article L. 411-2, paragraph II, of the French Monetary and Financial Code (private placement)</p> <p>(16<sup>th</sup> resolution)<sup>6</sup></p>	26 months	<p>€148,000 <sup>1</sup>,</p> <p>€270,147 <sup>4</sup>,</p> <p>and</p> <p>€100,000,000<sup>5</sup></p> <p>in the limit of 20% of the share capital per year, valued at the date of the decision of the Board making use of the delegation</p>	N/A
June 21, 2018	<p>Authorization to be granted to the Board of Directors in accordance with Articles L. 225-136(1), paragraph 2, and R. 225-119 of the French Commercial Code to set the issue price of the shares, equity securities conferring access to other equity securities or conferring the right to an allotment of debt securities and/or securities conferring access to equity securities, canceling preferred subscription rights, under the delegations of authority that are the subject of the 13<sup>th</sup> and 16<sup>th</sup> resolutions</p> <p>(17<sup>th</sup> resolution)</p>	26 months	<p>10% of the capital per year determined on the day of the decision of the Board making use of the delegation</p>	N/A
June 21, 2018	<p>Delegation of authority to the Board of Directors to increase the number of shares to be issued in the event of a capital increase with or without preferred subscription rights</p> <p>(18<sup>th</sup> resolution)</p>	26 months	<p>15% of the initial issue</p> <p>€270,147<sup>4</sup></p>	N/A



Date of the General Meeting of Shareholders	Subject of the delegation	Duration of validity	Ceiling (in nominal value when it is expressed in euros)	Date and terms of use by the Board of Directors
June 21, 2018	Delegation granted to the Board of Directors to issue shares and securities entailing a capital increase in consideration of non-cash contributions (19 <sup>th</sup> resolution)	26 months	10% of the capital of the Company existing at the date of the transaction, €270,147 <sup>4</sup> and €18 million for debt securities that could be issued under this delegation	N/A
June 21, 2018	Delegation of authority to the Board of Directors to issue shares and securities entailing a capital increase in the event of a public exchange offer initiated by the Company (20 <sup>th</sup> resolution)	26 months	€196,000 <sup>1</sup> €270,147 <sup>4</sup> and €100,000,000 <sup>5</sup>	N/A
June 21, 2018	Fixing the overall limitations of the amount of issues carried out under the delegations conferred (21 <sup>th</sup> resolution)	--	€270,147 <sup>4</sup> and €100,000,000 <sup>5</sup>	N/A
June 21, 2018	Authorization to the Board of Directors to grant share subscription and/or purchase stock options ("Options"), canceling shareholders' preferred subscription rights in favor of a specific category of persons (defined as:  employees and/or corporate officers (or some of them) of the Company or companies or groupings affiliated with it in accordance with the conditions set out in Article L. 225-180, paragraph I of the French Commercial Code. (22 <sup>nd</sup> resolution) <sup>2</sup>	38 months	€15,000 <sup>1</sup> , and 5% of capital on a fully diluted basis, recognized on the date of the decision of the allotment	<b>Board of September 27, 2018</b>  Use of the delegation for the allotment of 130,000 options to subscribe to a potential capital increase of €2,600 reserved for the benefit of certain employees
June 21, 2018	Delegation of authority to the Board of Directors to issue and allot ordinary share  warrants ("warrants"), canceling preferred subscription rights in favor of a  specific category of person (defined as:  (i) any individual or legal entity who are strategic partners of the Company, industrial or commercial entities in the pharmaceutical	18 months	€15,000 <sup>1</sup> , and 5% of capital on a fully diluted basis, recognized on the date of the decision of the allotment	N/A

Date of the General Meeting of Shareholders	Subject of the delegation	Duration of validity	Ceiling (in nominal value when it is expressed in euros)	Date and terms of use by the Board of Directors
	<p>sector, or persons who have entered into a service or consulting agreement with the Company or any of its subsidiaries;</p> <p>(ii) shareholders, senior management executives or employees of such entities in the case of legal entities;</p> <p>(iii) the senior management executives, corporate officers or employees of the Company or its subsidiaries)</p> <p>(23<sup>rd</sup> resolution)<sup>3</sup></p>			
June 21, 2018	<p>Authorization to the Board of Directors to allot free shares ("free share allocation"), whether existing or to be issued, canceling shareholders' preferred subscription rights in favor of a specific category of persons (defined as:</p> <p>employees, or certain categories of them, of the Company and/or entities directly or indirectly affiliated with it within the meaning of Article L. 225-197-2 of the French Commercial Code, as well as corporate officers of the aforementioned companies or entities, as determined by the Board of Directors in accordance with the provisions of Article L. 225-197-1 <i>et seq.</i> of the French Commercial Code, or some of them, and who, in addition, meet the conditions and, if applicable, the allotment criteria that will have been set by the Board of Directors)</p> <p>(24<sup>th</sup> resolution)</p>	38 months	<p>€15,000 <sup>1</sup>,</p> <p>and</p> <p>5% of share capital on a fully diluted basis recognized on the date of the decision of the allotment</p>	N/A
June 21, 2018	<p>Setting of the overall limits on the amount of the issues carried out pursuant to the authorizations to grant options and free shares and the delegations of authority to issue warrants</p> <p>(25<sup>th</sup> resolution)</p>	-	<p>5% of share capital on a fully diluted basis recognized on the date of the decision of the allotment</p>	N/A
June 21, 2018	<p>Delegation of authority to the Board of Directors to carry out a capital increase by issuing shares or securities conferring access to the company's capital restricted to members of a company savings plan, canceling preferred</p>	18 months	<p>€4,900 <sup>1</sup>,</p>	N/A

Date of the General Meeting of Shareholders	Subject of the delegation	Duration of validity	Ceiling (in nominal value when it is expressed in euros)	Date and terms of use by the Board of Directors
	subscription rights in favor of the aforementioned beneficiaries  (26 <sup>th</sup> resolution)			

<sup>1.</sup> Maximum nominal amount of the resolution concerned.

<sup>2.</sup> The issue price of the securities issued pursuant to this delegation of authority shall be set by the Board of Directors using a multi-criteria method, provided the share subscription price is not less than 80% of the weighted average of the share prices over the twenty (20) trading days preceding the date when the issue price is set, and the issue price of securities conferring access to capital is such that the sum immediately received by the Company at the time of this issue, plus, if applicable, any sum that it may subsequently receive for each share issued as a result of the issue of such securities, is not less than 80% of the weighted average of the share prices over the twenty (20) trading days preceding the date the issue price is set.

<sup>3.</sup> The subscription or purchase price of shares resulting from exercising the Options shall be determined by the Board of Directors on the date that the Options are granted, as follows:

- in the case of options to subscribe for new shares, the price shall not be less than 95% of the average, weighted by the volumes of the share prices over the twenty (20) trading days prior to the date the Option is granted;
- in the case of options to subscribe for existing shares, the price shall not be less than 95% of the average price of the twenty (20) trading days prior to the date the Option is granted, or of the average purchase price of the shares held by the Company in accordance with Articles L. 225-208 and L. 225-209 of the French Commercial Code

The subscription price of an ordinary share on exercise of a warrant will be determined by the Board of Directors at the time of the awarding of the warrants in the same manner: as long as the shares of the Company are admitted to trading on a regulated market, price at least equal to the average, weighted by the volumes of the price of the twenty (20) stock market sessions preceding the day of the decision of the Board to assign the warrants, reduced where applicable by a maximum discount of 5%.

<sup>4.</sup> Total nominal amount of the capital increases that may be carried out pursuant to the 12<sup>th</sup> to 16<sup>th</sup>, 19<sup>th</sup> and 20<sup>th</sup> resolutions (see the 21<sup>st</sup> resolution).

<sup>5.</sup> Total nominal amount of the debt securities that may be issued pursuant to the 12<sup>th</sup> to 16<sup>th</sup>, 19<sup>th</sup> and 20<sup>th</sup> resolutions (see the 21<sup>st</sup> resolution).

<sup>6.</sup> The issue price of the securities that may be issued pursuant to this delegation of authority shall be determined by the Board of Directors in accordance with the following terms and conditions: the sum that the Company receives or should receive for each share issued or created by subscription, conversion, exchange, redemption, exercise of warrants or otherwise shall be at least equal to an amount determined in accordance with the regulations applicable on the issue date (as of this date, the average, weighted by the volumes of the share prices over the last three trading days prior to the date the price is set, less a possible discount of no more than 5%, in accordance with Article R. 225-119 of the French Commercial Code). This is subject to the exception set out in the 17<sup>th</sup> resolution, that authorizes the Board of Directors to set the issue price of the securities issued pursuant to the delegations of authority that are the subject of the 13<sup>th</sup> and 16<sup>th</sup> resolutions, and up to the limit of 10% of the share capital per year as determined on the date of the Board of Directors' decision, as adjusted based on transactions that may subsequently affect this decision, at the price it shall determine based on a multi-criteria method, provided the subscription price is not less than 80% of the weighted average of the share prices over the five (5) trading days prior to the date the issue price is set, and that the issue price of securities conferring access to capital is such that the sum received immediately by the Company at the time of such issue, plus, if applicable, any sum it may subsequently receive for each share issued as a result of issuing such securities, is not less than 80% of the weighted average of the share prices over the five (5) trading days prior to the date the issue price is set.

#### **21.1.6. Information relating to the share capital of Group companies which is the subject of a conditional or unconditional agreement providing for it to be placed under option**

As far as the Company is aware, there are no call options, put options or other commitments in favor of the shareholders of the Company or made by them with regard to the Company's shares.

## 21.1.7. Changes in share capital

### 21.1.7.1. Table showing changes in share capital over the last three financial years

Reporting date	Nature of operations	Capital movement in €	Premium in €	Number of shares created	Number of shares constituting the capital	Nominal value in €	Share capital in €
	<b>As of December 31, 2015</b>	<b>389,648</b>	<b>81,923,706</b>	<b>11,036,872</b>	<b>19,482,394</b>	<b>0.02</b>	<b>389,648</b>
<b>March 2016</b>	Exercise of 45,834 warrants February 2016	917	182,415	45,834	19,528,228		390,565
<b>March 2016</b>	Exercise of 150 BSPCE February 2016	60	9,540	3,000	19,531,228		390,625
<b>July 2016</b>	Exercise of 950 BSPCE July 2016	380	49,220	19,000	19,550,228		391,005
<b>July 2016</b>	Capital increase (with cancellation of preferred subscription rights in favor of a category of persons, July 2016)	68,000	26,452,000	3,400,000	22,950,228		459,005
	<b>As of December 31, 2016</b>	<b>459,005</b>	<b>108,616,881</b>	<b>14,504,706</b>	<b>22,950,228</b>	<b>0.02</b>	<b>459,005</b>
<b>June 2017</b>	Exercise of 2,200 BSPCE January 2017	880	109,120	44,000	22,994,228		459,885
<b>June 2017</b>	Exercise of 2,000 BSPCE May 2017	800	127,200	40,000	23,034,228		460,685
<b>January 2018</b>	Exercise of 4,500 warrants, October 2017	1,800	298,215	90,000	23,124,228		462,485
<b>January 2018</b>	Exercise of 160 BSPCE, November 2017	64	7,936	3,200	23,127,428		462,549
	<b>As of December 31, 2017</b>	<b>462,549</b>	<b>109,159,352</b>	<b>14,681,906</b>	<b>23,127,428</b>	<b>0.02</b>	<b>462,549</b>
<b>February 2018</b>	Capital increase (with cancellation of preferred subscription rights in favor of a category of persons, February 2018)	28,628	12,138,264	1,431,399	24,558,827		491,177
<b>June 2018</b>	Exercise of 400 BSPCE	160	19,840	8,000	24,566,827		491,337
<b>September 2018</b>	Capital increase (with cancellation of preferred subscription rights in favor of a designated person, September 2018)	25,800	8,888,100	1,290,000	<b>25,856,827</b>		517,137
	<b>As of December 31, 2018</b>	<b>517,137</b>	<b>130,231,356</b>	<b>17,411,305</b>	<b>25,856,827</b>	<b>0.02</b>	<b>517,137</b>

### 21.1.7.2. Ownership of the Company's shares over the last three financial years

Shareholders	12/31/2016	12/31/2017	12/31/2018
Thomas Kuhn	6.54%	6.49%	5.80%
Other managers and employees	5.42%	4.36%	4.88%
<i>Total Management and employees</i>	<i>11.96%</i>	<i>10.85%</i>	<i>10.68%</i>
BPIfrance Investissement (FCPR Innobio)	10.81%	9.40%	8.41%

Shareholders	12/31/2016	12/31/2017	12/31/2018
Bpifrance Participations	7.39%	7.34%	7.20%
<i>BPI subtotal</i>	<i>18.21%</i>	<i>16.74%</i>	<i>15.61%</i>
Andera Partners	19.18%	18.85%	16.84%
Roivant Sciences Ltd	0%	0%	5.54%
OMNES CAPITAL Funds	7.09%	6.74%	(1)
JP Morgan Asset Management (UK) Limited	7.20%	4.85%	(1)
Merck Serono	4.74%	0%	0%
DeuteRx	0%	0%	4.99%
Public	31.63%	41.9%	46.20%
Treasury shares	0.073%	0.11%	0.15%
<b>Total</b>	<b>100%</b>	<b>100%</b>	<b>100%</b>

(1) The Company does not have information relating to the exact ownership of capital and voting rights of the OMNES Capital Fund and JP Morgan Asset Management at the date of this document de référence, as they own less than 5% of share capital or voting rights based on the shareholder disclosures received by the Company and the AMF.

#### 21.1.8. Items likely to have an impact in the event of a takeover bid

Items likely to have an impact in the event of a takeover bid are presented and explained in accordance with the provisions of Article L. 225-37-5 of the French Commercial Code.

##### 21.1.8.1. Structure of the Company's capital

The structure of the Company's capital is described in Chapter 21 "Additional Information" of this document de référence.

As far as the Company is aware, there are no other shareholders holding directly or indirectly, alone or in concert more than 5% of the capital or voting rights at the date of this report.

##### 21.1.8.2. Restrictions provided for in the bylaws on the exercise of voting rights and share transfers or clauses brought to the Company's attention pursuant to Article L. 233-11 of the French Commercial Code.

Not applicable.

**21.1.8.3. Direct or indirect shareholdings in the Company's capital of which it is aware pursuant to Articles L. 233-7 and L. 233-12 of the French Commercial Code**

As of the date of this *document de référence*, no shareholder individually holds either control of the Company, or a percentage likely to lead to the presumption of control of the Company within the meaning of the provisions of Article L. 233-3 of the French Commercial Code.

**21.1.8.4. List of the holders of any securities carrying special controlling rights and description of such securities**

The Company is not aware of the existence of special controlling rights.

**21.1.8.5. Control mechanisms provided for in any employee share ownership system, where the controlling rights are not exercised by the employees**

The Company has not set up any system of employee share ownership that may contain control mechanisms where the controlling rights are not exercised by the employees.

**21.1.8.6. Agreements between the shareholders of which the Company is aware and that may result in restrictions on the transfer of shares and in the exercise of the voting rights**

Not applicable.

**21.1.8.7. Rules applicable to the appointment and replacement of the members of the Board of Directors and to amendment of the bylaws**

The rules applicable in this respect are provided for in the bylaws and are in compliance with the law and the regulations in force.

**21.1.8.8. Powers of the Board of Directors, in particular the issuance or buyback of shares**

Information about delegations of authority can be found in Section 21.1.5 "Acquisition rights and/or obligations attached to the capital issued but not paid-in and capital increase commitment" of this *document de référence*.

**21.1.9. Agreements entered into by the Company that have been amended or end in the event of a change in control of the Company**

The Company entered into certain agreements, which involve stipulations relative to change of control of the Company.

Some terms and conditions of the securities giving access to capital also contain stipulations regarding an acceleration of the period of downtime in the event of a change of control of the Company (refer to Section 21.1.4 "Convertible or exchangeable securities or securities accompanied by warrants" of this *document de référence*).

## **21.2. Certificate of incorporation of the Company and bylaws**

### **21.2.1. Corporate purpose (article 2 of the Company's bylaws)**

The purpose of the Company, in France and any other country, is as follows:

- Research and development of new therapeutic strategies for humans, contract manufacturing and sale and marketing in all its forms of specialty pharmaceuticals previously tested in pre-clinical and clinical studies, as well as all applied research and medical development activities, filing and acquisition of all patents, trademarks and industrial property rights;
- Consultation and conduct of market surveys and studies relating to pharmaceutical regulations and pharmaceutical and clinical development;
- Participation of the Company, by any means, directly or indirectly, in all operations which may be related to its purpose through the incorporation of new companies, contribution, subscription or purchase of shares or share rights, merger or otherwise, creation, acquisition, rental, or management of a lease over any businesses or establishments; the taking, acquisition, exploitation or transfer of all processes and patents related to such activities.

And generally, all industrial, commercial, financial or non-trading transactions, in personal or real property, that may be directly or indirectly related to the corporate purpose or any similar or related purpose.

### **21.2.2. Provisions of the bylaws and other provisions relating to members of administrative and management bodies**

#### **21.2.2.1. Board of Directors (Articles 12-14 of the Company's bylaws)**

##### *21.2.2.1.1. Appointment of the members of the Board of Directors*

The Company is managed by a Board of Directors composed of between 3 and 18 members, who may be natural persons or legal entities, subject to the derogation provided for by law in case of a merger.

Any legal entity must, at the time of its appointment, appoint a natural person as its permanent representative on the Board of Directors. The length of the term of office of the permanent representative is the same as that of the legal entity director that it represents. When the legal entity removes its permanent representative from office, it must immediately arrange to replace him/her. The same provisions apply in the event of the death or resignation of the permanent representative.

No person over the age of 70 years shall be appointed as a Director. When directors cross this age limit during their term of office, thus bringing the number of directors aged over 70 to more than one-third, the oldest director shall be deemed to have automatically resigned.

Directors may or may not be shareholders of the Company.

During the life of the Company, Directors are appointed by a decision of the Ordinary General Meeting of Shareholders. The term of office of Directors is three (3) years. It ends at the close of the Ordinary General Meeting of Shareholders called to approve the financial statements for the previous financial year and held in the year during which their term of office expires.

In the event of a vacancy due to death or resignation of one or more Directors, the Board of Directors may make provisional appointments by co-optation in the period between two collective decisions by the shareholders. These appointments are then submitted to the next Ordinary General Meeting of

Shareholders for ratification. A director appointed to replace another director performs his/her duties for the remainder of his/her predecessor's term of office.

Directors may be re-elected. They can be removed from office at any time by a decision of the Ordinary General Meeting of Shareholders.

#### *21.2.2.1.2. Deliberations of the Board of Directors*

The Board of Directors meets as often as required by the best interests of the Company, but at least four times a year, after being convened by the Chairman. The Chief Executive Officer at any time, or one-third of the Directors if the Board of Directors has not held a meeting for over two months, may ask the Chairman to convene a Board meeting with regard to a specified agenda.

Invitations shall be sent in writing (fax, letter or e-mail), at least five business days prior to the meeting of the Board on the first call and at least two business days before the meeting of the Board on the second call. In case of emergency or if all the Directors accept, the period of prior notice may be shortened.

Meetings shall be held at the registered office or in any other place mentioned in the meeting notice. Within the limits provided for by law, the Board of Directors may meet and deliberate by any means, including in particular video, telex, fax, telephone conference, video conference, online or by any other means. Directors participating in the Board meeting by video conference or other means of telecommunication allowing the identification of participants and ensuring their effective participation in accordance with the conditions defined by the internal regulations of the Board of Directors are deemed to be present for the calculation of the quorum and majority.

