Teaching your cells to treat your disease

A French limited liability company (*société anonyme*) with capital of €2,577,465.20

Registered office: Les Cardoulines, Allée de la Nertière, 06560 Valbonne –Sophia Antipolis

Grasse Trade and Companies Register n° 435 361 209

2015
REGISTRATION DOCUMENT

DISCLAIMER

The English version of the registration document is a free translation of the official registration document prepared in France and registered with the French financial market authority (*Autorité des Marchés Financiers* – AMF) on May 24, 2016 under number R.16-048. Certain sections have been intentionally omitted.

All possible care has been taken to ensure that the translation is an accurate representation of the original. However, in all matters of interpretation of information, views or opinion expressed therein, the original version of the registration document in French takes precedence over this translation.

Copies of the French language version of this registration document can be obtained free of charge from TxCell (Les Cardoulines, Allée de la Nertière, 06560 Valbonne – Sophia Antipolis), on TxCell's website (www.txcell.com) and on the AMF's website (www.amf-france.org).

Note

In this registration document (the "*Document de Référence*"), the terms "TxCell" or the "Company" mean the company TxCell, a French limited liability company (*société anonyme*) whose head office is located at Les Cardoulines Sophia Antipolis – Allée de la Nertière – 06560 Valbonne, Sophia Antipolis, France, registered with the Grasse trade and companies register under number B 435 361 209.

The *Document de Référence* presents notably:

- the annual financial statements prepared according to French GAAP for the year ended December 31, 2015, and the corresponding statutory auditors' report, presented in paragraph 26.1 of the *Document de Référence*; and
- the annual financial statements prepared according to IFRS for the year ended December 31, 2015, and the corresponding statutory auditors' report, presented respectively in paragraph 20.1 and 20.2 of the *Document de Référence*.

A glossary defining certain terms used in the *Document de Référence* can be found in chapter 27 of the *Document de Référence*.

Disclaimer

Market and competition information

The *Document de Référence* contains, specifically in chapter 6 *"Overview of business activities"*, information relating to the Company's markets and competitive position. Unless otherwise stated, the information contained in the *Document de Référence* on markets and product categories are estimates made by the Company and are provided for illustrative purposes only. This information derives, specifically, from studies conducted by external sources. Publicly available information which the Company believes to be reliable has not been verified by an independent expert, and the Company cannot guarantee that a third party using different methods to collect, analyze and calculate data on these markets would obtain the same results. In addition, the Company's competitors may define markets and categories differently.

Forward-looking information

The *Document de Référence* contains information on the Company's prospects and development priorities. This information is sometimes identified by the use of the future or the conditional tense or forward-looking words such as "consider", "envisage", "think", "aim to", "expect", "understand", "should", "aspire to", "estimate", "believe", "wish", "could" or, where appropriate, the negative of those terms or any other variant or similar terminology. This information is not historical data and should not be interpreted as a guarantee that the facts and data set out herein will happen. This information is based on data, assumptions and estimates which the Company deems reasonable. It is subject to change or amendment due to uncertainties related, specifically, to the economic, financial, competitive or regulatory environment. This information is mentioned in various paragraphs of the *Document de Référence* and contains data about the Company's intentions, estimates and objectives, particularly regarding the market in which it operates, its strategy, growth, results, financial position, cash position and forecasts. The forward-looking information contained in the *Document de Référence* is provided only as at the date of the *Document de Référence*. The Company operates in a constantly changing competitive environment. It may therefore not be able to anticipate all the risks, uncertainties or other factors that may affect its business, their potential impact on its business or the extent to which the occurrence of a risk or a combination of risks could have significantly different results from those implied in any forward-looking information, it being noted that none of this forward-looking information constitutes a guarantee of actual results.

Risk factors

Investors are advised to carefully read the risk factors described in chapter 4 "*Risk Factors*" of the *Document de Référence* before making any investment decision. The occurrence of any or all of these risks may have a material adverse effect on the Company's business, financial position, results or prospects. In addition, other risks, not yet identified or deemed immaterial by the Company at the date of the *Document de Référence*, could also have a material adverse effect.