The presence of at least half of the Board members in office is necessary for the validity of the Board's deliberations. A register of attendance is signed by the Directors attending the meeting.

Decisions shall be taken by a majority vote of the members present or represented at each meeting. The Chairman of the Board of Directors has the casting vote.

Deliberations of the Board of Directors are recorded in minutes included in a special register and signed by the Chairman of the meeting and at least one director or, in the event that the Chairman is unable to do so, by at least two directors.

Copies or extracts of the minutes of the deliberations are validly certified by the Chairman of the Board of Directors, the Chief Executive Officer, or a duly empowered representative authorized for such purpose.

#### *21.2.2.1.3. Powers of the Board of Directors*

The Board of Directors determines the direction of the Company's business activities and oversees the implementation thereof.

Subject to the powers expressly attributed to General Meetings of Shareholders and within the limit of the corporate purpose, it addresses any matters affecting the proper governance of the Company and settles the matters that concern it through its deliberations.

The Board of Directors performs the checks and verifications that it considers appropriate.

Each director must receive the necessary information for the performance of his/her duties and can obtain all the documents he/she considers useful from the Executive Management.



In dealings with third parties, the Company is bound even by the acts of the Board of Directors which do not fall within the scope of the corporate purpose or exceed the limitations on the powers provided for in the bylaws applicable to it, if it cannot prove that the third party was aware that the act exceeded such purpose or limitations, or that it could not fail to be aware of it given the circumstances.

The Chairman organizes and directs the Board of Directors' work on which he/she reports to the General Meeting of Shareholders and executes its decisions.

He/she makes sure that the Board of Directors functions properly and ensures that the directors are in a position to carry out their duties.

Security, endorsements and guarantees given by the Company are mandatorily subject to authorization by the Board of Directors.

The Board of Directors has the capacity to decide on the issuance of bonds.

The provisions of Article L. 225-38 of the French Commercial Code apply to agreements entered into, directly or via an intermediary, between the Company and one of its Directors or Chief Executive Officers.

#### **21.2.2.2. General management (Article 15 of the Company's bylaws)**

##### *21.2.2.2.1. Chief Executive Officer (Directeur Général)*

###### Appointment - Removal

Depending on the choice made by the Board of Directors, the general management is carried out either by the Chairman or by a natural person appointed by the Board of Directors and with the title of Chief Executive Officer, who may be a director or not.

If the Board of Directors chooses to separate the duties of Chairman from those of Chief Executive Officer, it shall proceed with the appointment of the Chief Executive Officer, set the length of his/her term of office, determine his/her compensation and, where applicable, the limitations on his/her powers.

The Chief Executive Officer must be less than 65 years old to exercise his/her functions. When in the course of their duties this age limit is reached, the CEO will be deemed to have resigned from office.

The Chief Executive Officer may be removed from office at any time by the Board of Directors. When the Chief Executive Officer does not perform the duties of Chairman of the Board of Directors, his/her removal from office may give rise to damages, if it is decided without due cause.

###### Powers

When the general management of the Company is carried out by the Chairman of the Board of Directors, these provisions apply to him.

The Chief Executive Officer has the broadest powers to act in any circumstances in the name of the Company. He/she exercises these powers within the limit of the corporate purpose and subject to the powers that the law and the bylaws expressly attribute to General Meetings of Shareholders and to the Board of Directors and any limitations on the powers that are imposed on him/her by the Board of Directors.

The Chief Executive Officer represents the Company in its dealings with third parties. The Company is committed even by acts of the Chief Executive Officer that are not within the Company's purpose, unless it can prove that the third party knew that the act went beyond this purpose or could not have

been unaware thereof given the circumstances, mere publication of the bylaws not being sufficient to constitute such proof.

#### *21.2.2.2.2. Deputy Chief Executive Officers (Directeurs généraux délégués)*

On the proposal of the Chief Executive Officer, whether such duties are carried out by the Chairman of the Board of Directors or by another person, the Board of Directors may appoint one or more natural persons responsible for assisting the Chief Executive Officer with the title of Deputy Chief Executive Officer.

With regard to third parties the Deputy Chief Executive Officer(s) have the same powers as the Chief Executive Officer subject, where applicable, to the specific limitations on powers that may be imposed on them by the Board of Directors.

In the event of termination of the duties of the Chief Executive Officer or his/her inability to act, the Deputy Chief Executive Officers shall retain their duties and their responsibilities until the appointment of a new Chief Executive Officer unless otherwise decided by the Board of Directors.

#### **21.2.2.3. Internal regulations**

The internal regulations of the Board of Directors were adopted by the Board of Directors on March 12, 2014 and most recently updated on June 30, 2017.

The internal regulations of the Board of Directors, as well as the specialized Committees it describes, supplement the legal and regulatory provisions, in compliance with the French Commercial Code and the Middlednext Code of Corporate Governance.

They set out, in particular, the role, the powers, the composition and the functioning of the Board of Directors, duties and ethical obligations of its members, the conditions of their compensation and of good information provision.

#### **21.2.2.4. Ethical charter**

The Company has implemented an ethical charter that was adopted by the Board of Directors on November 16, 2018.

The ethical charter reminds the Company's Directors, executive managers and employees of the Company's fundamental values of ethics and proper conduct. This document guides the Company's Directors, executive managers and employees in their decisions taken to ensure that they are in line with the Company's legal obligations and fundamental values of ethics.

#### **21.2.3. Rights, privileges and restrictions attached to the Company's shares (Articles 10 and 11 of the Company's bylaws)**

##### **21.2.3.1. Forms of the securities**

The shares shall be in registered or bearer form, at the option of the shareholder, subject to the provisions of laws and regulations in force. Shares that have not been paid up in full shall mandatorily be in registered form.

##### **21.2.3.2. Voting rights**

The voting right attached to shares is proportionate to the percentage of capital represented by the shares and each share carries the right to at least one vote. The General Meeting of Shareholders held

on January 8, 2015 decided to remove the automatic double voting rights as provided for by French law No. 2014-384 of March 29, 2014 aimed at recapturing the real economy (known as the “Florange” law).

#### **21.2.3.3. Rights to dividends and profits**

Each share entitles the holder to ownership of the corporate assets, to a share of the profits and the liquidating dividend pro rata to the percentage of the share capital that it represents.

#### **21.2.3.4. Preferred subscription rights**

All of the Company's shares carry preferred subscription rights in the event of any capital increases.

#### **21.2.3.5. Limits on voting rights**

None.

#### **21.2.3.6. Identification of the holders of bearer shares**

The Company is entitled, under the legal and regulatory provisions in force, to request at any time, at its own cost, from the central depository which is responsible for keeping its securities issuance account, the name or corporate name, nationality, year of birth or year of incorporation, and address of the holders of securities granting voting rights at its own General Meetings of Shareholders immediately or in future, together with the quantity of securities held by each of them, and where applicable, the restrictions to which the securities may be subject and, more generally, to make use of the provisions of Article L. 228-2 of the French Commercial Code with regard to identification of the holders of securities granting voting rights at its own General Meetings of Shareholders immediately or in future.

#### **21.2.3.7. Company's repurchase of its own shares**

See Section 21.1.3 “Number, book value and nominal value of the shares held by the Company or for the Company” of this *document de référence*.

#### **21.2.4. Changes in the shareholders' rights**

Only the Extraordinary General Meeting of Shareholders of the Company is empowered to make decisions with the effect of changing the rights of the shareholders provided by the Company's bylaws.

#### **21.2.5. General Meetings of Shareholders**

##### **21.2.5.1. Common rules that apply to all General Meetings of Shareholders (article 20 of the Company's bylaws)**

General Meetings of Shareholders are called under the conditions provided for by law.

General Meetings of Shareholders are held at the registered office or in any other location indicated in the notices or letters calling them to the meeting, in France or in any other country.

The agenda is set in accordance with the provisions of the laws and regulations in force.

Participation in General Meetings of Shareholders, in any form whatsoever, shall be subject to registering or recording shares under the conditions and within the time periods provided for by regulations in effect.

A shareholder may give a proxy in order to be represented at any General Meetings of Shareholders in accordance with the legal provisions in force. The specific proxy for each General Meeting is signed by the person granting the proxy who states his/her last name, first names and address.

For any proxy from a shareholder without an indication of the proxy, the Chair of the General Meeting of Shareholders casts a vote in favor of adoption of the draft resolutions presented or approved by the Board of Directors and a vote against the adoption of all other draft resolutions.

Correspondence voting takes place in accordance with the terms and conditions set by the provisions of the laws and regulations. Legal entities participate in General Meetings through their legal representatives or any other person duly and properly authorized by them.

General Meetings are chaired by the Chairman of the Board of Directors. In his/her absence, the General Meeting elects its chair itself.

The duties of vote-tellers are carried out by the two members of the General Meeting present and accepting such duties who hold the largest number of votes either in their own name or as proxy holders. If they do not accept, the General Meeting elects its vote-tellers itself.

The officers of the Meeting appoint the secretary, who can be chosen from outside the shareholders.

An attendance sheet is kept under the conditions provided for by law.

The deliberations of the General Meeting of Shareholders are recorded in minutes signed by the officers of the Meeting; these minutes must be included in a minute-book kept in accordance with regulatory provisions.

#### **21.2.5.2. Special provisions applicable to Ordinary General Meetings of Shareholders (article 21 of the Company's bylaws)**

The Ordinary General Meeting of Shareholders is composed of all the shareholders regardless of the number of shares they hold, on condition that all the amounts due thereon have been paid up.

In order to validly deliberate when called for the first time, the General Meeting must be composed of a number of shareholders representing at least one-fifth of the shares with voting rights.

If this condition is not met, the General Meeting of Shareholders is adjourned and called again in accordance with the forms provided for above. At this second meeting and, the deliberations made with regard to the same agenda as the previous meeting are valid regardless of the number of shares represented.

The deliberations of the Ordinary General Meeting of Shareholders are taken by a majority of the votes of the shareholders present or represented.

The Ordinary General Meeting of Shareholders can make any decisions other than those with the effect of amending the bylaws either directly or indirectly.

It is held at least once a year, within six months of the end of the Company's financial year, to approve the annual financial statements, unless this time period is extended by an order of the President of the Commercial Court deciding upon an application by the Board of Directors.

#### **21.2.5.3. Special provisions with regard to Extraordinary General Meetings of Shareholders (Article 22 of the Company's bylaws)**

Only the Extraordinary General Meeting of Shareholders is empowered to make decisions with the effect of amending the bylaws either directly or indirectly.

The Extraordinary General Meeting of Shareholders is composed of all shareholders regardless of the number of shares they hold, on condition that all the amounts due thereon have been paid up.

In order to validly deliberate when called for the first time, the General Meeting must be composed of a number of shareholders representing at least one-fourth of the shares with voting rights.

If this condition is not met, the General Meeting of Shareholders shall be adjourned and called again in accordance with the forms provided for above. At this second meeting and, where applicable, any subsequent meetings, the deliberations made with regard to the same agenda as the previous meeting are valid if the General Meeting is composed of a number of shareholders representing at least one-fifth of the shares with voting rights. If no quorum is reached, the second General Meeting may be extended until a date no more than two months later than that on which it was called.

The deliberations of the Extraordinary General Meeting of Shareholders are taken by a majority of two-thirds of the votes of the shareholders present or represented.

By way of exception, the Extraordinary General Meeting of Shareholders may decide under the quorum and majority requirements provided for Ordinary General Meetings of Shareholders when the increase in capital takes place via the capitalization of reserves, profits or share premiums.

#### **21.2.6. Mechanisms making it possible to delay, defer or prevent a change of control**

The Company's bylaws do not provide any mechanism that may delay, defer or prevent a change of control.

#### **21.2.7. Crossing of ownership thresholds (Article 10 of the Company's bylaws)**

In addition to the legal obligations of declaration of crossing of thresholds, any natural person or legal entity, acting alone or in concert, who becomes the holder, in any manner whatsoever within the meaning of Articles L. 233-7 *et seq.* of the French Commercial Code, of a fraction equal to 2% of the share capital or voting rights, or any multiple of this percentage, must inform the Company of the total number of shares and voting rights of the Company that it owns (or that it may subsequently own in accordance with the meaning of Article L. 233-7 of the French Commercial Code), before and after the transaction that led to the crossing of such threshold, and the nature of this transaction. This declaration shall be made via a registered letter with return receipt requested (or by any equivalent means for persons who are resident outside France) sent to the registered office, at the latest, prior to the close of trade on the fourth trading day following the day on which the shareholding threshold is crossed.

This obligation applies under the same conditions as those provided for in Articles L. 233-7 *et seq.* of the French Commercial Code, whenever the fraction of the capital or voting rights held falls below one of the thresholds provided for in the aforementioned articles.

In the event of non-compliance with the above provisions, a shareholder who has not duly and properly made the declaration shall be deprived of the voting rights attached to the shares exceeding the fraction that has not been duly declared for any General Meeting of Shareholders that may be held, until the expiration of the time period provided for by French law and regulations in force following the date on which the notification is duly made. This sanction will only be applied upon a request, recorded in the minutes of the General Meeting of Shareholders, of one or more shareholders holding at least three percent (3%) of the Company's capital.

**21.2.8.** Specific conditions governing changes to the share capital

In the Company's bylaws, there is no specific provision governing the change in its share capital that would be stricter than the legal provisions.

## 22. MATERIAL AGREEMENTS

Except for the agreements described below, the Company has only entered into agreements in the normal course of business.

### 22.1. Merck Serono agreement

The Company entered into a transfer and license agreement with Merck Serono on March 19, 2009, amended on July 30, 2009, June 22, 2010, May 23, 2014 and November 28, 2014 (the “MS Agreement”), as part of the spin-off of Merck Serono’s research and development activities in the cardiometabolic field. The MS Agreement was amended on July 30, 2009, to include an additional patent on the list of patents for which Merck Serono granted a license to the Company.

Pursuant to the terms of the MS Agreement, Merck Serono transferred certain patents and granted a license for other patents and know-how to the Company for research and development, and the marketing of pharmaceutical products. This license is exclusive covering a list of 25 molecules, by program, selected by the Company.

To support its research and development activities and given Merck Serono’s economic interest in the development of Poxel, Merck Serono paid the Company a total non-refundable amount of €7.2 million.

In exchange for rights that were granted under the MS Agreement, Merck Serono was entitled to the following compensation:

- a. royalties on net sales of the products covered by patents granted or awarded under license by Merck Serono at a rate equivalent to the high single-digits in the higher portion of the range for Imeglimin, and at a low single-digit rate in the lower part of the range for the other products;
- b. a percentage of the revenue from any partnership agreement relating to the drug-candidates covered by the patents, granted or awarded under license, at a low double-digit rate near the bottom of the range.

In the event of a sale of the Company, the latter was to pay Merck Serono an amount corresponding to a percentage of the sale price of the Company’s shares at a decreasing single digit-rate based on said sale price. This commitment was valued in the financial statements presented in accordance with IFRS as of December 31, 2014 and December 31, 2015.

Within the scope of the Company’s initial public offering, pursuant to the amendment to the agreement signed on May 23, 2014, Merck Serono agreed to surrender its rights in case of sale of the Company only if the initial public offering was successful and in consideration of 1,088,531 ordinary shares, representing 7.69% of the Company’s share capital on a fully diluted basis prior to the public offering.

The debt to Merck Serono ceased to exist upon completion of the Company’s initial public offering on February 6, 2015. At that date, the financial debt was reassessed at fair value on the basis of the issue price of €6.66 per share and was then reclassified as equity for a total of €7,249,000.

The expiration date of the MS Agreement must be analyzed on a country-by-country, and product-by-product basis. The MS Agreement remains in effect until the later of: (i) the final expiration date of any patent relating to products containing substances covered by patents granted or licensed to the Company by Merck Serono in the country in question; or (ii) ten years from the first sale to the general public of the products in the country concerned, following regulatory approval for said product in that country.

## 22.2. Contract with SUMITOMO DAINIPPON PHARMA

On October 30, 2017 the Company signed a license with Sumitomo Dainippon Pharma (“SDP”) for the co-development and marketing of Imeglimin, a drug-candidate for type 2 diabetes.

Under this contact, SDP has an exclusive marketing right for Japan, China, South Korea, Taiwan and nine other countries in Southeast Asia, for all human and veterinary indications, including type 2 diabetes.

The two parties will co-finance certain development activities within the limit of 1.2 M EUR for the Company. SDP will assume development costs above this limit, as well as marketing costs.

SDP made an initial payment to the Company in the amount of 4.750 billion yen (approximately 36 million euros). The contract also provides for staggered payments, subject to attainment of the clinical development objectives of Imeglimin for a maximum amount of 2.75 billion yen (approximately EUR 21 million), as well as payments subject to marketing goals for a maximum amount of 26.5 billion yen (approximately 198 million euros). The contract includes the payment of two-digit royalties to the Company, whose percentage grows according to the level of sales, on net sales made by SDP.

## 22.3. Contract with ROIVANT SCIENCES GMBH

On February 9, 2018 the Company signed an exclusive contract with Roivant Sciences GmbH (“Roivant Sciences” or “Roivant”) for development and marketing of Imeglimin, an oral drug-candidate developed by the Company for treatment of type 2 diabetes, in the United States, Europe and other countries not covered by the existing partnership in Eastern and Southeast Asia between the Company and Sumitomo Dainippon Pharma (described in Section 22.2 “Contract with Sumitomo Dainippon Pharma” of this *document de référence*). The agreement provides that prior to the marketing of Imeglimin, the parties may agree to a potential of co-promotion agreement.

The agreement includes an initial payment of \$35 million (approximately EUR 28 million) to the benefit of the Company. Payments linked to attainment of the objectives of regulatory development and sales, up to a maximum of 600 million dollars (approximately 486 million euros), are also planned. The contract includes the payment of two-digit royalties on net sales made by Roivant, the percentage of which is growing according to the level of sales.

Roivant will assume the costs of development and marketing of Imeglimin, and the Company will participate in the program for the development of up to \$25 million (approximately EUR 20 million) for two years.

In addition, Roivant has invested \$15 million (approximately EUR 12 million) in the share capital of Poxel, by subscription of 1,431,399 new ordinary shares of the company at a price of 8.50 euros per share.

## 22.4. Contract with DEUTERX

On August 29, 2018 the Company entered into a purchase contract with DeuteRx for DRX-065, a drug-candidate under clinical development for the treatment of non-alcoholic steatohepatitis (NASH), a portfolio of other potential deuterated drug-candidate for the treatment of rare and speciality metabolic diseases, and all related industrial and intellectual property rights of DeuteRx. In consideration for this acquisition the Company paid DeuteRx €6.8 bn (\$8 bn) and issued 1.29 million new ordinary shares to DeuteRx, representing 4.99% of the Company’s share capital. The Company



must also pay DeuteRx, in cash or in Company shares, as the case may be, amounts tied to attaining certain development and regulatory objectives for products under the acquired programs, in cash or in shares, from the moment of publication of the positive results of phase II; payments linked to sales targets for the products; and royalties based on net sales.

## **23. INFORMATION FROM THIRD PARTIES, STATEMENTS BY EXPERTS AND DECLARATIONS OF INTEREST**

None

## 24. DOCUMENTS AVAILABLE TO THE PUBLIC

Copies of this *document de référence* are available without charge at the Company's registered office, 259/261 Avenue Jean Jaurès – Immeuble le Sunway – 69007 Lyon.

This *document de référence* is also available at the Company's website ([www.poxel.com](http://www.poxel.com)) and the website of the AMF ([www.amf-france.org](http://www.amf-france.org)).

The Company's bylaws, the minutes of general meetings of shareholders and other corporate documents, as well as historical financial information and all expert valuations and statements issued at the Company's request that must be made available to its shareholders under applicable laws can be examined, without charge, at the Company's registered office.

From the date of listing of the Company's shares for trading on the Euronext market in, regulated information (as defined by the AMF General Regulation) will also be available on the Company's website ([www.poxel.com](http://www.poxel.com)).

## **25.INFORMATION ON SHAREHOLDINGS**

Information regarding the companies in which Poxel holds a portion of the share capital that may have a material impact on the assessment of its assets and liabilities, financial position or results is provided in Sections 7 “Organization structure” and 20 “Financial information concerning the assets, financial position and results of the Group” of this *document de référence*.

## 26.APPENDIX

### 26.1. Statutory financial statements established for the year ended December 31, 2018

#### 26.1.1. Assets

POXEL Balance sheet – assets (K€)	Notes	31/12/2018			31/12/2017
		Amount	Amort. Prov.	Carrying amount	Carrying amount
Uncalled subscribed capital					
<b>INTANGIBLE ASSETS</b>					
Startup costs					
Development costs					
Concessions, patents and similar rights	3	16 580	4	16 577	0
Goodwill					
Other intangible assets	3				
Advance payments on intangible assets					
<b>TANGIBLE FIXED ASSETS</b>					
Land					
Buildings					
Technical installations, equipment and tools	3				
Other tangible fixed assets	3	464	169	295	143
Fixed assets in progress					
Advances and payments					
<b>FINANCIAL ASSETS</b>					
Equity-accounted investees					
Other investments	3	154	154		
Receivables from equity interests					
Other equity investments					
Loans					
Other financial assets	3	579	13	566	517
<b>TOTAL FIXED ASSETS</b>		<b>17 778</b>	<b>340</b>	<b>17 438</b>	<b>661</b>
<b>INVENTORIES AND WORK IN PROCESS</b>					
Raw materials and supplies					
Goods in process					
Services in process					
Intermediate and finished products					
Goods					
Advances, prepayments/orders	4	3 061		3 061	6 435
<b>RECEIVABLES</b>					
Trade receivables and related accounts	4	17 546		17 546	8 192
Other receivables	4	5 433	437	4 996	5 316
Subscribed capital, called and unpaid					
<b>OTHER</b>					
Investment securities	5	59 445		59 445	50 019
Cash at hand	5	7 127		7 127	4 145
<b>ACCRUALS</b>					
Prepaid expenses	7	1 081		1 081	552
<b>TOTAL CURRENT ASSETS</b>		<b>93 692</b>	<b>437</b>	<b>93 255</b>	<b>74 658</b>
Exchange rate adjustments on assets		1 037		1 037	0
<b>TOTAL ASSETS</b>		<b>112 506</b>	<b>777</b>	<b>111 730</b>	<b>75 319</b>

## 26.1.2. Liabilities

POXEL			31/12/2018	31/12/2017
Balance sheet – liabilities (in €K)		Notes		
<b>SHAREHOLDERS' EQUITY</b>				
Shareholders' equity or individual equity capital	8		517	463
Share issuance, merger and contribution premiums	8		113 669	92 623
Reserves	8		16 643	16 643
Legal reserve				
Statutory or contractual reserves				
Regulated reserves (3) (of which curr. prov. res.)				
Other reserves (of which purchase of original works)				
Retained earnings	8		-81 717	-69 662
<b>INCOME FOR THE PERIOD (profit or loss)</b>	8		11 400	-12 054
Investment subsidies				
Regulated provisions				
<b>TOTAL EQUITY</b>			<b>60 513</b>	<b>28 012</b>
<b>OTHER EQUITY</b>				
Income from the issue of equity securities				
Conditional advances	11		615	803
<b>TOTAL OTHER EQUITY</b>			<b>615</b>	<b>803</b>
<b>PROVISION FOR CONTINGENCIES AND CHARGES</b>				
Provisions for contingencies	10		1 055	84
Provisions for charges				
<b>TOTAL PROVISIONS</b>			<b>1 055</b>	<b>84</b>
<b>LIABILITIES</b>				
Convertible bonds				
Other bonds				
Loans and bank borrowings	5		8	755
Loans and financial debt Other	6		13 646	
Advances and prepayments on current orders			1 257	1 317
Trade payables and related accounts	13		21 250	9 008
Tax and social security liabilities	13		1 151	937
Payables on fixed assets and related accounts				
Other liabilities	12			95
<b>ACCRUALS</b>				
Prepaid income	12		12 086	34 301
<b>TOTAL DEBTS</b>			<b>49 398</b>	<b>46 414</b>
Exchange rate adjustments on liabilities			149	6
<b>TOTAL LIABILITIES</b>			<b>111 730</b>	<b>75 319</b>

### 26.1.3. Income statement

POXEL		Notes	31/12/2018	31/12/2017
Income statement in K€				
OPERATING INCOME				
Sales of goods				
Production sold	14.1	74 599	8 579	
NET REVENUE		74 599	8 579	
Operating subsidies				
Reversals of depreciation and provisions and transferred charges	14.2	79	6	
Other income		722	13	
TOTAL OPERATING INCOME		75 401	8 598	
OPERATING EXPENSES				
Purchases of goods				
Change in inventory of goods				
Purchase of raw materials and other supplies				
Change in inventory (raw materials and supplies)				
Other purchases and external expenses	14.3	58 171	19 499	
Taxes and duties	14.3	272	100	
Salaries and wages	14.3	2 421	2 090	
Social security charges	14.3	1 164	937	
OPERATING ALLOWANCES				
Fixed asset depreciation expense	3	61	38	
Provisions on current assets				
Provisions for contingent liability	10	122	84	
Other Charges	14.3	5 773	730	
TOTAL OPERATING CHARGES		67 983	23 477	
OPERATING INCOME		7 418	-14 878	
Financial income				
Financial expenses	16	2 770	64	
	16	2 244	413	
FINANCIAL INCOME		525	-349	
CURRENT INCOME BEFORE TAX		7 943	-15 228	
Non-recurring income				
Non-recurring expenses	16	70	147	
	16	88	96	
EXTRAORDINARY INCOME		-18	51	
Employee profit-sharing				
Income taxes	17	-3 476	-3 122	
PROFIT OR LOSS FOR THE PERIOD		11 400	-12 054	

### 26.1.4. Notes to the financial statements

#### Note 1: Presentation of the business activities and major events

The following information constitutes the Appendix to the parent company financial statements and is an integral part of the summary financial statements for the fiscal years ended December 31, 2017 and December 31, 2018. Each of these fiscal years covers a period of twelve months from 1 January to 31 December.

### **1.1 General information on the Company and its business activities**

Established in March 2009 following a spin-off from Merck Serono, Poxel S.A. is a French société anonyme (public limited liability company) with its registered office at 259 Avenue Jean Jaurès, 69007 LYON, registered in the Lyon Trade and Companies Register under number 510 970 817 RCS, further to be referred to as “the Company”), with the business activity of developing innovative molecules for the treatment of metabolic diseases, of which type 2 diabetes and non-alcoholic steatohepatitis (NASH).

The Company has incurred operating losses every year, except for the financial year of its inception. Such losses result principally from internal and external research and development expenses, related in particular to conducting numerous pre-clinical and clinical trials, primarily as part of the development of Imeglimin. In October 2017, the Company signed an initial contract of strategic partnership with Sumitomo Dainippon Pharma for the development and marketing of Imeglimin, drug candidate for the treatment of type 2 diabetes in Japan, China and eleven other countries in Asia. In February 2018, the Company also signed a partnership agreement with Roivant Sciences for development and marketing of Imeglimin in the United States, Europe and other Asian countries not covered by the agreement with Sumitomo Dainippon Pharma. On August 30, 2018, the Company signed a strategic agreement with DeuteRx for the acquisition of an innovative drug candidate at the clinical development stage for the treatment of NASH, as well as other programs for the treatment of metabolic diseases.

The Company’s future development depends on a combination of several factors, including: (i) the success of its research and development operations; (ii) the continuation of partnership agreements entered into by the Company; (iii) obtaining regulatory approval and market acceptance of the future products proposed by the Company; (iv) obtaining the necessary financing; and (v) the development of competing products by other companies. Consequently, the Company was able, on the short/medium term, to finance itself through new partnerships for the development and marketing of its drug candidates and through the issuance of new equity instruments.

### **1.2 Significant events**

#### **Acquisition of assets**

On August 30, 2018, the Company announced the signing of a strategic agreement with DeuteRx for the acquisition of DRX-065, an innovative drug candidate at the clinical development stage for the treatment of NASH, as well as other programs for the treatment of metabolic diseases. The Company thus acquired the exclusive worldwide ownership of DRX-065 (R-pioglitazone stabilized by deuterium substitution), a clinical development program for the treatment of NASH. It also acquired other programs, including deuterated drug candidates for the treatment of rare and specialized metabolic diseases.

This agreement resulted in an initial payment of 6.8 M€ (8 M\$) and the issuance for the benefit of DeuteRx of 1.29 million new common shares of Poxel at the price of 6.91 € per share, representing 4.99% of the capital of Poxel.



## **Signature of a contract with Roivant Sciences GmbH**

On 9 February, 2018 we signed an exclusive contract with Roivant Sciences GmbH (“Roivant”) for development and commercialisation of Imeglimin, oral drug candidate developed by us from treatment of type 2 diabetes, in the United States, in Europe and in other countries not covered by the partnership existing in Eastern and South-Eastern Asia between us and Daiippon Pharma.

The agreement includes an initial payment of \$35 million (approximately EUR 28 million) to the benefit of the Company. Payments linked to attainment of the objectives of regulatory development and sales, up to a maximum of 600 million dollars (approximately 486 million euros), are also planned. The contract includes the payment of two-digit royalties on net sales made by Roivant, the percentage of which is growing according to the level of sales.

Roivant will assume the costs of development and marketing of Imeglimin, and the Company will participate in the program for the financing of the development of up to \$25 million (approximately EUR 20 million) for two years.

In addition, Roivant has invested \$15 million (approximately 12 million euros) in the capital of Poxel, by subscription of 1,431,399 new common shares of the Company at a price of 8.50 € per share.

## **Increases in capital**

Several capital increases took place in the 2018 financial year:

- As part of the agreement signed in February 2018, discussed above, the Company issued 1,431,399 new common shares to Roivant Sciences at a price of 8.50 € per share, representing a capital increase of 29 K€ and an issue premium of 12,138 K€.
- On May 21, 2018 an employee exercised 400 founders’ warrants, giving right to subscribe to 8,000 common shares at a price of 2.5€, representing a capital increase of 0.2 K€, together with a share premium of 20 K€.
- In August 2018, in the context of the agreement with DeuteRx (see above), the Company issued 1.29 million new ordinary shares of Poxel at the price of €6.91 per share.

Accordingly, the share capital is €517,136.84 as of December 31, 2018, divided in 25,856,827 shares of €0.02 of nominal value.

## **Establishing a subsidiary in Japan**

In March 2018, the Company established a subsidiary in Japan, (“POXEL JAPAN KK”), registered in Tokyo. This subsidiary is fully owned by POXEL SA. Its share capital is 20 million yen.

## **Note 2: Principles, rules and accounting policies**

### **2.1 Principles used for drawing up the financial statements**

The accounts for the year end have been prepared and presented in accordance with the accounting rules in the respect of the principles laid down by Articles 121-1 and 121-5 and following of the General Accounting Plan 2014. The accounting policies have been applied in compliance with the provisions of the French Commercial Code, the accounting decree of November 29, 1983 and ANC Regulation 2014-03 relative to the rewriting of the General Accounting Plan applicable to the closing of the fiscal

year. The basic method used for the assessment of the elements entered in the accounts is the method of historical costs.

The general accounting conventions have been applied, in the respect of the principle of prudence, in accordance with the following assumptions:

- Continuity of the operation;
- Permanence of accounting methods from one fiscal year to another; being specified that since 31 December, 2015, the company has opted for the preferred method of imputing costs related to the capital increases occurring during the fiscal year to the emission premium.
- Independence of the years.

The hypothesis of the continuity of operation has been chosen given the financial capacity of the Company (cash available) in the light of its financing needs of the next 12 months.

For a better understanding of the accounts presented, the main modes and methods of assessment chosen are specified below, including when:

- A choice is offered by the legislation;
- An exception provided by the legislation is used;
- The application of a accounting prescription is not sufficient to give a faithful image;
- There is an exemption from the accounting requirements.

## **2.2 Intangible assets**

Payments made for the acquisition of a product portfolio are recognized as “Other intangible assets” when they meet the definition of an intangible asset, i.e. when it is a controlled resource, from which the Company expects future economic benefits, and which is identifiable, i.e. separable or resulting from contractual or legal rights.

The first recognition criterion, relating to the probability of future economic benefits generated by the intangible asset, is deemed to be met for research and development work when they vest separately.

In this context, amounts paid to third parties in the form of initial payments or milestone payments relating to proprietary medicinal products that have not yet received marketing authorization, are recognized as assets. These rights are amortized on a linear basis over their useful life from the time the marketing authorization is obtained. Unamortized rights (before marketing authorization) are subject to impairment tests in accordance with the procedures defined in Note 2.5.

Intangible assets consist of software.

The intangible assets are evaluated at the cost of their acquisition or at the cost of their production. They are depreciated linearly over the duration of their use by the Company, or:

Elements	Depreciation periods
Licenses and software development	1 to 3 years

The expenditure related to the registration of patents are registered as a charge.

### 2.3 Tangible assets

Tangible capital assets are valued at their cost of acquisition (purchase price and direct accessory costs) or their cost of production by the Company.

The depreciation schedule of the assets is determined using actual useful life.

The depreciation periods and methods used are primarily the following:

Elements	Depreciation periods
Facilities and fixtures	5 to 10 years - Linear
Computer hardware	1 to 3 years - Linear
Furniture	5 years - Linear

### 2.4 Financial assets

The financial assets are mainly:

- Equity interests in the Japanese subsidiary created in 2018;
- Guarantee deposits paid in the framework of contracts of simple rental contracts of French premises;
- The liquidity agreement (cash part and "own shares" part).

### 2.5 Recoverable value of fixed assets

The assets having an indefinite useful life are not amortized and are subject to an annual test of depreciation. The depreciated assets are subject to an impairment test whenever there is an internal or external index showing that an asset could have lost its value.

The impairment test consists of comparing the net book value of the tested asset to its recoverable amount. The test is performed per asset group.

An impairment is recognized up to a maximum of the excess of the carrying value on the recoverable value of the asset. The recoverable value of an asset corresponds to its fair value minus costs of assignment or its useful value, if the latter is higher.

Impairment tests are performed at the closing date of the financial year for unamortized assets (whether or not there is an indication of impairment), based on forecast cash flows determined by management, according to the base of revisions of development costs, sales and cost of sales over the term of patent protection.

The fair value minus the disposal costs is the amount, which can be obtained from the sale of an asset during a transaction in conditions of normal competition between well informed and willing parties.

The value in use is the present value of estimated future cash flows expected to arise from the continued use of an asset and from its disposal at the end of its useful life. The value in use is determined on the basis of estimated cash flows based on the development plan for the assets and the resulting expected sales, and are discounted using long-term after-tax market rates that reflect market estimates of the time value of money and the specific risks of the assets. The terminal value is determined from the infinity update of the last cash flows of the test.

As of December 31, 2018:

- The Company has no intangible assets with an indefinite life. However, as explained in Note 3, the Company has a recognized product portfolio, which will be amortized as soon as the marketing authorization is obtained, and which has no indication of impairments.
- No non-current asset present an internal or external index of loss of value.

## **2.6 Claims and accounts of regularization**

Receivables are measured at nominal value. An impairment is recognised, where applicable, on a case-by-case basis through a provision to take into account collection difficulties which are likely to occur.

Other receivables include the nominal value of the Research Tax Credit which is recognised as a receivable for the period corresponding to the fiscal year in which the eligible expenses that gave rise to the tax credit were incurred.

The accounts of active regularization correspond to the expenses recognized in advance. They relate to the costs incurred in the current activity of the Company.

## **2.7 Securities**

The securities are listed in the assets for their acquisition value.

The provisions for possible depreciation are determined by comparison between the acquisition value and the likely disposal value.

## **2.8 Foreign currency operations**

The charges and products in foreign currencies are recorded for their counter-value at the date of the operation.

The debts and liabilities in foreign currencies existing at the end of the financial year are converted during in force at this date.

The difference resulting from the conversion of debts and claims in foreign currency to this last course is included in the balance sheet in the positions of "conversion differences" of assets and liabilities. The conversion differences are the subject of a provision for risks and charges by an equivalent amount, where appropriate.

## **2.9 Provisions for Risks and Charges**

These provisions, registered in compliance with the CRC Regulation No. 2000-06, are the intended to cover the risks and charge that current events or developments make probable, whose amount is quantifiable as to their object, but whose achievement, the maturity or the amount are uncertain.

## **2.10 Retirement benefits**

The amounts of the future payments corresponding to the benefits granted to employees are assessed according to an actuarial method, taking the assumptions regarding the evolution of wages, the age of retirement and mortality. These assessments are then recognized at their present value.

These commitments are not the subject of provision but are included in the off-balance sheet commitments.

See Note 19.1.

## **2.11 Borrowings**

The borrowings are valued at their nominal value. The costs of issuance are immediately supported.

The accruals are recorded on the liabilities side, at the rate of interest provided for in the contract.

## **2.12 Public subsidies to be received**

### **Conditional advances**

The advances received from public agencies for the financing of the research activities of the company or for the territorial commercial prospecting, whose refunds are conditional, are presented on the liability side under the heading "other own funds" and their characteristics are detailed in note 10.

In the event of declared failure, abandoning of granted credit is recognised as a subsidy.

### **Subsidies**

Subsidies received are recognised in the financial statements as soon as the corresponding receivable becomes certain, in the light of the conditions required for granting the subsidy.

Operating subsidies are recognised in the financial statements as current income, taking into consideration, where applicable, the pace of corresponding expenditures in order to comply with the concept of matching revenues and expenses.

### **Research tax credit**

The Research Tax Credit (Crédit d'Impôt Recherche) is granted to companies by the French government to promote technical and scientific research. The companies which justify of expenditure fulfilling the required criteria (expenditure on research from licensed companies, located in France or, since 1 January, 2005 within the European Community or in another State that is a party to the Agreement on the European Economic Area and having concluded a tax convention with France, containing a clause of administrative assistance) benefit from a tax credit, which can be used for the payment of corporate income tax due for of achievement of the expenditure and the following three fiscal years or, where appropriate, be reimbursed for its share in surplus.

The research tax credit is presented in the income statement to the credit of the line "taxes on profits".

The Company has received the Research Tax Credit since its incorporation.

### **2.13 Revenue**

The revenue corresponds to the fair value of the consideration received or to be received for goods and services sold in the context of the Company's activities. It is presented net of value added tax, returns of merchandise, rebates and reductions.

In the Company's ordinary activities, it may enter into partnership agreements with pharmaceutical groups. The compensation received in relation to these agreements is generally based on:

- payment of a premium upon signing (i.e., upfront fees);
- payments for specific developments on the achievement of technical milestones;
- payment for research and development efforts;
- Income from future sale of products.