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1. PERSONS RESPONSIBLE

1.1 Person responsible for the *Document de Référence*

Mr. Stéphane Boissel, Chief Executive Officer.

1.2 Statement of the person responsible

I hereby certify that, having taken all reasonable measures in this respect, the information contained in the *Document de Référence* is, to the best of my knowledge, in accordance with reality and does not contain any omission likely to affect its meaning.

I have received a letter of completion of work from the statutory auditors in which they state that they have verified the information concerning the financial position and the financial statements presented in the *Document de Référence*, and have carried out an overall review of the *Document de Référence*.

The financial statements prepared according to IFRS for the year ended December 31, 2015 presented in the *Document de Référence* were approved without reservation in a report by the statutory auditors, presented on pages 187 and 188 of the *Document de Référence*, which contains the following observation: *"Without questioning the opinion expressed above, we would like to draw your attention to note 2.2 "Going-concern principle" of the notes to the financial statements, which states the financial position of the company at December 31, 2015, and the measures envisaged for the company to cover its cash requirements."*

The financial statements prepared according to IFRS for the year ended December 31, 2014, incorporated by reference in the *Document de Référence* were approved without reservation in a report by the statutory auditors, presented on pages 176 and 177 of the *document de référence* registered with the AMF on June 11, 2015 under the number R.15-049. This report contains no observations.

The financial statements prepared according to IFRS for the year ended December 31, 2013, incorporated by reference in the *Document de Référence* were approved without reservation in a report by the statutory auditors, presented on pages 192 and 193 of the *document de base* registered with the AMF on March 13, 2014 under the number I.14-008, which contains the following observation: *"Without questioning the opinion expressed above, we would like to draw your attention to note 5.3.2 "Going-concern principle" of the notes to the financial statements, which states the financial position of the company at December 31, 2013, and the measures taken by the company to cover its cash requirements."*

French original signed in Valbonne, France
on May 24, 2016

Stéphane Boissel
Chief Executive Officer

2. STATUTORY AUDITORS

2.1 Principal statutory auditors

ERNST &YOUNG AUDIT

represented by Cédric Garcia, partner

Tour First, 1 place des Saisons

Paris La Défense – 92400 Courbevoie – France

Start date of first term: December 20, 2013

Term of office expiry date: at the annual general meeting convened to vote on the financial statements for the financial year ending December 31, 2018.

AUDIT CONSEIL EXPERTISE SAS, a member of PKF INTERNATIONAL

represented by Guy Castinel, partner

17, boulevard Augustin Cieussa

13007 Marseille – France

Start date of first term: Bylaws of the Company incorporated on April 12, 2001

Term of office expiry date: at the annual general meeting convened to vote on the financial statements for the financial year ending December 31, 2018.

2.2 Alternate statutory auditors

AUDITEX

Tour First, 1 place des Saisons

Paris La Défense – 92400 Courbevoie – France

Start date of first term: December 20, 2013

Term of office expiry date: at the annual general meeting convened to vote on the financial statements for the financial year ending December 31, 2018.

FIDEA CONTROLE SARL

101, rue de Miromesnil

75008 Paris – France

Start date of first term: May 22, 2013

Term of office expiry date: at the annual general meeting convened to vote on the financial statements for the financial year ending December 31, 2018.

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

2.3 Fees paid to the statutory auditors

The following table sets out the amount of fees charged by the statutory auditors and members of their network to the Company in 2014 and 2015:

In thousands of euros	Audit Conseil Expertise member of PKF International				Ernst & Young			
	2015		2014		2015		2014	
	Amount excluding taxes	%	Amount excluding taxes	%	Amount excluding taxes	%	Amount excluding taxes	%
Statutory audit	52	90%	47	53%	84	87%	77	38%
Other audit-related services	6	10%	42	47%	12	13%	128	62%
Total fees	**58**	**100%**	**89**	**100%**	**96**	**100%**	**205**	**100%**

There were no other services directly linked to the statutory auditors' mission rendered by any members of the network of the statutory auditors to the Company.