When the agreement provides that the Company still has obligations to render within the scope of the partnership, non-refundable advances are deferred and recognized as revenue staggered over the period of the collaboration agreement.

The milestone payments represent amounts received from partners under these cooperation agreements. Their perception depends on the achievement of certain development, regulatory or commercial objectives. The milestone payments are recorded in the result when the generator fact occurs and that there no conditions precedent to their payment. The generator facts can be stages of development, or even the regulatory steps or the marketing of products derived from development work conducted in the framework of the agreement.

### **2.14 Industry information**

The Company operates in one single segment: the development of innovative molecules for the treatment of metabolic diseases, in particular diabetes type 2 diabetes and non-alcoholic steatohepatitis (NASH).

### **2.15 Research and development expenses**

Research and development costs are systematically expensed.

The amount of research costs incurred in the financial year 2018 is approximately 51 M€.

### **2.16 Financial income (expense)**

The financial income (expense) corresponds mainly to loan interest, VMP products and term accounts and exchange losses and gains.

## 2.17 Non-recurring income

The costs and income outside of ordinary activities of the Company constitute the exceptional income.

## 2.18 Earnings per share

Basic loss per share is calculated by dividing income attributable to equity holders of the Company by the weighted average number of outstanding ordinary shares for the period.

Diluted loss per share is measured by adjusting the income attributable to the holders of ordinary shares and the weighted average number of outstanding ordinary shares for the effects all the dilutive potential ordinary shares.

If, in the calculation of diluted loss per share, instruments giving deferred rights to capital such as stock options or warrants (BSAs, warrants, BSP, free shares) do not generate an antidilutive effect, these instruments are not taken into account.

## Note 3: Intangible, tangible and financial assets

GROSS VALUES OF FIXED ASSETS (Amounts in K€)	31/12/2017	Acquisitions	Disposals	Reclassification	31/12/2018
Start-up costs and development expenses					
Other intangible fixed assets line items	2	16 578			16 580
<b>Total intangible assets</b>	<b>2</b>	<b>16 578</b>	<b>0</b>	<b>0</b>	<b>16 580</b>
Machinery and equipment					0
General installations, fixtures and fittings	111	128			239
Transportation equipment	0				0
IT and office equipment and furniture	143	83			226
Tangible fixed assets in progress	0				0
<b>Total tangible fixed assets</b>	<b>254</b>	<b>210</b>	<b>0</b>	<b>0</b>	<b>464</b>
Treasury shares	163	154			317
Liquidity Agreement deposit	130				130
Other financial assets	227	112	52		287
<b>Total financial assets</b>	<b>519</b>	<b>266</b>	<b>52</b>	<b>0</b>	<b>733</b>
<b>GRAND TOTAL</b>	<b>775</b>	<b>17 054</b>	<b>52</b>	<b>0</b>	<b>17 778</b>

AMORTIZATION, DEPRECIATION AND IMPAIRMENT OF FIXED ASSETS (Amount in K€)	31/12/2017	Allocations	Reversals	Reclassification	31/12/2018	Net values 12/31/2018
Start-up costs and development expenses						
Other intangible fixed assets line items	2	2			4	16 577
<b>Total intangible assets</b>	<b>2</b>	<b>2</b>	<b>0</b>	<b>0</b>	<b>4</b>	<b>16 577</b>
Machinery and equipment	0				0	0
General installations, fixtures and fittings	27	20			47	192
Transportation equipment	0				0	0
IT and office equipment and furniture	84	39			122	103
Tangible fixed assets in progress	0				0	0
<b>Total tangible fixed assets</b>	<b>111</b>	<b>59</b>	<b>0</b>	<b>0</b>	<b>169</b>	<b>295</b>
Treasury shares	0				0	317
Equity interests	0	154			154	-24
Other financial assets	2	13	2		13	274
<b>Total financial assets</b>	<b>2</b>	<b>167</b>	<b>2</b>	<b>0</b>	<b>167</b>	<b>566</b>
<b>GRAND TOTAL</b>	<b>114</b>	<b>227</b>	<b>2</b>	<b>0</b>	<b>340</b>	<b>17 438</b>

In 2018, under the contract signed with DeuteRx (see Note 1.2), the Company acquired an innovative drug candidate under clinical development for the treatment of NASH (DRX-065), as well as other programs for the treatment of metabolic diseases for 15,780 K€, of which 8,914 K€ was paid in shares and \$8 million (6,866 K€) in cash. This acquisition is recognized for an amount of 16,572 K€, which includes 791 K€ in acquisition costs.

The implementation of the depreciation tests described in note 2.5 revealed no depreciation on the presented financial years. In the context of the sensibility tests, the Company has not identified any variation of the key assumptions likely to lead to a depreciation, the actualized value of the flows related to the activated project being very superior to the book value of the assets related to the project. The principal retained assumptions are:

- Discount rate : 11 %
- Projected cash flow of 15 years.

Because of the risks and uncertainties related to the process of research and development, the six criteria of capital property are not deemed to be met for any of development projects in progress. Consequently, all costs incurred by the company are recognised as an expense.

The Company does not hold any financial lease contracts.

#### Note 4: Credits

The tables below detail the components of the "Receivables" items at December 31, 2018 as well as their breakdown up to or more than one year:

Receivables (17,545 K€) correspond to 17,500 K€ to the chargeback to Sumitomo Dainippon Pharma of research expenses incurred under the Imeglimin phase 3 TIMES program in Japan. The amount of these receivables is recognized as and when the program costs advance.

In the absence of a taxable result, and of corporate taxes at least equal to the amount of the debt to the State relating to the research tax credit ("CIR"), the amount not imputed to the IS debt is refundable in the year following the year of its finding, when the Company has the status of SMES in the European sense.

VAT receivables primarily relate to input VAT as well as to the requested refund of VAT.



The advances and payments on account correspond mainly to the royalties paid to Merck Serono following the signature of the contract of partnership with Sumitomo Dainippon Pharma (see Note 19.5). Its accounting treatment follows that of patent lease contracts. As well, recognition as operating charge is being done according to the recognised revenue. This line item also includes advances and deposits paid to suppliers performing research and development services.

Other tax receivables correspond to a payment of 382 by the Company following a tax notification contested by the Company. The analysis carried out by the Company makes it possible to consider its right to recover the paid sums as reasonable. As a result, no provision is recognized in this respect.

STATEMENT OF RECEIVABLES (Amounts in K€)	31/12/2018		
	Gross amount	One year maximum	Due in more than one year
<b>Fixed assets</b>			
Other financial assets	579		579
<b>Total fixed assets</b>	<b>579</b>	<b>0</b>	<b>579</b>
<b>Current assets</b>			
Trade receivables	17 546	17 546	
Employees and related accounts			
Statement - Research Tax Credit	3 552	3 552	
Value added tax	931	931	
Advances and payments	3 061	3 061	
Subsidies receivable	0	0	
Accrued holdings	81	81	
Other receivables	870	870	
<b>Total current assets</b>	<b>26 039</b>	<b>26 039</b>	<b>0</b>
Prepaid expenses	1 081	1 081	
<b>Grand total</b>	<b>27 700</b>	<b>27 120</b>	<b>579</b>

## Note 5: Securities and cash flow

The cash accounts include term accounts.

The table below shows the detail of the securities and the net cash flow:

INVESTMENT SECURITIES AND NET CASH (Amounts in euros)	31/12/2018		31/12/2017	
	Carrying value	Market value	Carrying value	Market value
Money-market SICAVs	0	0	0	108
Term accounts	59 445		50 019	
Cash in bank and cash at hand	7 127		4 145	
Bank facilities	0		-751	
<b>Total investment securities and Net cash</b>	<b>66 571</b>		<b>53 412</b>	

## Note 6: Loans and various financial liabilities

As regards the Roivant Sciences' contract, the Company received an initial payment of \$35 million and has also committed to contribute \$25 million to the financing of the development of Imeglimin in the United States and Europe. The portion of the initial payment that is counterpart to the obligation to participate in the cofinancing of Roivant's development program has been treated as a debt. The remaining balance to be paid at the closure, amounting to 13,646 thousand euros, is fully classified as current financial debts.

This agreement provides that, until the Company has fully paid its obligation to participate in the financing of Roivant's development plan, and in the event that the Company's immediately available cash, less expected disbursements within 30 days, is less than 3 times the amount of such residual obligation, for at least 10 consecutive days, then, the Company would be required to establish an irrevocable letter of credit with a leading bank for the benefit of Roivant, for the residual amount of such obligation calculated on such date. Roivant may return this letter of credit for collection if the Company defaults in the repayment of its obligation, or in the event of termination of the contract at Roivant's initiative and under certain conditions. If the Company is unable to obtain a letter of credit, or if it is cancelled, then, the amounts due to Roivant by the Company on that date will be immediately payable.

At the closure date, the Company is in compliance with the terms of the contract on the basis of its available cash balances amounting to 66,571 thousand euros.

## Note 7: Prepaid expenses

The amount of the prepaid expenses by nature is broken down as follows:

<b>PREPAID EXPENSES (Amounts in K€)</b>	<b>31/12/2018</b>	<b>31/12/2017</b>
Real estate leases	66	40
Insurance	258	89
Fees, subscriptions	55	35
Studies	606	220
Travel expenses	92	45
Other	4	123
<b>Total prepaid expenses</b>	<b>1 081</b>	<b>552</b>

## Note 8: Shareholders' equity

### Note 8.1: Changes in Equity

The variation of the equity of analysis as follows:

POXEL Change in equity Amounts in K€	Capital Number of shares	Capital	Share premiums	Reserves	Retained earnings	Income	Shareholders' equity
<b>At December 31, 2016</b>	<b>22 950 228</b>	<b>459</b>	<b>92 057</b>	<b>16 643</b>	<b>-46 775</b>	<b>-22 888</b>	<b>39 497</b>
Appropriation of 2016 income					-22 888	22 888	0
2017 net income						-12 054	-12 054
Dividends							0
Share issue	177 200	4	542				546
Share issue costs							0
Issue of warrants			24				24
Other							0
<b>At December 31, 2017</b>	<b>23 127 428</b>	<b>463</b>	<b>92 623</b>	<b>16 643</b>	<b>-69 662</b>	<b>-12 054</b>	<b>28 012</b>
Appropriation of 2017 income					-12 054	12 054	0
2018 net income						11 400	11 400
Dividends							0
Share issue	2 729 399	55	21 046				21 101
Share issue costs			-41				-41
Issue of warrants			41				41
Other							0
<b>At December 31, 2018</b>	<b>25 856 827</b>	<b>517</b>	<b>113 669</b>	<b>16 643</b>	<b>-81 717</b>	<b>11 400</b>	<b>60 513</b>

## Note 8.2: Composition of the share capital and detail by categories of shares

The capital at December 31, 2018 was 517,136,84€, divided into 25,856,827 common shares of 0.02 € nominal value each, fully paid, after taking into account the various capital increases occurred in 2018, shown in Note 1.2 (creating 2,729,399 shares).

COMPOSITION OF SHARE CAPITAL	31/12/2018	31/12/2017	31/12/2016
Capital (in euros)	517 137	462 549	459 005
Number of shares	25 856 827	23 127 428	22 950 228
Nominal value (in €)	0,02 €	0,02 €	0,02 €

## Note 8.3: History of the share capital

Date	Nature of operations	Capital movements in €	Share premium in €***	Number of shares created	Number of shares constituting the capital	Nominal value in €	Share capital in €
<b>At December 31, 2016</b>		<b>459 005</b>	<b>112 993 977</b>	<b>3 467 834</b>	<b>22 950 228</b>	<b>0,02</b>	<b>459 005</b>
<b>January 2017</b>	Exercise of employee founder's warrant	880	109 120	44 000	22 994 228		459 885
<b>May 2017</b>	Exercise of employee founder's warrant	800	127 200	40 000	23 034 228		460 685
<b>June 2017</b>	Subscription of warrants/founder's warrant				23 034 228		460 685
<b>Oct 2017</b>	Exercise of warrants	1 800	298 215	90 000	23 124 228		462 485
<b>Nov 2017</b>	Exercise of employee founder's warrant	64	7 936	3 200	23 127 428		462 549
<b>At December 31, 2017</b>		<b>462 549</b>	<b>113 536 448</b>	<b>177 200</b>	<b>23 127 428</b>	<b>0,02</b>	<b>462 549</b>
<b>February 2018</b>	Roivant capital increase	28 628	12 138 264	1 431 399	24 558 827		491 177
<b>May 2018</b>	Exercise of employee founder's warrant	160	19 840	8 000	24 566 827		491 337
<b>August 2018</b>	DeuteRx capital increase	25 800	8 888 100	1 290 000	25 856 827		517 137
	Subscription of warrants/founder's warrant		40 575		25 856 827		517 137
<b>At December 31, 2018</b>		<b>517 137</b>	<b>134 623 227</b>	<b>2 729 399</b>	<b>25 856 827</b>	<b>0,02</b>	<b>517 137</b>

(\*) Issuance premium has been allocated to a specific unavailable reserve account

(\*\*) the share capital fees assigned to the issuance premium are not presented in this table.

#### Note 8.4: Distribution of dividends

The Company has made no distribution of dividends during the financial years ended December 31, 2017 and 2018.

#### Note 9: The equity instruments

##### Note 9.1: Share subscription warrants

Date of allotment	Type	Number of warrants issued	Number of lapsed stock options	Number of outstanding stock options	Maximum of shares to be issued*	Exercise price in €*	Duration of exercise
Board Meeting of July 5, 2010	Warrants for directors	4 500	0	0	0	3,33 €	10 years
<b>At December 31, 2010</b>		<b>4 500</b>	<b>0</b>	<b>0</b>	<b>0</b>		
<b>At December 31, 2011</b>		<b>4 500</b>	<b>0</b>	<b>0</b>	<b>0</b>		
<b>At December 31, 2012</b>		<b>4 500</b>	<b>0</b>	<b>0</b>	<b>0</b>		
Board Meeting of February 20, 2013	Warrants 10/31/2012	2 500	0	2 500	50 000	4,00 €	10 years
<b>At December 31, 2013</b>		<b>7 000</b>	<b>0</b>	<b>2 500</b>	<b>50 000</b>		
Board Meeting of March 12, 2014	Warrants 10/31/2012	2 500	0	2 500	50 000	4,00 €	10 years
<b>At December 31, 2014</b>		<b>9 500</b>	<b>0</b>	<b>5 000</b>	<b>100 000</b>		
Board Meeting of January 8, 2015	Warrants 07-25-2014	42 500	0	42 500	42 500	4,00 €	10 years
Board Meeting of April 29, 2015	Warrants 06-16-2015	42 500	0	42 500	42 500	9,37 €	10 years
Board Meeting of May 7, 2015	Warrants 06-16-2015	240 000	0	240 000	240 000	9,62 €	10 years
<b>At December 31, 2015</b>		<b>334 500</b>	<b>0</b>	<b>330 000</b>	<b>425 000</b>		
Board Meeting of January 29, 2016	Warrants 01-29-2016	42 500	0	42 500	42 500	9,05 €	10 years
Board Meeting of January 29, 2016	Warrants 01-29-2016	42 500	0	42 500	42 500	9,05 €	10 years
Board Meeting of March 31, 2016	Warrants 01-29-2016	42 500	0	42 500	42 500	9,26 €	10 years
<b>At December 31, 2016</b>		<b>462 000</b>	<b>0</b>	<b>457 500</b>	<b>552 500</b>		
Board Meeting of January 27, 2017	Warrants 01-27-2017	62 500	0	62 500	62 500	7,17 €	10 years
Board Meeting of June 30, 2017	Warrants 06-30-2017	25 000	0	25 000	25 000	6,90 €	10 years
<b>At December 31, 2017</b>		<b>549 500</b>	<b>0</b>	<b>545 000</b>	<b>640 000</b>		
Board Meeting of January 25, 2018	Warrants 2018	90 000	0	0	90 000	6,60 €	10 years
<b>At December 31, 2018</b>		<b>639 500</b>	<b>0</b>	<b>635 000</b>	<b>730 000</b>		

\* After splitting of stock by 20

##### Note 9.2: Founders' warrants

Date of allotment	Type	Number of warrants issued	Number of options lapsed/exercised	Number of outstanding stock options	Maximum of shares to be issued*	Exercise price in €*	Duration of exercise
Board Meeting of June 20, 2010	BCE 06-10-2010-1	5 000	3 310	1 690	33 800	2,50 €	10 years
Board Meeting of December 17, 2010	BCE 06-10-2010-2	3 000	3 000	0	0	2,50 €	10 years
<b>At December 31, 2010</b>		<b>8 000</b>	<b>6 310</b>	<b>1 690</b>	<b>33 800</b>		
Board Meeting of September 20, 2011	BCE 06-10-2010-2	1 500	0	1 500	30 000	2,50 €	10 years
<b>At December 31, 2011</b>		<b>9 500</b>	<b>6 310</b>	<b>3 190</b>	<b>63 800</b>		
<b>At December 31, 2012</b>		<b>9 500</b>	<b>6 310</b>	<b>3 190</b>	<b>63 800</b>		
<b>At December 31, 2013</b>		<b>9 500</b>	<b>6 310</b>	<b>3 190</b>	<b>63 800</b>		
Board Meeting of March 12, 2014	BCE 10-31-2012	5 000	2 300	2 700	54 000	3,20 €	10 years
<b>At December 31, 2014</b>		<b>14 500</b>	<b>8 610</b>	<b>5 890</b>	<b>117 800</b>		
<b>At December 31, 2015</b>		<b>14 500</b>	<b>8 610</b>	<b>5 890</b>	<b>117 800</b>		
Board Meeting of July 29, 2016	BSPCE 07-29-2016	45 000	45 000	0	0	8,45 €	10 years
<b>At December 31, 2016</b>		<b>59 500</b>	<b>53 610</b>	<b>5 890</b>	<b>117 800</b>		
Board Meeting of March 31, 2017	BSPCE 03-31-2017	100 000	0	100 000	100 000	5,91 €	10 years
Board Meeting of June 30, 2017	BSPCE 2017-2	177 500	15 000	162 500	162 500	7,26 €	10 years
Board Meeting of September 21, 2017	BSPCE 2017-3	15 000	0	15 000	15 000	6,01 €	10 years
<b>At December 31, 2017</b>		<b>352 000</b>	<b>68 610</b>	<b>283 390</b>	<b>395 300</b>		
							10 years
<b>At December 31, 2018</b>		<b>352 000</b>	<b>68 610</b>	<b>283 390</b>	<b>395 300</b>		

\* After splitting of stock by 20

### Note 9.3: Stock-options

Date of allotment	Type	Number of warrants issued	Number of lapsed stock options	Number of outstanding stock options	Maximum number of shares to be issued	Exercise price in €	Duration of exercise
Board Meeting of March 31, 2016	Stock options	80 000	0	80 000	80 000	12,55 €	10 years
Board Meeting of November 23, 2016	Stock options	150 000	0	150 000	150 000	6,47 €	10 years
<b>At December 31, 2016</b>		<b>230 000</b>	<b>0</b>	<b>230 000</b>	<b>230 000</b>		
Board Meeting of January 27, 2017	Stock options	12 500	0	12 500	12 500	6,76 €	10 years
Board Meeting of January 27, 2017	Stock options	185 000	0	185 000	185 000	6,76 €	10 years
Board Meeting of June 30, 2017	Stock options	97 500	5 000	92 500	92 500	6,61 €	10 years
<b>At December 31, 2017</b>		<b>525 000</b>	<b>5 000</b>	<b>520 000</b>	<b>520 000</b>		
Board Meeting of January 25, 2018	Stock options	215 000	7 500	207 500	207 500	6,79 €	10 years
Board Meeting of September 27, 2018	Stock options	130 000	0	130 000	130 000	6,82 €	10 years
<b>At December 31, 2018</b>		<b>870 000</b>	<b>12 500</b>	<b>857 500</b>	<b>857 500</b>		

### Note 9.4: Free shares

Date of allotment	Type	Number of free shares issued	Number of free shares lapsed	Number of free shares vested	Number of free shares outstanding	Maximum number of shares to be issued	Exercise price	Duration of exercise
<b>At December 31, 2017</b>		<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>			
Board Meeting of January : Free shares		126 500	5 750	0	120 750	120 750	N/A	N/A

### Note 9.5: Equity instruments granted to executives

Warrants, BSPCE and SO						
Name of the beneficiary	Nature of the instrument	Free shares, Warrants, SO issued allocated and subscribed	Free shares, Warrants, SO allocated and which can be subscribed	Free shares, Warrants, SO exercable at the closure (lapse of time)	Free shares, Warrants, SO exercable at the closure with conditions	Decision to issue the warrants, Free shares, SO
Thomas Kuhn	Actions gratuite	33300	22200	11100	0	25-janv-18
Pierre Legault	SO	30000	30000	0	0	25-janv-18
Pierre Legault	SO	12500	0	12500	0	27-janv-17
Thomas Kuhn	BSPCE	50000	33333	16667	0	30-juin-17
Pierre Legault	BSA	42500	14167	28333	0	29-janv-16
Pierre Legault	BSA	42500	14167	28333	0	31-mars-16
Pierre Legault	SO	150000	50000	100000	0	23-nov-16
Thierry Hercend	BSA	1875	0	1875	0	12-mars-14
Thierry Hercend	BSA	1000	0	1000	0	20-févr-13
Thierry Hercend	BSA	4500	0	4500	0	05-juil-10
Thierry Hercend	BSA	1875	0	1875	0	12-mars-14
Thierry Hercend	BSA	1000	0	1000	0	20-févr-13
Thierry Hercend	BSA	4500	0	4500	0	05-juil-10
Thierry Hercend	BSA	1000	0	1000	0	20-févr-13
Thierry Hercend	BSA	4500	0	4500	0	05-juil-10
Thierry Hercend	BSA	4500	0	4500	0	05-juil-10
Thierry Hercend	BSA	4500	0	4500	0	05-juil-10

## Note 10: Provisions for risks and charges and provisions for depreciation

### Litigation and liabilities

The Company may be involved in judicial, administrative or regulatory procedures in the normal course of its activity. A provision is recorded by the Company as soon as there is a sufficient likelihood that such disputes will entail costs for the Company.

In 2017, the Company established a provision of 83 K€ for social and tax risks. In 2018 this provision was reversed to the amount of 65 K€, corresponding to a tax administration adjustment not contested by the Company.

In addition, at December 31, 2018 the Company recognized a provision for exchange losses of 1,037 K€.

### Note 11: Conditional advances

The other own funds are composed of repayable advances granted by public bodies (Bpifrance Financement) as well as the subsidies which the definitive allocation was conditioned.

The table below shows the composition and the evolution of the other own funds:

CHANGE IN REPAYABLE ADVANCES (Amount in K€)	Repayable advances		Total
	PXL770	Imeglimin (New Formulation)	
<b>At December 31, 2016</b>	<b>118</b>	<b>826</b>	<b>944</b>
(+) Collection of funds			0
(-) Refund of expenses	-73	-69	-142
(+/-) Other movements			0
<b>At December 31, 2017</b>	<b>45</b>	<b>757</b>	<b>803</b>
(+) Collection of funds			0
(-) Refund of expenses	-45	-143	-188
(+/-) Other movements			0
<b>At December 31, 2018</b>	<b>0</b>	<b>615</b>	<b>615</b>

#### **Repayable advance from Bpifrance Financement / ERDF - PXL770**

On August 31, 2011, the Company obtained a repayable, interest-free grant from Bpifrance Financement as part of the European Regional Development Fund, or ERDF fund, for a maximum amount of 250 K€ in the context of the “development and selection of a new AMPK activator drug for the treatment of diabetes.”

Following the technical success of the project, the repayment of this innovation assistance was made according to a schedule that began in 2013 and was completed in the 2018 financial year.

#### **Repayable advance from Bpifrance Financement Innovation - Imeglimin (New Formulation)**

In October 2011, the Company obtained 950 K€ as a repayable, interest-free innovation support grant from Bpifrance Financement for the “development of a new formulation of Imeglimin for the treatment of diabetes”.

Payments from Bpifrance Financement were made in instalments between the signature date of the contract and the end of the project, the main stages of which were as follows:

- first installment of 700 K€ on January 16, 2012;
- the balance, limited to €150 K on September 2, 2016.

Following the technical success of the project, the repayment of this innovation subsidy began in 2013 and continues as follows:

- €12 K for the last two quarters of 2016;
- €12 K for the first two quarters of 2017 and €22,500 for the next two quarters;
- €22 K for the first two quarters of 2018 and €48,750 for the next two quarters;
- €49 K for the first two quarters of 2019 and €71,250 for the next two quarters;
- €71 K for the first two quarters of 2020 and €83,000 for the next two quarters;
- the balance in 2021.

## Note 12: Due dates of debts and other own funds at the closing date

STATEMENT OF DEBTS (Amounts in K€)	31/12/2018			
	Gross amount	One year maximum	1 - 5 years	More than five years
<b>Conditional advances (other equity)</b>	<b>615</b>	<b>240</b>	<b>375</b>	
<b>Financial liabilities</b>				
Other borrowings and financial debts	13 646	13 646		
Loans and bank borrowings	8	8		
<b>Total financial liabilities</b>	<b>13 654</b>	<b>13 654</b>	<b>0</b>	<b>0</b>
<b>Operating payables</b>				
Trade payables and related accounts	21 250	21 250		
Employees and related accounts	138	138		
Social security and other social bodies	1 008	1 008		
VAT, other taxes, duties and similar payments	5	5		
Group and associates	0	0		
Prepaid income	12 086	11 388	698	
<b>Total operating payables</b>	<b>34 486</b>	<b>33 788</b>	<b>698</b>	<b>0</b>
<b>Grand total</b>	<b>48 756</b>	<b>47 683</b>	<b>1 073</b>	<b>0</b>

The company did not use trade instruments to pay its suppliers.

Prepaid income been recorded in the framework of the contract concluded with Sumitomo Dainippon Pharma.

Deferred income relates to the initial payment received under the Sumitomo Dainippon Pharma contract, which is recognized as an advance on the costs of the TIMES Phase 3 program for Imeglimin in Japan (see Note 17).

Under the Roivant Sciences contract, the Company is committed to contributing to the financing of the development of Imeglimin in the United States and in Europe for 25 million dollar. This commitment is recognized under current financial liabilities (see Note 6).

## Note 13: Details of expenses to pay

The charges to pay are broken down as follows:



<b>BREAKDOWN OF ACCRUED EXPENSES</b> <b>(Amounts in K€)</b>	<b>31/12/2018</b>	<b>31/12/2017</b>
<b>Financial liabilities</b>		
Accrued interest		
<b>Trade payables and related accounts</b>		
Accrued supplier liabilities	12 091	5 758
<b>Total trade payables and related accounts</b>	<b>12 091</b>	<b>5 758</b>
<b>Tax and social security liabilities</b>		
Personnel - provision for paid leave	138	108
Personnel accrued expenses	372	356
Social security charges payable	186	181
State - accrued liabilities	245	37
<b>Total tax and social security liabilities</b>	<b>941</b>	<b>683</b>
Other liabilities	0	95
<b>Total other liabilities</b>	<b>0</b>	<b>95</b>
<b>Grand total</b>	<b>13 032</b>	<b>6 536</b>

## **Note 14: Result of operation**

### **14.1: Turnover**

<b>REVENUE AND INCOME FROM OPERATIONS</b> <b>(Amounts in K€)</b>	<b>31/12/2018</b>	<b>31/12/2017</b>
<b>Revenue</b>	<b>74 599</b>	<b>8 579</b>
Sumitomo Contract	66 088	8 579
Roivant Contract	8 192	
Management fees	318	
Enyo contract	0	0

In 2018, revenue reflected the contract signed with Sumitomo Dainippon Pharma in October 2017 and the contract signed with Roivant Sciences GmbH in February 2018 (see Significant events in the financial year).

At December 31, 2017, the recognized turnover is linked to the Sumitomo contract.

### **Accounting treatment of the Roivant Sciences GmbH contract:**

On February 9, 2018 the Company signed an exclusive contract with Roivant Sciences GmbH ("Roivant") for the development and marketing of Imeglimin, an oral drug candidate developed by the Company for treatment of type 2 diabetes, in the United States, in Europe and in other countries not covered by the existing partnership in Eastern and South-Eastern Asia between the Company and Dainippon Pharma (see Note 4.1).

This contract is analyzed as the assignment to Roivant of an exclusive license for Imeglimin.

The contract price on the transaction date was valued at \$10 million. This price is made up of a non-refundable fixed payment of \$35 million, less \$25 million granted by the Company in the form of a firm commitment to take part in financing Roivant's development program.

This amount was therefore recognized in full at the date of signing the contract, as its payment is certain and the Company has fulfilled its obligations at that date.

The portion of the initial payment that is counterpart to the obligation to participate in the financing of Roivant's development program has been treated as a debt. The remaining balance to be paid at the closure, amounting to 13,646 k€, is fully classified as current financial debts (see Note 6).

The license agreement also provides for payments for development, regulatory and marketing milestones. Their payment is not probable at December 31, 2018. They are therefore not recognized on that date.

#### **Accounting treatment of the Sumitomo contract:**

In October 2017, the Company signed a partnership agreement with Sumitomo Dainippon Pharma (see note 1.2), under the terms of which the two companies will jointly develop Imeglimin for the treatment of type 2 diabetes in Japan. Sumitomo Dainippon Pharma will finance the external costs of phase 3 and commercialisation costs.

This Contract provides:

- That the Company receive an initial payment of €36,031 K, which pays for the license and the exclusive rights granted to Sumitomo Dainippon Pharma as well as the co-development;
- That the Company receive the reimbursement of costs of external development engaged in the framework of the Phase 3 and under the conditions laid down in the contract.

The company is engaged to carry out work in the context of co-development with Sumitomo Dainippon Pharma, so the product generated by the initial payment is not acquired during the year and its recognition is deferred over the expected duration of the contract

The recognition of this income is for the advancement of direct costs, on the basis of the estimate of the direct costs expected on the duration of the contract, a method that best represents the progress of the work. The Company expects to achieve a positive margin on this contract. In the opposite case, a loss would have been found upon termination.

Therefore:

- The initial payment is counted in turnover and is spread over the duration of the planned development to the contract (3 years), on the basis of the progress of the direct costs incurred on the program.
- Charge-backs are recorded in revenue, up to the amount of the costs incurred, over the same period as that of the cost commitment.

For the 2017 and 2018 financial years, revenue relating to this contract are 8,579 K€ and 66,088 K€, respectively, of which:

- 1,729 K€ and 22,215 K€ under the averaging of initial payment received by the Company, the balance of 34,302 K€ in 2017 and 12,086 K€ in 2018 being recognized in deferred income;
  - 6,848 K€ and 43,872 K€ as charge-backs to Sumitomo Dainippon Pharma for development costs of phase 3 of Imeglimin in Japan and invoices submitted to that extent.

This contract also provides for payments relating to the achievement of the objectives of development and sales. Since no milestones had been reached at the reporting date, no income was recognized at December 31, 2018.

#### 14.2: Transfer of charges

Transfers of charges constitute benefits in kind.

<b>TRANSFERT DE CHARGES (Montants en K€)</b>	<b>31/12/2018</b>	<b>31/12/2017</b>
Avantages en nature	14	6
Reprise de provisions	66	
<b>Total des transferts de charges</b>	<b>79</b>	<b>6</b>

#### 14.3: Operational costs

##### External costs

External costs are presented below:

<b>External expenses (Amounts in K€)</b>	<b>31/12/2018</b>	<b>31/12/2017</b>
Subcontracting, studies and research	51 028	13 576
Compensation Temporary workers Fees	3 222	2 261
Personnel on secondment	1 492	1 802
Travel, Missions and Receptions	1 219	904
Intellectual property fees	251	340
Other Charges	959	616
<b>Total</b>	<b>58 171</b>	<b>19 499</b>

Research and development expenses mainly reflect the studies on the Imeglimin and PXL770 projects. The Company is performing its studies through its network of sub-contracted service providers. The remuneration of these contracts constitutes the essential part of its operating expenses in the field of research.

The major part of the increase in subcontracting costs is related to the TIMES program for which expenses of €46 million were recorded in 2018. This amount also includes the fees to be paid to Merck Serono under the contract signed with Roivant Sciences GmbH, for which a provision was created

according to the Company's best estimate on the balance sheet date. (this item is a contingent liability, as mentioned in Note 20.4)

### Taxes and dues

Taxes and dues mainly correspond to the CET tax.

### Personnel costs

The personnel costs can be broken down in the following manner:

<b>Personnel expenses (Amounts in K€)</b>	<b>31/12/2018</b>	<b>31/12/2017</b>
Salaries	2 421	2 090
Social security charges	1 164	937
<b>Total</b>	<b>3 585</b>	<b>3 027</b>

The change in personnel expenses is primarily linked to the reinforcement of the clinical research teams.

The ICCC is used to improve the competitiveness of the company and enable it to achieve of efforts in the field of investment, research, innovation, training and recruitment.

### Other Charges

<b>Other expenses (Amounts in K€)</b>	<b>31/12/2018</b>	<b>31/12/2017</b>
License	4 509	258
License fees	171	96
Attendance fees	333	362
Other	759	14
<b>Total</b>	<b>5 773</b>	<b>730</b>

## Note 15: Products and financial charges

<b>FINANCIAL INCOME (Amounts in K€)</b>	<b>31/12/2018</b>	<b>31/12/2017</b>
Interests	368	63
Financial income from investments	1	0
Foreign exchange gains	2 401	0
<b>Total investment income</b>	<b>2 770</b>	<b>64</b>

<b>FINANCIAL EXPENSES (Amounts in K€)</b>	<b>31/12/2018</b>	<b>31/12/2017</b>
Provisions for risks	1 506	0
Foreign exchange losses	738	398
Interest expenses	0	13
Other financial expenses	0	2
<b>Total financial expenses</b>	<b>2 244</b>	<b>413</b>

## Note 16: Non-recurring income and expenses

<b>EXTRAORDINARY INCOME</b> <b>(Amounts in K€)</b>	<b>31/12/2018</b>	<b>31/12/2017</b>
Gain on disposal of treasury shares	68	147
Prior-year income	2	
<b>Total extraordinary income</b>	<b>70</b>	<b>147</b>

<b>EXTRAORDINARY EXPENSES</b> <b>(Amounts in K€)</b>	<b>31/12/2018</b>	<b>31/12/2017</b>
Loss on disposal of treasury shares	75	94
Extraordinary amortization/depreciation of fixed assets	13	2
Other extraordinary expenses	0	0
<b>Total extraordinary expenses</b>	<b>88</b>	<b>96</b>

## Note 17: Income taxes

The amounts recorded in the income statement as corporate income tax are related essentially to the Research Tax Credit (CIR) and amounted to:

- 3,122 K€ in 2017
- 3,476 K€ in 2018.

The amount of Company's fiscal deficits indefinitely carried over at December 31, 2018 was 105,991K€. They represent a relief in future tax debt of 26,498 K€ (based on a tax rate of 25%). No other reprocessing will increase or reduce the future tax debt.

In 2018, the Company charged €1,508 K of prior tax loss carryforwards against revenues generated by partnership contracts signed during the year, which constitute non-recurring revenues.

The tax rate applicable to the Company for its profits excluding long-term capital gains, is the applicable rate in France, i.e., 33.33%. The tax rate voted for subsequent years is 31% in 2019, 28% in 2020, 26.5% in 2021 and 25% as from 2022.

The tax rate that applies to the Company for its long-term capital gains is the applicable rate in France, i.e., 15%. The tax rate adopted for subsequent years is 15% in 2017 as well as in 2018.

## Note 18: Earnings per share

### Basic earnings

The base earnings per share is calculated by dividing the net loss attributable to shareholders of the Company by the weighted average number of outstanding common shares for the year.

The set of instruments giving right to the capital in a deferred way (BSA, BSPCE and bonds) are regarded as anti dilutive when they induce a reduction in the loss per share. In that case, the diluted loss per share is identical to the base loss per share.

### Diluted earnings

Diluted earnings per share are calculated on the same basis as net income, by taking into account the conversion of all dilutive instruments in the average number of shares outstanding.

In 2017, the set of instruments giving right to the capital in a deferred way (BSA, BSPCE and stock options) are regarded as non-dilutive because they induce a reduction in the loss per share. This way, the diluted loss per share in 2017 is identical to the base loss per share.

<b>BASIC EARNINGS PER SHARE</b> <b>(Amounts in €)</b>	<b>31/12/2018</b>	<b>31/12/2017</b>
Weighted average number of shares outstanding	24 833 831	23 033 299
Net income for the period	11 400 318	-12 054 408
<b>Basic earnings per share (€/share)</b>	<b>0,46</b>	<b>(0,52)</b>
<b>Diluted earnings per share (€/share)</b>	<b>0,45</b>	<b>(0,52)</b>

## Note 19: Related parties

The Company has not concluded any significant transactions at abnormal market conditions with related parties.

### Remuneration of executives (outside of allocation of capital instruments)

In application of Article 531-3 of the General Accounting Plan, executives of a business corporation with a Board of Directors are the Chairman of the Board of Directors, CEO as well as directors who are natural or legal persons (and their permanent representatives).

The compensation paid to executives is broken down as follows (EUR):

<b>Compensation of corporate officers</b> <b>(K€)</b>	<b>31/12/2018</b>	<b>31/12/2017</b>
Fixed compensation due	331	191
Variable compensation due	123	46
Benefits in kind	9	6
Employer's contributions	120	96
Attendance fees	333	362
<b>TOTAL</b>	<b>917</b>	<b>701</b>

No advantage posterior to the employment is granted to members of the Board of Directors.

The terms of the allocation of the variable parts are established on the basis of qualitative and quantitative objectives set at 100% on the respect of goals at the level of the Company, common to all of the employees.

For the attribution of equity instruments assigned to executives see Note 8.

## Note 20: Commitments given

### 20.1 Retirement benefits

#### Methodology of calculation

The purpose of the actuarial valuation is to produce an estimate of the present value of the commitments of the Company in respect of severance pay to the planned retirement by the collective agreements.

These obligations related to the legal or conventional retirement compensation have been evaluated at the closing dates of the years presented. These allowances are not the subject of an accounting in the form of provision in the accounts of the company, but constitutes a commitment off balance sheet.

This amount is determined on different dates of closure on the basis of an actuarial evaluation, which is based on the use of the projected unit credit method, taking into account the rotation of staff and probabilities of mortality.

### Actuarial Assumptions

The main actuarial assumptions used for the evaluation of severance benefits at retirement are the following:

ACTUARIAL ASSUMPTIONS	31/12/2018	31/12/2017
Retirement age	Voluntary retirement at 65/67 years	
Collective bargaining agreements	Pharmaceutical industry	
Discount rate (IBOXX Corporates AA )	1,83%	1,68%
Mortality table	INSEE 2017	INSEE 2017
Rate of salary revaluation	2%	2%
Turnover rate	Low	Low
Social security expenses rate	50%	50%

### Calculated commitments

The commitments calculated for severance benefits to retirement are as follows:

RETIREMENT BENEFITS (Amounts in K€)	31/12/2018	31/12/2017
Amount of commitments	279	230

These commitments are not covered by plan assets.