3. SELECTED FINANCIAL INFORMATION

The selected financial information presented below is selected from the Company's annual financial statements for the financial years ended December 31, 2015 and 2014, which are set out in paragraph 20.1 of the *Document de Référence* and prepared in accordance with International Financial Reporting Standards ("IFRS") as adopted by the European Union.

The Company's unconsolidated annual financial statements for the financial year ended December 31, 2015 prepared in accordance with the applicable French accounting standards, which are the only legally valid financial statements, are included in the statutory auditors' report on the financial statements and reproduced in paragraph 26.1 of the *Document de Référence*. The Company's annual financial statements for the financial year ended December 31, 2014 prepared in accordance with the applicable French accounting standards are incorporated by reference to the *Document de Référence* (see chapter 24 of the *Document de Référence*).

The key figures summarized below should be read in conjunction with (i) the Company's audited financial statements prepared in accordance with IFRS for the financial years ended December 31, 2015 and 2014, presented in paragraph 20.1 of the *Document de Référence* or incorporated by reference (ii) the review of the Company's results and financial position presented in chapter 9 of the *Document de Référence* or incorporated herein by reference (iii) the review of the Company's cash flow and equity position presented in chapter 10 of the *Document de Référence* or incorporated herein by reference.

Extracts of the financial information for the financial years ended December 31, 2015 and December 31, 2014 (in accordance with IFRS)

Selected financial information from income statement

In thousands of euros	31/12/2015	31/12/2014
Revenue	920	1,327
Other income	3,718	2,094
Total current operating expenses	(14,782)	(11,694)
Current operating profit / (loss)	(10,145)	(8,273)
Other operating income and expenses	(1,167)	0
Operating profit / (loss)	(11,312)	(8,273)
Financial income and expenses	15	4
Net profit / (loss) before tax	(11,297)	(8,269)
Net profit / (loss)	(11,297)	(8,269)
Basic earnings per share (in €) *	-0.92	-0.78

* The Company's shareholders' meeting held on March 7, 2014 approved the Company's reverse stock split at a ratio of five existing shares for one new share. According to IAS 33 "Earnings per share", the net earnings per share is presented with a retrospective adjustment of the reverse stock split for all financial years presented, in order to allow comparability.

Selected financial information from balance sheet

In thousands of euros	31/12/2015	31/12/2014
Total assets	**20,720**	**20,043**
Non-current assets	**6,939**	**1,543**
Intangible assets	5,907	8
Property, plant and equipment	876	1,404
Financial assets	155	131
Current assets	**13,781**	**18,501**
Trade receivables	4	1,000
Other current assets	4,570	3,583
Cash and cash equivalents	9,208	13,917
Total liabilities	**20,720**	**20,043**
Shareholder's equity	**11,589**	**14,712**
Non-current liabilities	**1,664**	**1,990**
Portion of long and medium-term financial payables maturing over one year	1,641	1,627
Other non current liabilities	23	363
Current liabilities	**7,467**	**3,341**
Trade payables	1,608	1,395
Other payables	5,087	1,554
Current provisions	772	392

Selected financial information from cash-flow statement

In thousands of euros	31/12/2015	31/12/2014
Cash flows generated from / (used in) operations	(9,687)	(6,148)
Change in working capital	(379)	(785)
Net cash flows generated from / (used in) operating activities	**(10,066)**	**(6,933)**
Net cash flows generated from / (used in) investing activities	**(2,274)**	**(656)**
Net cash flows generated from / (used in) financing activities	**7,631**	**20,830**
Net increase / (decrease) in cash and cash equivalents	(4,710)	13,242
Cash and cash equivalents at the beginning of the year	13,917	676
Cash and cash equivalents at the end of the year	9,208	13,917

4. RISK FACTORS

Investors are advised to consider all of the information contained in the *Document de Référence*, including the risk factors described in this chapter before deciding to acquire or subscribe for shares in the Company. When preparing the *Document de Référence*, the Company conducted a review of the risks that could have a material adverse effect on the Company, its business, financial position or ability to achieve its objectives, and has identified no material risks other than those described below. However, investors' attention is drawn to the fact that there may or could be other risks, which are unknown or deemed, at the date of the *Document de Référence*, unlikely to have an adverse effect on the Company, its business, financial position, results or prospects.