### 20.2 Finance leases

The Company does not hold any financial lease contracts.

### 20.3 Commercial Leases

#### Real estate leases

In 2015, in relation with its activities, the Company moved its headquarters and entered into a commercial lease in Lyon with an effective date of July 1, 2015. Its term is nine complete and consecutive years, until June 30, 2024. The Company has the possibility to provide notice to terminate only every three years.

In November 2017, the Company entered into a commercial lease enabling it to enlarge the office space at its headquarters, effective from April 1, 2018. Its term is nine complete and consecutive years, until March 31, 2027. The Company has the possibility to provide notice to terminate only every three years.

The Company also subleased an office in Paris for a 12-month term which is renewable annually, effective January 1, 2013, and a lease for premises in Japan effective January 15, 2018, with a two-year commitment.

### **Contractual obligations and commitments**

The following table summarizes the Company's commitments as at December 31, 2018:

<b>Engagements financiers (Montants en K€)</b>	<b>A 1 an au plus (hors indexation)</b>	<b>De 1 à 3 ans (hors indexation)</b>	<b>De 3 à 5 ans (hors indexation)</b>	<b>&gt; 5 ans</b>	<b>Total</b>
Locations	251	346		-	597

### **20.4 Obligation under contract signed with Merck Serono when the Company was established**

The Company entered into a transfer and license agreement with Merck Serono on March 19, 2009 amended on July 30, 2009, June 22, 2010, May 23, 2014 and then November 28, 2014 (the "MS Agreement"), which falls within the scope of the spin-off of Merck Serono's research and development activities in the cardiometabolic field.

Pursuant to the terms of the MS Agreement, Merck Serono transferred certain patents and granted a license for other patents and know-how to the Company for research and development, and the marketing of pharmaceutical products. This license is exclusive for a list of 25 molecules, by program, selected by the Company.

In consideration of the rights that have been granted in the framework of the MS Contract, the Company must pay to Merck Serono:

- Royalties on net sales of products covered by the patents assigned or licensed in license by Merck Serono at a high single digit rate for the Imeglimin, and at a low single digit rate for other projects;
- a percentage of the income from any partnership agreement relating to the drug candidates covered by the patents granted or licensed, at a low double digit rate. For other products, if the Company enters into a partnership agreement, it would have to pay a percentage of the income from the partnership for the products covered by the patents transferred or licensed from Merck Serono, at a rate depending on the product and its stage of development at the time of the partnership.



As part of the application of this contract to the partnership agreement signed with Roivant in February 2018, the company and Merck Serono have a different interpretation of Poxel's revenue base to be subject to royalties. The Company considers, with its advisors, that its interpretation is justified by well-founded legal arguments and that the probability of an outflow of resources beyond the amount recorded is remote. Consequently, this discrepancy, applied to payments already received from Roivant on 31 December 2018 has not been the subject of a provision but constitutes a contingent liability for the company

## 20.5 Obligation under the DeuteRx contract

On August 29, 2018 the Company entered into a purchase contract with DeuteRx for DRX-065, a potential medication under clinical development for the treatment of non-alcoholic steatohepatitis (NASH), a portfolio of other potential specialty medications for the treatment of rare metabolic diseases, and all related industrial and intellectual property rights of DeuteRx.

This agreement specifies, for the entire product portfolio, the issue of up to 4 million shares in the Company in favor of DeuteRx, and milestone payments linked to the attainment of development, regulatory and sales targets, amounting to a maximum of \$545 million, part of which may be paid through the issue of shares in the Company. It also provides for the payment of royalties at a low-range figure on sales. The first milestone payment corresponds to the Company's decision to commence the phase 3 clinical development program for the drug candidates covered under that agreement, and will be made exclusively through the issue of shares in the Company.

## 20.6 Obligation under other agreements

In the framework of its activities, the Company regularly uses subcontractors and concludes research and partnership agreements with various organizations, or CRO, which perform preclinical trials and clinical studies in relationship with the drug candidates, mainly Imeglimin and to a lesser extent, PXL 770. The cost of the services rendered by the CROs is counted as an operating cost when it is engaged, or, depending on the nature, for their result at the date of the financial statements.

## Note 21: Number of Employees

The mean number of employees of the Company is:

AVERAGE WORKFORCE	Financial year 2018	Financial year 2017
Managerial staff	29	24
Non-managerial staff	1	1
<b>Average total workforce</b>	<b>30</b>	<b>25</b>

In 2017 the mean workforce integrates the portage staff of the Tokyo and Boston offices at 3 and 4, respectively. Following the creation of the Japanese subsidiary, the 5 employees in the Boston offices are now integrated into the average 2018 workforce.

## Note 22: Subsidiaries and equity holdings

Table of subsidiaries and holdings (Amounts in K€)	Capital	Reserves and retained earnings before appropriation of income	Proportion of ownership interest held	Carrying amount of shares held		Loans and advances granted by the company (gross amount)	Profit or loss of last fiscal year	Dividends	Comments
				Gross	Net				
POXEL JAPAN KK	154	0	100.0%	154	-	437	(491)	-	Impairment on equity interest: €295 K Impairment on related receivable: €603 K Guarantees and sureties: none Dividends: none Closing rate: 125.85 Average rate: 130.39

Poxel SA is the leading and consolidating company of the Group. POXEL JAPAN KK is full consolidated.

## Note 23: Post-balance sheet closing date events

None

## Note 24: Management and assessment of financial risks

The principal financial assets held by the Company are cash and cash equivalents held to finance the business activities and development of the Company and the client receivables in the context of the partnership contracts. The Company may be exposed to different types of financial risks: market risk, credit risk and liquidity risk. When appropriate, the Company uses simple ways proportionate to its size in order to minimize potentially adverse effect of these risks on financial performance. It is not the Company's policy to invest in financial instruments for speculative purposes.

### Interest rate risk

The Company has a very low exposure to interest rate risk, considering that:

- its liquid assets include fixed term deposits;
- the repayable advances are not subject to interest rate risk;
- no debt has been entered into at a variable interest rate.

### Credit risk

The credit risk is associated with the deposits with banks and financial institutions. For its cash investments, the Company uses first-rate financial institutions and does not bear any significant credit risk with regard to its cash.

### Foreign currency risk

The Company is exposed to foreign exchange risk taking into account the volume of transactions that it carries out in yen in the framework of the contract signed with Sumitomo Dainippon Pharma. However, it covers this risk in application of the principle provided in the contract, according to which the company re-bills Sumitomo Dainippon Pharma in the same currency as that in which it has been charged for its purchases.

The Company is also exposed to the foreign currency risk due to 13.6m€ liability towards Roivant (in USD). In any case, the Company has covered the major part of the risk by having subscribed to currency term accounts for an amount of 11.4m€ as of December 31, 2018.

At this stage, the Company has not adopted any other recurring mechanism of coverage to protect its activity against currency fluctuations. From time to time, the Company may nevertheless subscribe currency term accounts in order to cover a commitment in currency as mentioned above.

In the future, with the growth of its activity, which could expose the Company to the exchange risk in a more significant manner, it will consider using a suitable policy to cover these risks.

### Shares risk

The Company does not hold any equity investments or marketable securities traded on a regulated market.

### Liquidity risk

The Company is not exposed in the short term to liquidity risk, taking into account the fact that the cash available on December 31, 2018, which amounts to 66,571 K€, is sufficient to finance the development of the Company in the course of the next twelve months.

## Note 25: Statutory auditors' fees

	Exercice 2018			Exercice 2017		
	PwC	Mazars	Total	PwC	Mazars	Total
Commissariat aux comptes	60	60	120	39	39	78
Services Autres que la Certification des Comptes	12	12	24	23	19	42
<i>Requis par les textes</i>	12	12	24	23	19	42
<i>Autres SACC</i>	0	0	0	0	0	0
<b>Total des honoraires</b>	<b>72</b>	<b>72</b>	<b>144</b>	<b>62</b>	<b>58</b>	<b>120</b>

## 26.2. Audit report of Statutory Auditors on financial statements for the financial year ended December 31, 2018

### Auditors' report on the financial statements for the twelve months ended December 31, 2018

To the General Meeting of Shareholders

**Poxel**

*Le Sunway Building*

259 avenue Jean Jaurès

69007 Lyon

### Opinion

In accordance with the assignment entrusted to us by Poxel's General Meeting of Shareholders, we have audited the annual financial statements of Poxel for the year ended December 31, 2018, as attached to this report.

We certify that, in accordance with French accounting rules and principles, the annual financial statements give a true and fair view of the results of operations for the past financial year and of the company's financial position and assets at the end of that year.

The opinion expressed above is consistent with the content of our report to the audit committee.

### ***Basis of opinion***

#### ***Audit standards***

We conducted our audit in compliance with the professional standards applicable in France. We consider that the information we have collected is sufficient and appropriate to provide a basis for our opinion.

Our responsibilities under these standards are described in the section "Liability of the auditors for the audit of the annual financial statements" of this report.

#### ***Independency***

We conducted our audit in compliance with the rules of independence applicable to us, for the period from January 1, 2018 to the date of issue of our report, and in particular we did not provide services prohibited by article 5(\$1) of Regulation (EU) No 537/2014 or by the Code of Ethics for Auditors.

#### **Justification of the assessments - Key points of the audit**

In accordance with the requirements of articles L. 823-9 and R. 823-7 of the French Commercial Code (*code de commerce*) relating to the justification of our assessments, we bring to your attention the key points of the audit relating to the risks of material misstatement which, in our professional opinion, were the most significant for the audit of the financial statements for the year, as well as the responses we provided to those risks.

These assessments were made in the context of the audit of the financial statements taken as a whole and the formation of our opinion expressed above. We do not express an opinion on individual items in these financial statements.

#### ***Recognition of revenue from collaborative, licenses and services agreements***

*(Note 1.2 « Significant events », notes 2.13 and 14.1 « Revenues »)*

#### ***Identified Risk***

Poxel generates revenues from collaboration and licensing agreements for its drug-candidates and its own technologies with biopharmaceutical and pharmaceutical companies for a total amount of €74.3 million as of December 31, 2018.

These agreements provide for different types of payments: upfront payments, payments for the achievement of clinical and regulatory objectives, payments for research and development services, payments based on sales objectives and royalties which are determined on the basis of sales of marketed products.

The method for accounting for the corresponding income depends in particular on the nature of the rights granted and the types of payments provided for in these agreements. A misinterpretation of the agreements signed with the partners may lead to inadequate acknowledgement of the related income.

Agreements may provide for cases where income is to be acknowledged as progress on the basis of costs incurred. In this case, management must make estimates of the costs on completion and monitor the costs incurred for these services.

Revenue acknowledgement is a key element of the audit because of the diversity of contractual clauses that determine the accounting treatment and the estimates required to determine the revenue to be recognized.

#### *Response*

We have reviewed the license and partnership agreements entered into with Sumitomo Dainippon Pharma and Roivant Sciences GmbH and have carried out an analysis of these elements, including the obligations of the parties, the services to be provided and the compensation components.

We have obtained management's analyses and estimations to calculate the amount of revenue related to these agreements.

We evaluated the relevance of the methods used and the coherence of management's evaluations to calculate the amount of revenue related to these agreements.

With the help of our specialists, we examined the compliance of the accounting processing with the applicable standards and verified that the transactions satisfy the criteria for the accounting processing used.

For revenue recognized on a percentage-of-completion basis, we corroborated, on a test basis, the hypothesis and data used by the management to determine the costs to be completed with internal and external justifications (including agreements with subcontractors) and the justifications for the costs incurred.

Finally, we verified that appropriate information was provided in the notes to the annual financial statements.

#### ***Accounting treatment and valuation of the portfolio of products acquired from DeuteRx***

*(Note 1.2 "Significant events", notes 2.2 and 3 "Intangible assets", note 2.5 "Recoverable amount of fixed assets" and note 20.5 "Requirements under agreement with DeuteRx")*

#### *Identified Risk*

In August 2018, Poxel acquired, through a strategic agreement with DeuteRx, the DRX-065 drug-candidate in clinical development for the treatment of non-alcoholic steatohepatitis ("NASH") as well as other programs including deuterated drug-candidates for the treatment of rare and specialized metabolic disorders.

Poxel paid DeuteRx an upfront payment of €6.9 million (\$8 million) and 1.29 million new ordinary shares of Poxel at a price of €6.91 per share, representing 4.99% of the share capital (or €8.9 million at the time of the transaction). As indicated in Note 25.3, this agreement also provides for:

- Poxel payments to DeuteRx related to the achievement of certain clinical and regulatory objectives and product sales objectives (in cash or in Poxel shares, as applicable)
- Payment of royalties on sales.

This transaction appears significant and non-recurrent for Poxel, which led the Company to question the appropriate accounting treatment for this transaction.

At December 31, 2018, Poxel recognized an intangible asset for €16.6 million corresponding to the upfront payment of €15.8 million and €0.8 million in acquisition costs.

We considered the accounting processing of this agreement as a key element of the audit because this transaction seems material and non-recurrent for the Company.

#### *Response*

We obtained the agreement entered into with DeuteRx and analyzed it, in particular by reviewing the terms of payment and transfer of intellectual property.

With the help of our specialists, we reviewed the compliance of the accounting processing with the applicable standards.

Finally, we verified that appropriate information was provided in the notes to the annual financial statements.

#### ***Recognition and valuation of royalties paid under the sale and license agreement with Merck Serono***

*(Notes 4 « Details of expenses and income by function », note 14.3 “Operating expenses” and note 20.4 « Requirements under agreement executed with Merck Serono when the company was created »)*

#### *Identified Risk*

Poxel entered into a sale and license agreement with Merck Serono on March 19, 2009, amended on July 30, 2009, June 22, 2010, May 23, 2014 and November 28, 2014. This agreement provides, in particular, that the company must pay Merck Serono, in the form of a royalty, a percentage of the revenues from any partnership agreement relating to drug-candidates covered by patents assigned or licensed to which Imeglimine is a part.

As mentioned in Note 1.2 to the schedule to the annual financial statements, the Company has entered into an exclusive contract with Roivant Sciences GmbH for the development and marketing of Imeglimin in the United States, Europe and other countries.

A percentage of the revenues related to this contract must be paid to Merck Serono in the form of royalties. As indicated in Note 20.4, Merck Serono has a different interpretation of the basis for calculating royalties to be paid.

We considered the accounting and valuation of these royalties as a key point of the audit, the estimation of the expense recorded in this regard in the accounts requiring the exercise of management's judgment, in particular to determine the basis for calculating the royalties.

#### *Response*

We reviewed the agreement and its amendments signed with Merck Serono and the agreement signed with Roivant.

We consulted the discussions between Poxel and Merck Serono. We sought external confirmation from Poxel's counsel and analyzed the response to this request as part of this divergence of interpretation. We examined the merits of the arguments put forward by Poxel and his advisors to determine the elements to be included or excluded from the basis for calculating the royalties.

We evaluated the relevance of the methods used to calculate these royalties on the basis of the analysis conducted by the management and its advisors.

Finally, we verified that appropriate information was provided in the notes to the annual financial statements.

## **Specific audits**

We have also conducted, in accordance with the professional standards applicable in France, the specific audits required by legal and regulatory texts.

### ***Information given in the management report and in other documents on the financial situation and annual accounts addressed to shareholders***

We have no matters to report regarding the fairness and consistency with the annual financial statements of the information given in the Board of Directors' management report and in the other documents on the financial position and the annual financial statements addressed to the shareholders.

We certify that the information relating to payment periods mentioned in article D.441-4 of the French Commercial Code is true and fair and consistent with the annual financial statements.

### ***Corporate Governance Report***

We certify that the corporate governance report contains the information required by articles L. 225-37-3 and L. 225-37-4 of the French Commercial Code.

Concerning the information provided in accordance with the provisions of article L. 225-37-3 of the French Commercial Code on the compensation and benefits paid to the corporate representatives and on the commitments made in their favor, we have reviewed its consistency with the financial statements or the data used to prepare these financial statements and, where applicable, with the information collected by your Company from the companies controlling your Company or controlled by it. On the basis of this audit, we certify the accuracy and fairness of these information.

Concerning the information relating to the elements that your Company considered likely to have an impact in the event of an IPO or a public exchange offer, provided in accordance with the provisions of article L. 225-37-5 of the French Commercial Code, we have reviewed their compliance with the documents from which they are derived and which have been provided to us. On the basis of this audit, we have no matters to report on this information.

### ***Other information***

In accordance with the law, we have ensured that the various information relating to the identity of the holders of share capital or voting rights has been disclosed to you in the management report.

### **Information resulting from other legal and regulatory requirements**

#### ***Appointment of auditors***

We were appointed auditors of Poxel by your general meeting of 29 January 2016 for Mazars Paris and 31 January 2014 for PricewaterhouseCoopers Audit.

At December 31, 2018, PricewaterhouseCoopers Audit was in the fifth year of its engagement without interruption and Mazars Paris in the fourth year. Previously, Mazars Lyon, also a member of the Mazars network, was Poxel's auditor from 2009 to 2014. In consequence, the PricewaterhouseCoopers

Audit and Mazars networks are in their fourth year of operation without interruption since the Company's shares were admitted to trading on a regulated market.

### **Liability of management and persons constituting corporate governance with regard to the annual accounts**

It is the liability of the management to prepare financial statements that present a true and fair view in accordance with French accounting rules and principles and to establish the internal control that it believes is necessary for the preparation of financial statements that are free from material misstatement, whether due to fraud or error.

By preparing the consolidated financial statements, the management is in charge of evaluating the Company's ability to continue its business, presenting in these financial statements, if any, all information related to the business continuity and applying business accounting policy, unless it is intended to winding up the Company or to cease its business.

The audit committee is responsible for monitoring the process of preparing financial information and for monitoring the effectiveness of internal control and risk management systems, as well as, where applicable, internal audit, with respect to procedures related to the preparation and processing of accounting and financial information.

The annual financial statements have been approved by the Board of Directors.

### **Liability of the auditors in regard to the audit of the annual accounts**

#### *Audit objective and approach*

It is our liability to prepare a report on the annual financial statements. Our objective is to obtain reasonable assurance that the financial statements taken as a whole are free from material misstatement. Reasonable assurance is a high level of assurance, but does not guarantee that an audit conducted in accordance with professional standards of practice will consistently identify any material misstatement. Misstatements may result from fraud or error and are considered material when it can reasonably be expected that they could, individually or in aggregate, influence the economic decisions that users of the accounts make based on them.

As indicated by article L. 823-10-1 of the French Commercial Code, our mission of certification of the accounts does not consist in guaranteeing the viability or quality of the management of your Company.

As part of an audit conducted in accordance with professional standards applicable in France, the auditor exercises professional judgment throughout the audit. In addition:

- it identifies and evaluates the risks of material misstatement of the annual financial statements, whether due to fraud or error, defines and performs audit procedures to address these risks, and obtains information that it considers sufficient and appropriate to form an opinion. The risk of not detecting a material misstatement due to fraud is higher than that of a material misstatement due to error, as fraud may involve collusion, falsification, willful misrepresentation, misrepresentation or circumvention of internal control;
- it reviews the internal control relevant to the audit in order to design audit procedures that are appropriate under the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the internal control;



- it evaluates the adequacy of the accounting policies used and the reasonableness of the accounting estimations made by management, as well as the information relating to them provided in the annual financial statements;
- it evaluates the appropriateness of management's application of the going concern accounting policy and, depending on the information collected, whether or not there is a material uncertainty related to events or circumstances that could affect the Company's ability to continue as a going concern. This evaluation is based on the information collected up to the date of its report, it being recalled, however, that subsequent circumstances or events could jeopardize the continuity of operations. If it concludes that a material uncertainty exists, it draws the attention of the readers of its report to the information provided in the annual financial statements about that uncertainty or, if these information are not provided or are not relevant, it issues a qualifying certification or a refusal to certify;
- it evaluates the overall presentation of the annual financial statements and evaluates whether the annual financial statements reflect the underlying transactions and events in such a way as to give a true and fair view.

#### *Report to the Audit Committee*

We deliver to the Audit Committee a report that includes the scope of the audit work and the work program implemented, as well as the conclusions arising from our audit. We also report to it, where applicable, the material weaknesses in internal control that we have identified with respect to the procedures relating to the preparation and processing of accounting and financial information.

Among the elements communicated in the report to the Audit Committee are the risks of material misstatement, which we consider to have been the most important for the audit of the annual financial statements for the year and which therefore constitute the key audit issues, which we are required to describe in this report.

We also provide the Audit Committee with the declaration provided for in article 6 of Regulation (EU) No. 537-2014 confirming our independence, within the meaning of the rules applicable in France as defined in particular by articles L. 822-10 to L. 822-14 of the French Commercial Code and in the Code of Ethics for the Auditors. If necessary, we discuss with the Audit Committee the risks to our independence and the safeguards applied.

Lyon and Courbevoie, April 8, 2019

The auditors

PricewaterhouseCoopers Audit

MAZARS

Elisabeth L'hermite

Séverine Hervet

## 26.3. Non-financial information

### ***Non-financial information:***

Poxel is a dynamic biopharmaceutical company developing innovative treatments for metabolic diseases, in particular type 2 diabetes and nonalcoholic steatohepatitis (NASH). Based in Lyon (France), Poxel was spun out in 2009 from Merck Serono, which was at the time one of the global leaders in the field of metabolic disorders. Our registered office is in Lyon, France and we also have offices in Paris, Boston and Tokyo.

Our expertise is based on the understanding of the key mechanisms involved in metabolic diseases and our ability to develop innovative solutions for treating patients. Our management team and our Board of Directors have extensive experience in the pharmaceutical industry, ranging from molecular research, through development and marketing, to patient access and the management of the drug life cycle.

Our expertise consists in:

- Developing first-in-class treatments for type 2 diabetes, NASH and other metabolic diseases with significant unmet medical needs;
- Leading the clinical development of drug candidates for treating metabolic diseases;
- Establishing global strategic partnerships.

### ***A diversified portfolio product designed to act on metabolic diseases***













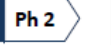




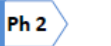








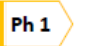



We study the potential of innovative molecules to fight against metabolic diseases, in particular type 2 diabetes and NASH. We are committed to developing new therapeutic options that are safe and effective for patients.

Type 2 diabetes is a major public health challenge, the incidence of which is growing steadily. It is the most common form of diabetes, affecting about 90% of the diabetic population.

Nonalcoholic steatohepatitis (NASH) is a metabolic disease with no clear disease origin that is becoming a pandemic. It is characterized by an accumulation of fat in the liver, which induces inflammation and fibrosis. The disease can remain silent for a long time. However, when it starts to progress, it can quickly develop towards severe damage and liver cirrhosis, which can significantly impair liver function and even lead to liver failure or liver cancer.

The Company has developed a diversified product portfolio for the treatment of these two diseases:

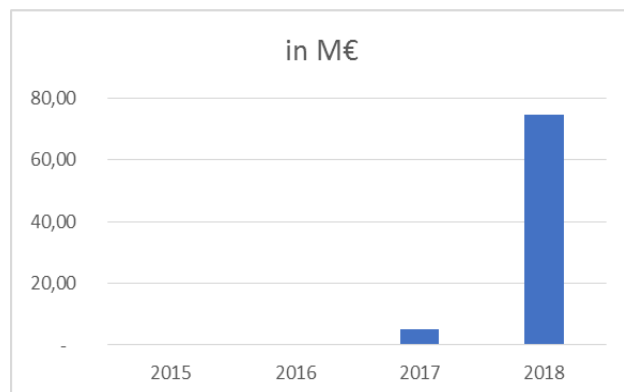
- For type 2 diabetes, Imeglimin is the first representative of a new chemical class of oral agents, Glimins. It targets mitochondrial bioenergetics. It is currently in Phase III clinical development.
- For NASH, the Company continues the development of two drug-candidates with separate and complementary action mechanisms: PXL770, a first-in-class direct activator of adenosine monophosphate-activated protein kinase (AMPK), currently in Phase II clinical development, and PXL065, the R-stereoisomer of pioglitazone stabilized by deuterium substitution, currently in Phase I clinical development.

	Indication	MOA	Preclinical	Phase 1	Phase 2	Phase 3	Partner/ Rights	Next Steps
Imeglimin Japan/ Asia*	Type 2 Diabetes	Mitochondrial Bioenergetics						<ul style="list-style-type: none"> <li>Phase 3 TIMES completion</li> <li>Target JNDA submission 2020</li> </ul>
Imeglimin US/ EU/ Other**	Type 2 Diabetes	Mitochondrial Bioenergetics						<ul style="list-style-type: none"> <li>Manufacturing drug for Phase 3</li> <li>Differentiation studies in CKD patients w/ T2D</li> </ul>
PXL770	NASH/ metabolic diseases	Direct AMPK activator						<ul style="list-style-type: none"> <li>Initiate Phase 2a program in NASH</li> </ul>
PXL007 (EYP001)	Hepatitis B NASH	FXR agonist						<ul style="list-style-type: none"> <li>Complete Phase 1 program by Enyo Pharma</li> </ul>
PXL065 (formerly DRX-065)	NASH	MPC Inhibitor						<ul style="list-style-type: none"> <li>Complete Phase 1, tox, CMC</li> <li>Initiate Phase 2</li> </ul>
Poxel/ DeuteRx programs	Metabolic (AMN/ALD, NASH, etc.)	Direct AMPK activator/ MPC Inhibitor						<ul style="list-style-type: none"> <li>Complete preclinical studies</li> </ul>

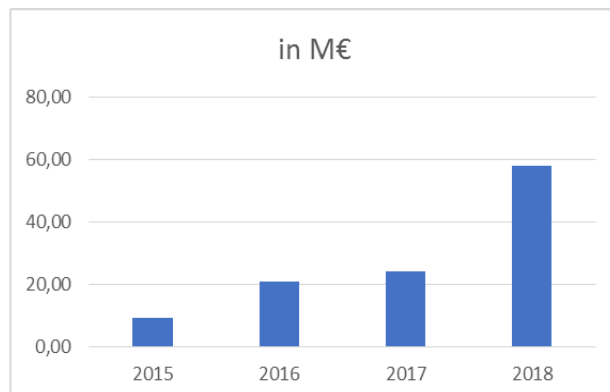
### Main economic data

Our business model is focused on research and development and the conclusion of strategic partnerships for developing, manufacturing and marketing drugs.

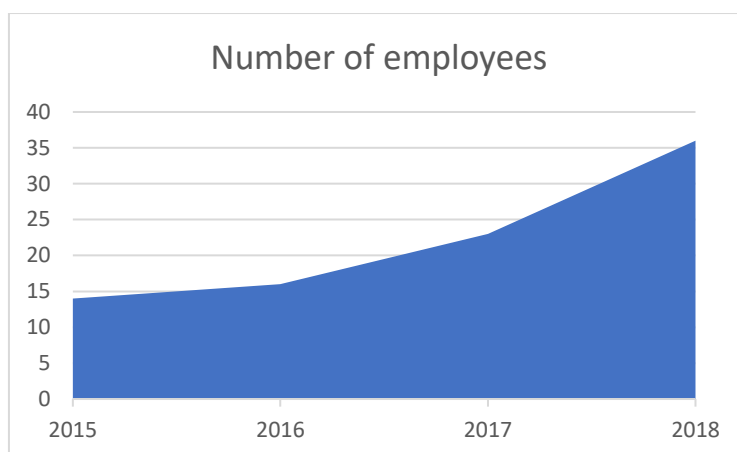
#### Revenue



#### Research and development costs

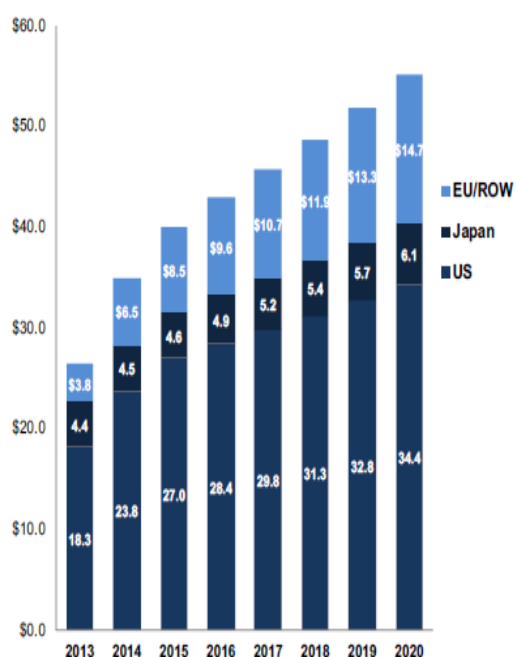


### Number of employees



### *Imeglimin target markets*

Global Type 2 Diabetes Market (Sales in \$B)



Source: Oppenheimer & Co. estimates



### Japan and Asia

The Japanese market, worth nearly \$6 billion and fast expanding, offers a unique opportunity for value creation. In Japan, China and 11 other Asian countries, our strategic partner for Imeglimin is Sumitomo Dainippon Pharma. In Japan, Poxel and Sumitomo Dainippon Pharma have co-developed Imeglimin and are leading the Phase III program, which is financed by Sumitomo Dainippon Pharma, also responsible for marketing the product on this market.

### United States and Europe

American and European markets represent an opportunity of roughly \$32 billion. We have finalized a license agreement with Roivant Sciences, our strategic partner for these two markets and for other countries that are not covered by the agreement with Sumitomo Dainippon Pharma. The preparatory work for the Phase III program began in 2018. The Company's objective is to initiate the Phase III program in 2019.

### *Other partnerships finalized to diversify the drug-candidates portfolio and our target markets*

Under an agreement with DeuteRx LLC, we acquired the exclusive worldwide rights to a novel clinical stage drug-candidate for treating NASH, as well as several other deuterated drug candidates for the treatment of rare and specialty metabolic diseases. The lead drug candidate, PXL065 currently in Phase I clinical development, will continue to be developed for the treatment of NASH.

We also signed a license agreement with Enyo Pharma for our FXR (farnesoid X receptor) agonist. Enyo has launched the phase 1b program for hepatitis B and is studying its development potential for NASH. We also work closely with academic leaders in the areas of metabolic and cardiovascular diseases as well as mitochondrial dysfunctions. We collaborate with many reputed universities in our fields:

- CarMeN Laboratoire de recherche Cardiovasculaire, Métabolisme, Diabétologie et Nutrition, Université Lyon UMR INSERM 1060, France
- INSA Lyon, Hospices Civils
- Kobe University, Japan
- Université de Grenoble U1042 & UMR\_S 1055, and Université de Rouen UMR INSERM 1096, France
- Yale University, New Haven, CT, USA

We intend to continue our development through a proactive policy of strategic partnerships and development of our drug-candidates portfolio.

### **1) Social and environmental information**

On December 31, 2018, an Executive Committee of eight people ran the Company (four men and four women). The members of this Executive Committee collectively have expertise which covers all of the value chain involved in the development of a new drug. All have held positions of high responsibility in large groups and, for the most part, have key experience working in pharmaceutical companies with widely known diabetes franchises. The Executive Committee consists of four of the co-founders, as well as the Executive Vice-President, Business Development & US Operations, the Senior Vice President, Investor Relations & Public Relations, the Executive Vice-President, Late Clinical Development, Reg & Medical Affairs, and the Chief Financial Officer.

#### **1.1. Employment and social information**

The Company carries out research and development in the medical sector. As such, its employees are at the heart of its business model. To motivate and retain in the long term all of its key people, the Company has implemented a policy of talent management. POXEL was incorporated in March 2009 and employed 36 persons on December 31, 2018. In nine years, the Company has hired qualified and competent staff, especially around Lyon.

#### **a) Employment:**

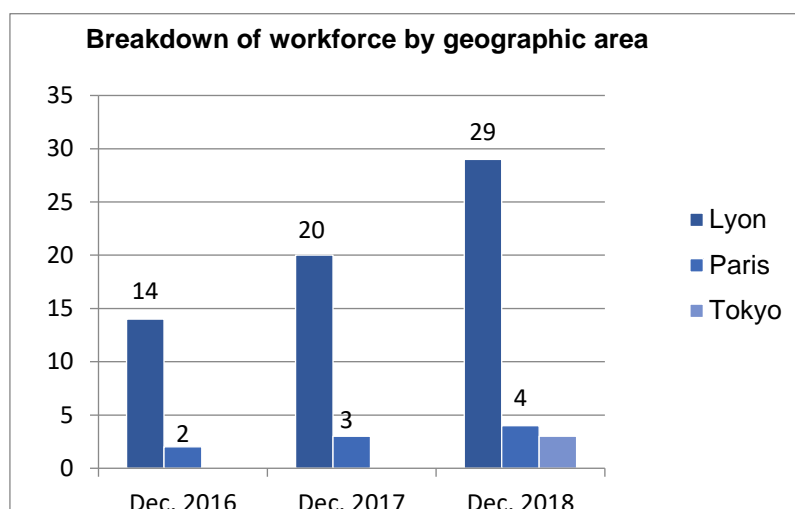
##### **Workforce:**

On December 31, 2018, the Company's workforce was composed of 36 employees in France and Japan and five temporary workers in Boston. These five persons exercise their functions in the areas of clinical and medical affairs, business development, investor relations and public relations. In 2018, the Company's workforce increased by 12. This change is due to 15 new hires (12 in France and 3 in Japan) and 3 departures.

The workforce indicators presented below describe information for employees with an employment contract in France or Japan at the end of each financial year.

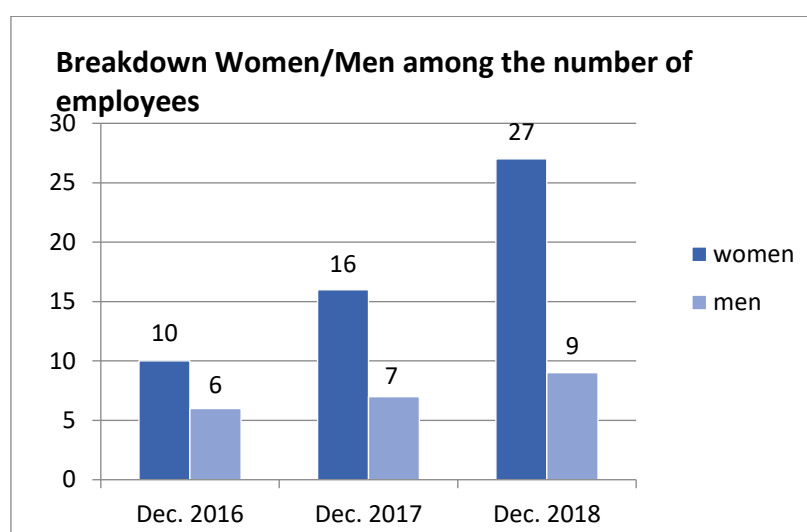
##### **Breakdown by geographic area:**

Employees work in two main sites in France: Lyon and Paris. There is also a site in Tokyo, Japan. The head office is located in Lyon. The Company has a secondary office in Paris.



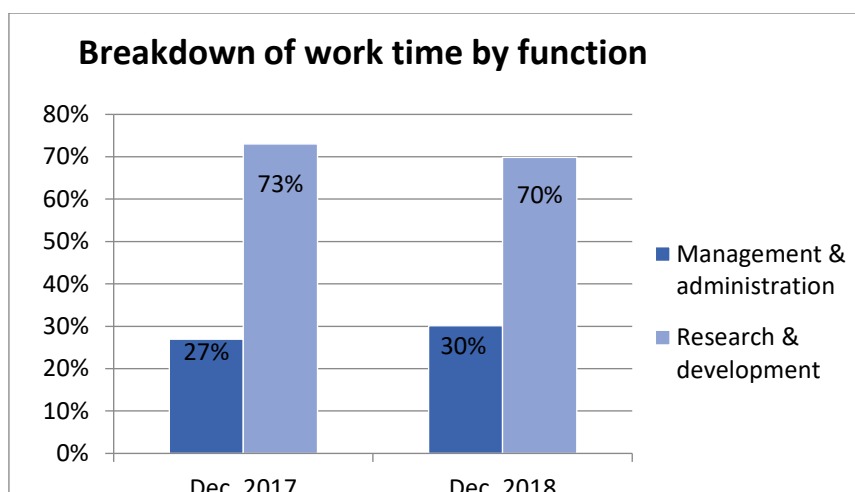
**Men/women breakdown:**

On December 31, 2018, women accounted for about 75% of the Company's contractual workforce, compared to 70% on December 31, 2017. The distribution of employees by sex is as follows:



**Breakdown by function:**

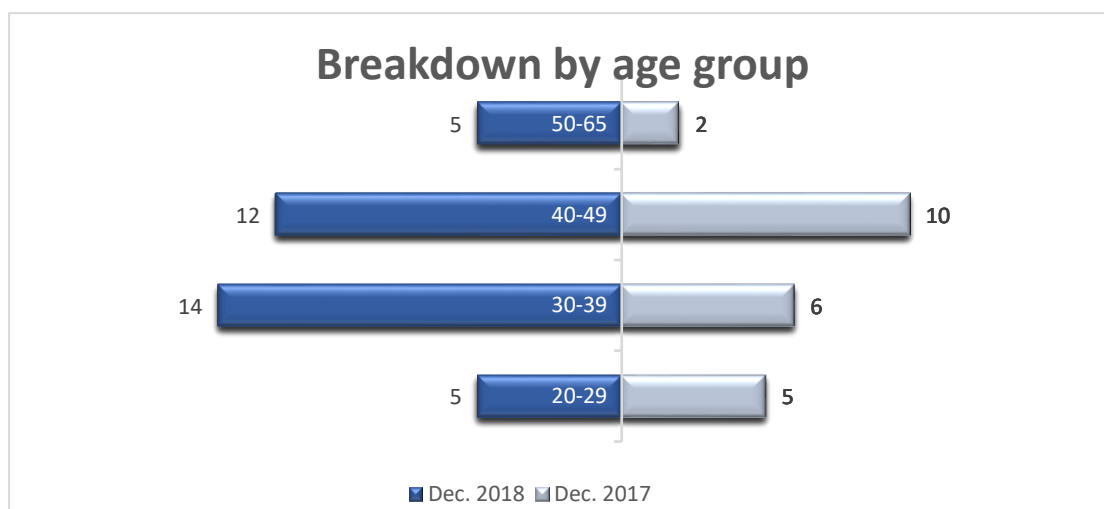
The staff has extensive experience in the management of research and innovation. As shown in the table below, employees spend most of their working hours on research and development, i.e., more than 70% of their working hours:



**This shows the importance given to research within POXEL.**

### **Seniority:**

On December 31, 2018, the average age of the staff was 40 years (slightly down compared with 2017), with an average length of service of approximately two years and eight months (against an average length of service of approximately three years and two months on December 31, 2017). The decline in seniority is explained by the large number of recruitments made the previous year.