Risks presented below are summarized in the following table:

Section	Nature of the risk	Summary of the risk	Risks specific to	
			the Company	the sector
4.1	**Risks associated with the Company's business**			
4.1.1	Risks associated with clinical development	*Development of the Company's products may be delayed or unsuccessful*	X	
		The clinical trials are subject to authorizations from regulatory authorities		X
		The clinical trials are submitted to continuous monitoring from the regulatory authorities		X
		The Company has limited experience in the clinical development of products	X	
		The development of a new type of cell therapy generates many uncertainties	X	
4.1.2	Risks related to the manufacturing process for products developed by the Company	*The transfer of the manufacturing of the product Ovasave® could cause additional delays to the clinical trials CATS29*	X	
		The optimization of the manufacturing process is necessary to the financial viability of the products of the Company	X	
		The drug candidates of the Company are biologics and their manufacture is complex. The Company may encounter difficulties in production, particularly with respect to process development or scaling-out of manufacturing capabilities. If the Company or any of its CMOs encounter such difficulties, its ability to provide supply of its drug candidates for clinical trials could be delayed or stopped, or the Company may be unable to maintain a commercially viable cost structure.	X	
4.1.3	Risks associated with the technology platform	*The ongoing products are based on the same platform of products, safety or therapeutic efficacy issues could question this platform*	X	
4.1.4	Risks associated with the market and competition	*The Company could be dependent on its most advanced product, Ovasave®, due to the less advanced stage of development of its other products*	X	
		Competition on the market of the treatment of diseases targeted by the Company is intense		X
		The commercial success of the Company's products cannot be guaranteed		X
4.1.5	Risks associated with the Company's business and strategic development	*Obtaining marketing authorizations and other certifications prior to any marketing may be uncertain*		X
4.1.6	Risk of dependence on third parties	*The Company could encounter a dependency situation vis-à-vis subcontractors to which it will outsource the manufacturing of the products it develops*	X	
		The supply of specific raw materials and products needed to conduct clinical trials and manufacture the Company's products is not guaranteed	X	
		The Company could find itself in a situation where it is dependent on the subcontractors to whom it outsources its clinical trials	X	
4.2	**Regulatory and legal risk**			
4.2.1	Risks associated with the Company's intellectual property rights	*Protection of the Company's patents, patents applications and other intellectual property rights is uncertain*		X
		The Company benefits from certain intellectual property rights through joint ownership or licenses	X	
		The Company cannot guarantee that it will not infringe intellectual property rights or that its own rights will not be infringed		X
		The Company may not be able to prevent the disclosure to third parties of confidential information likely to have an impact particularly on its future intellectual property rights		X
4.2.2	Risks associated with product liability	*Criminal complaints or lawsuits could be filed or brought against the Company by patients, regulatory agencies, pharmaceutical companies or any other third party using or marketing its products*		X