The Company benefits from a balanced distribution of its workforce, between young professionals and more experienced employees.

### **Remuneration:**

Personnel expenses (from the IFRS accounts) rose by 13% in 2018. They were one of the Company's main operating expense items. This increase primarily reflects the expansion of clinical development activities.

Personnel expenses per fiscal year	2 018	2 017	2 016	2 015	2 014
As a percentage of operating expenses	8,32%	16,01%	11,36%	13,55%	15,98%
<b>Total amount in k€</b>	<b>5 462</b>	<b>4 852</b>	<b>3 134</b>	<b>1 856</b>	<b>1 418</b>

The pay scale only varies based upon the position of each employee and the associated seniority.

The Company has implemented a bonus policy based on reaching of common objectives of the Company and on reaching measurable individual objectives. The weight of the objectives in the bonus calculation varies according to the employees' seniority. The attribution criteria and bonus amount are defined at the annual review of employees, in function of objectives set the previous year at their meeting with their line manager. A summary review of the previous year is compiled in order to validate the meeting of objectives and the final allocation of the bonus. The objectives for the current year are also discussed.

#### **b) Organization of labor:**

The employment contracts of the employees are submitted to the Collective Agreement of the Pharmaceutical industry.

Since October 1, 2015 the working time of managerial staff is calculated based on the total working days in a year ("forfait-jour"). A teleworking agreement was prepared in 2018 and signed in January 2019, thus ushering in a new work organizational structure. Teleworking is a solution to the need to ease the constraints related to the organization of work and the needs of employees. A company collective agreement on the right to disconnect was also prepared in 2018 and signed in January 2019, in order to bring the proper use of IT and digital tools in line with the necessary respect of rest and holiday periods, as well as with work-life balance.

Absenteeism remains very low in the Company. There was practically no absenteeism between 2016 and 2018.

Absenteeism	2016	2017	2018
total days worked	6 224	7 602	9 892
work outage / illness in days	6	26	6
<b>% absenteeism / days worked</b>	<b>0,1%</b>	<b>0,3%</b>	<b>0,1%</b>

Absenteeism is calculated on the basis of the hours worked by the entire staff of the company (employees on permanent contract versus employees on temporary contracts).

#### **c) Labor relations:**

Labor relations are organized around the Company institutions representing the personnel, mainly the staff representatives. The Company has four staff representatives (two principal and two deputy representatives) who were elected in June 2018 for a four-year term. The Company maintains a constructive dialog with staff representatives; a dialog driven by transparency, consultation, and attention.

#### **d) Health and Safety:**

The safety of the personnel and the management of the working conditions are fundamental for the sustainable development of the Company. The Company has made the compulsory reports concerning its facilities and has received approvals to perform its activities. The control and maintenance of the



technical and electric facilities has been made according to the applicable legislation. The staff has the necessary clearances and training for using the equipment and for keeping up with the health and safety requirements.

The single occupational risk assessment document is also regularly updated. These documents are at the disposal of the whole staff. As stated earlier, the company is working on teleworking agreements in order to reduce commuting, and on the right to disconnection, in order to prevent information overload and stress. The Internal Regulations were updated in May 2017. It summarizes the main rules of workplace health and safety that employees must follow, and presents the common rules applicable to all employees to allow them to evolve in satisfactory work and safety conditions.

Upon hiring, the new employee follows an integration pathway, intended to allow him to meet key persons and learn about the rules of operation of the Company. At the end of a period of one month, an informal intake report is prepared. A recruitment medical examination is organized for all staff. Subsequently, a medical examination is organized every two years.

Following negotiations with various agencies, the Company has signed a medical insurance contract offering guarantees to its employees in respect of the Responsible Contract, which took effect as of January 1, 2016. The Company provided access to restaurant coupons to its employees in 2017.

In 2018, the Company did not identify any work or commuting accidents. No occupational disease or professional character has been declared in 2018 nor in the previous financial year. No permanent incapacity has been notified to the Company for this financial year and the previous years.

#### **e) Training:**

The Company has implemented a HR management policy, which aimed at attracting and retaining the best profiles. This is achieved by pursuing a proactive compensation policy and keeping the training budget adapted to the needs of the employees and their activities. Moreover, individual career-building support is offered to each employee. The staff is highly skilled and the Company attaches great importance to maintaining this high individual level of knowledge and skill of each employee.

A training plan has been established since 2017. It is analyzed in the table below. It included a seminar to which all the Company's employees were convened, and which represented 406 training hours in 2017, as well as collective training courses in 2018 (including 500 hours of Japanese language lessons, 231 hours on the corporate culture and 75 hours on intercultural relations).

Employees can make specific requests during the year depending on their specific needs. Their requests are thus submitted to the line manager for validation.

<b>Monitoring of training plans</b>	<b>2018</b>	<b>2017</b>	<b>2016</b>	<b>2015</b>	<b>2014</b>
Number of training courses attended by employees	19	12	13	18	12
Number of training hours attended	1 397	522	97	135	133
<i>Note: 2017 &amp; 2018 training courses with collective training are taken into account</i>					

Staff training in the Company mainly focuses on technical training and management training.

#### **f) Equality of treatment:**

In 2017, Ms. Kumi Sato was appointed a director. This increased the percentage of women on the Board of Directors to 25%, in accordance with regulations.

When hiring, in order to avoid any discrimination during hiring procedures, the Company strives to make an objective selection based on the concrete needs of the Company. In this framework, a job description is drafted for each of the proposed positions. It describes the missions entrusted, the responsibilities related to the position, the people with whom the new employee will interact and the skills required for the position. This ensures a non-discriminatory recruitment process that is based solely on the criteria of skills and talent.

In order to clarify and facilitate recruitment, the company has also added a Careers section to its Internet site where offers of employment are posted.

The Company pursues a non-discriminatory wage policy. Regardless of their occupational group ("catégorie professionnelle"), the compensation management and individual profile evaluation procedures are identical for both men and women. The Company hires without any discrimination every person presenting all the qualifications required for its development.

This also applies to the access to training. The Company, concerned by the insertion of young professionals on the labor market, offers employment to young people whenever possible, namely through traineeships.

## 1.2. Environmental information

Due to its activity (research & development), the Company considers that its environmental impact is low. Its activities do not include any industrial manufacturing or distribution, the heavy use of raw materials, or significant discharges into the environment. Its activities do not require the use of mains gas, nor specialty gases. The Company does not generate any particular noise nuisance for the staff or the local population. The Company estimates that the discharges into the air related to its activity are not significant and have little impact on the air quality. The details concerning the greenhouse gas emissions related to plane travel are indicated below.

In addition, the Company operates within a highly constrained regulatory framework, to which it complies. The Company has all the necessary approvals to carry out its activities.

In this context, only the following issues have been identified as relevant and will therefore be dealt with in the rest of the Report:

- General environmental policy
- Measures taken to preserve and develop biodiversity
- Sustainable use of resources:
  - o Energy consumption
  - o Greenhouse gas emissions

### **General environmental policy:**

**In order to limit travel and its impact on the environment, the Company attempts to use video conferencing and teleconferencing tools whenever possible in the course of its internal and external meetings.**

In Lyon, the Company has leased premises in a building certified BBC (*Bâtiment Basse Consommation*), rated B for energy consumption (53.7 kWhPE/sq.m/year, almost class A, for which the limit is 50) and

A for greenhouse gas emissions (0.6 kg eq. CO<sub>2</sub>/sq.m/year) This building was recognized by the Prebat (Program of Research on Energy in Buildings) in 2009.

For the activities and investments for which it is responsible, the Company also seeks to limit its impact on the environment.

- For example, the Company generates little waste. It mainly generates administrative waste, paper or office consumables (printer cartridges). For office consumables, the Company has signed a contract for the collection of this waste by a specific contractor in charge of recycling them. Special containers have been installed in the offices in Lyon to collect paper, thin cardboard, bottles and coffee pods.

The Company has set up a specific follow-up process for the manufacturing, packaging, use and destruction of the active ingredients that are used in the pre-clinical and clinical studies performed by external providers. As such, the Company checks the destruction certifications obtained by the CRO (the contract research organization that performs the external clinical tests).

#### **Measures taken to preserve and develop biodiversity:**

The Company does not directly conduct pre-clinical or clinical studies. In order to protect biodiversity in the framework of carrying out such tests, the Company demands that its service providers comply with strict safety rules and with the regulations applicable in the countries, where the studies are carried out. In addition, the studies outsourced by the Company do not have a direct impact on global climate change and the evolution of biodiversity.

#### **Circular economy: waste prevention and management:**

The Company has signed contracts with specialized service providers for the recovery of used consumables and the disposal of its archives. Printer consumables are collected directly by a service provider. The Company also has a contract with a specialized provider for the disposal and recycling of waste electric and electronic equipment.

The company does not operate in the agri-food area, so measures relating to the food waste are not applicable.

#### **Circular Economy: Sustainable use of resources:**

The Company's activity is focused on research and not on manufacturing. Therefore, it does not buy significant quantities of raw materials. Similarly, energy and water consumption is limited to servicing IT tools (and other electrical facilities) and the sanitary installations of the employees. This consumption is not significant.

Therefore, the main greenhouse gas emissions remain limited to releases related to the consumption of electricity (main factor of scope 2) and employees' travel (cars/aircraft/trains, main factor of scope 3) whose impact is described in the following paragraphs. There are no other significant emission factors involved in the cycle of activity of the Company.

Electricity consumption was 16,449 kWh in 2018 for premises leased on the two floors of the building in Lyon (compared with 13,512 kWh in 2017), representing emissions of roughly 1.2 tons of CO<sub>2</sub> equivalent. These data correspond to electricity consumption on the basis of actual data for 2017 and

2018. The Company does not monitor the electricity consumption of its offices in Paris, Tokyo and Boston which were deemed to be non-significant given the surface areas occupied.

Given its activity, Company employees have had to travel by plane on domestic and international flights many times over the past two years. Consequently, the Company has set up criteria to monitor CO<sub>2</sub> emissions caused by those trips. This information has been estimated from data collected internally. It does not take into account the impact of fuel combustion for air travel.

Greenhouse gas emissions in teq CO <sub>2</sub>			
	2016	2017	2018
TOTAL	285	405	568

Train travel of employees is insignificant, and its impact is estimated at approximately 0.5 tons of CO<sub>2</sub> equivalent releases of greenhouse gases for all 2018 trips.

## 2) Information relating to societal sustainable development commitments

### Measures granted in favor of consumer health and safety:

The Company focuses on consumer health and safety: researching and developing an innovative treatment of metabolic diseases, namely type 2 diabetes and NASH. These research activities are described in the *document de référence* published for the December 31, 2018 year-end.

The development of a new drug-candidate follows a rigorous evaluation process, in which the safety related to the use of the drug-candidate is the most important concern for the Company that develops the product and the competent authorities in charge of its evaluation. As a consequence, the Company has to comply with the applicable rules (Good Manufacturing Practices, Good Laboratory Practices, Good Clinical Practices), and the rules set up by the bodies in charge of the evaluation of those new drugs and the public health protection, as the European Medicine Agency (EMA), the Pharmaceuticals and Medical Devices Agency (PMDA) in Japan, of the Food and Drug Administration (FDA) in the United States.

At the date of publication of this document, both the pre-clinical and clinical studies carried out on the three main products of the Company, Imeglimin, PXL770 and PXL065, have highlighted good tolerance of these three drug candidates.

In October 2017, the Company has entered into a strategic partnership with Sumitomo Dainippon Pharma for the development and marketing of Imeglimin in Japan, China, South Korea, Taiwan and in nine other countries of Southeast Asia. The Company and Sumitomo Dainippon Pharma co-pilot the phase III development of Imeglimin in Japan. Sumitomo Dainippon Pharma bears all the development costs associated with this program and will be responsible for the marketing of Imeglimin in Japan. In China, South Korea, Taiwan, and in nine other countries of South- East Asia, Sumitomo Dainippon Pharma alone will act and pilot the development and the marketing of Imeglimin.

At the end of 2017, Imeglimin entered into phase III in type 2 diabetic patients in Japan. This program continued in 2018 and will be completed in 2019. Phases I and II of the development of Imeglimin

conducted in more than 1,200 patients with type 2 diabetes in the United States, Europe and Japan have demonstrated its efficacy and good tolerance, as monotherapy and in combination with other diabetic treatments.

PXL770, the second drug-candidate, is a direct activator of adenosine monophosphate-activated protein kinase (AMPK). AMPK is a central regulator of several metabolic pathways that have a role in the metabolism of lipids, glucose homeostasis and inflammation. Based on this central role, the targeting of AMPK offers the opportunity to pursue a wide range of indications to treat chronic metabolic disease, including diseases affecting the liver, such as nonalcoholic steatohepatitis (NASH). Phase Ib with the administration of multiple and increasing doses on nearly 50 subjects demonstrated a favorable safety and tolerability profile with no reported serious adverse effects or any particular sign of toxicity. Phase IIa development will be launched in 2019 to demonstrate the efficacy and safety of PXL770 on nearly 120 patients suffering from nonalcoholic steatohepatitis (NASH).

It must be noted that in 2016, the Company has obtained a protection by patent awarded by the United States Patent and Trademark Office (USPTO) for this product.

In August 2018, the Company signed a strategic agreement with DeuteRx for the acquisition of PXL065, an innovative drug-candidate at the clinical development stage for the treatment of NASH, as well as other programs for the treatment of metabolic diseases. PXL065 is currently in Phase I development studies, and the results available on the date of writing this report show its safety and excellent tolerability, without any undesirable events.

#### **Sponsoring and philanthropy:**

To enhance its visibility with researchers, the Company was one of the sponsors for the “MEETOCHONDRIE” conference held in May 2017 and May 2018. This patronage has led to media coverage for the Company thanks to the presence of its logo on communication media. Poxel was also a sponsor of the ALD Connect 2018 meeting held in Philadelphia in November.

#### **Outsourcing and suppliers:**

The Company has not set up any specific CSR criteria in its supplier selection procedure. Its selection criteria are based on the supplier’s ability to meet the Company’s requirements, which may be related to products, manufacturing procedures, process and equipment, staff qualifications, quality management systems or implementation times of the services entrusted.

A specific operating process related to supplier selection and management was set up and is available to any employee. Every Company supplier is submitted to this process. As a consequence, the following supplier families are concerned:

- The CRO (Clinical Research Organizations) which performs studies;
- The CMO (Clinical Manufacturing Organizations) which provides the Company with the research necessary material.

Poxel thus creates shared value by involving the suppliers and health professionals in its corporate responsibility approach. The R&D strategy is structured into development projects, which are coupled with specifications in order to entrust the implementation to one or several sub-contractors, who may be industrial partners, Contract Research Organizations, academia (e.g., University Hospital Centers,

CNRS, INSERM, Yale University in the United States, etc.), sometimes with the help of recognized experts, with which the Company maintains relations for the development of its molecules.

Several sub-contractors are contacted for each development project. Their selection is based on objective criteria defined upstream (incorporating, at minimum, aspects of expertise in the field, quality, successful experience, cost and timing). The collaboration of the Company with its service providers is part of a process of continuous quality improvement. In this respect, during its collaborations, Poxel performs audits to confirm that these stakeholders comply with best practices and regulatory standards.

**Methodology note:**

**This report presents CSR data concerning Poxel (the “Company”) for fiscal 2017 and Poxel and its Japanese subsidiary for fiscal 2018. Financial year 2017 covers the period between January 1, 2017 and December 31, 2017. Financial year 2018 covers the period between January 1, 2018 and December 31, 2018. The Company has two geographical locations in France: its head office in Lyon and an office in Paris, as well as an office in Tokyo, Japan since September 1, 2018. Unless specified in the report, the data presented aggregates information relating to these three sites.**

**All the indicators are monitored by the Financial Controller, Director of Human Resources, the Chief Administrative Officer and the Chief Financial Officer. The employment indicators are established based on a non-accounting summary, supported by employment data arising from salaries and personnel files.**

**Concerning environmental indicators, non-accounting monitoring is performed. Based on this monitoring, actual electricity consumption is calculated on the basis of consumption billed. We used a CO<sub>2</sub> equivalent emission factor of around 72g CO<sub>2</sub>/kWh based on the ADEME carbon accounting v7.1.**

**Information was collected by the Human Resources Director and the Chief Administrative Officer. The information was checked by the Financial Controller and the Chief Financial Officer.**

## 27.CONCORDANCE TABLES

The table of concordance below allows you to identify in this *document de référence*:

Information comprising the annual financial report (Article L. 451-1-2 of the French Monetary and Financial Code and Article 222-3 of the AMF General Regulation),

Information comprising the annual management report (Article L. 225-100 and following of the French Commercial Code).

### 27.1. Table of concordance with the Annual Financial Report

Annual Financial Report		Document de référence	Pages
1	Certification of the person responsible for the annual financial report	Section 1	13
2	Management report	See index below	
3	Report on business governance	See index below	
4	Communication of auditors' fees	Section 20.11	245
5	Financial statements prepared in accordance with IFRS standards	Section 20.1	191
6	Report of the statutory auditors on the consolidated financial statements prepared in accordance with IFRS standards	Section 20.2	237
7	Annual financial statements	Section 26.1	278
8	Report of the Statutory Auditors on the annual financial statements	Section 26.2	308

### 27.2. Table of concordance with the management report

Annual management report		Document de référence	Pages
1	Situation of the Company and activity during the past financial year	Sections 6 and 20	57 and 191
2	Objective and exhaustive analysis of the Company's business development, results and financial situation, in particular the debt situation of the Company and the Group	Sections 9, 10 and 20	91, 103 and 191
3	Allocation of results	Section 20.6	244
4	Expenses not deductible for tax purposes	Section 20.7	244
5	Summary of dividends distributed	Section 20.5.1	243

6	Key financial and non-financial performance indicators, including information on environmental and personnel matters	Section 3 and 26.3	15 and 315
7	Principal risks and uncertainties the company is facing / Use of financial instruments by the Company / Technological risks	Section 4	17
8	Information on financial risks related to the effects of climate change	Section 4.8	50
9	Internal control and risk management procedures relating to the preparation and processing of accounting and financial information	Section 16.6	173
10	Information on timeframes for payment of suppliers	Section 20.9	245
11	Activity in research and development	Sections 9.1.3 and 11	94 and 112
12	Foreseeable developments and prospects for the future	Sections 6 and 12.2	57 and 140
13	Important events that have occurred since the close of the year	Section 20.10	245
14	Participation of employees in the capital at the end of the financial year	Section 17.3	179
15	Summary of operations of the executives and the persons mentioned in Article L. 621-18-2 of the French Monetary and Financial Code on Company securities sold during the financial year	Section 18.4	181
16	Taking into account the social and environmental consequences of the activity, including the consequences on climate change and the use of goods and services produced, as well as societal commitments to sustainable development, the circular economy, the fight against food waste and the fight against discrimination and the promotion of diversity	Section 26.3	315
17	Activities of subsidiaries and controlled companies	Sections 7 and 25	97 and 280
18	Significant stakes assumed in companies having their headquarters in France, or assuming control of such companies; transfers of said stakes	Sections 7 and 25	89 and 277
19	Information relating to the distribution of capital and the self-assessment - Share Buyback Program	Section 18 and 21.1.3	180 and 247
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