Section	Nature of the risk	Summary of the risk	Risks specific to	
			the Company	the sector
4.2.3	Risks associated with a restrictive and evolving regulatory framework	*The cell therapy treatment developed by the Company being very innovative, regulations on the subject are still being drawn up, additional requirements may come into play*		X
4.2.4	Risks associated with the pharmaceutical company status of the Company or its manufacturers	*The Company's subcontractors could lose their pharmaceutical company status*		X
		The Company could have to produce itself the drugs it develops but cannot guarantee that it will the pharmaceutical company status will be granted, nor that they be partially or fully suspended or revoked	X	
4.3	**Risks associated with the Company's organization**			
4.3.1	The Company could lose key employees and not be able to attract other qualified personnel	*The Company competes with other research entities and academic institutions to recruit and retain highly qualified scientific, technical and management personnel*	X	
4.3.2	The Company's development will depend on its ability to manage growth	*As part of the Company's growth strategy, the Company will likely be required to develop its operational capacity, which could use a significant amount of its internal resources*	X	
4.4	**Industrial risks**	*The Company's operations involve the handling of biological and chemical materials during research and manufacturing, which exposes it to health risks (occupational diseases)*	X	
4.5	**Risks related to information systems**	*The Company has formalized rules to protect the safety of information systems and their users, but cannot guarantee absolute safety and availability of the information system as well as the integrity and the confidentiality of data*	X	
4.6	**Financial risks**			
4.6.1	Risks associated with historical and future losses	*The Company could have to seek for other sources of financing and cannot guarantee that the terms proposed by any new partner would be identical or even financially acceptable*	X	
4.6.2	Risks relating to the business model	*The duration of treatment will vary depending on each patient and according to their response to the treatment, revenues and margins could therefore vary for each patient, given that production costs are concentrated on the manufacturing phase of the personalized product, regardless of the length of the treatment*	X	
4.6.3	Risk associated with research tax credit	*The Company cannot exclude the possibility of the tax authorities challenging the methods used by the Company for calculating research and development expenditure or of the CIR being called into question (for past or future fiscal years) pursuant to a regulatory change or it being challenged by the tax authorities*	X	X
4.6.4	Risks associated with carrying losses forward in the future	*It cannot be excluded that regulatory or legislative developments regarding corporation tax will call into question, in whole or in part, the possible offsetting of these prior losses against future profits, or impose a time limit on such offsetting*	X	X
4.6.5	Risks related to access to public grants and advances	*In the event the Company does not comply with the contractual conditions set out in innovation grant agreements entered into, it may be required to repay any advances early*	X	
4.6.6	Dilution risk	*Exercise of instruments giving entitlement to the outstanding capital as well as all new issuances or allotments would lead to a potentially significant dilution for the current and future shareholders of the Company*	X	
4.7	**Market risk**			
4.7.1	Liquidity risk	*The Company may need to strengthen its capital base or seek additional funding to ensure its development*	X	
4.7.2	Foreign exchange rate risk	*The Company considers that it is not exposed to foreign currency exchange risks in that only a small portion of its supplies are obtained outside the euro zone and invoiced in foreign currencies*	X	
4.7.3	Credit risk	*Credit risk relating to liquid assets, equivalents and short term financial instruments is not significant in view of the quality of the co-contracting financial institutions*	X	
4.7.4	Interest rate risk	*The Company does not have any variable-rate debt. Its debt repayments are not subject to interest rate risk*	X	
4.7.5	Equity risk	*The Company considers that it is not exposed to any risk associated with equities or other financial instruments, given that it does not hold any interest or security in listed companies*	X	
4.8	**Insurance and risk cover**	*Quantification of potential risks in the absence of direct loss or loss indicators for its industry, makes it difficult to determine an insurable amount*		X
4.9	**Significant events and legal action**	*The Company could be subject to governmental, judiciary or arbitration proceedings. With the exception of an adjustment notice for a non-material amount of €12 thousand, there are no other ongoing procedures to the Company's knowledge*		X

4.1 Risks associated with the Company's business

4.1.1 Risks associated with clinical development

Development of the Company's products may be delayed or unsuccessful

The Company conducts preclinical and clinical programs with an aim over time to market personalized cell therapies for the treatment of severe chronic inflammatory diseases, in particular of the bowel (such as Crohn's disease) or ocular area (such as uveitis) (please refer to paragraph 6.1.1 of the *Document de Référence*).

The development of a drug candidate is a long and expensive process consisting of several phases which aim to demonstrate the therapeutic benefit of the drug candidate for one or more specific indications. The failure of any one of the various clinical phases for a given indication could delay the development, manufacturing and marketing of the therapeutic drug concerned or halt its development. Similarly, during clinical trials, patient recruitment might not be carried out according to a timetable compatible with the development needs or testing of the Company's products.

Ovasave®, the first drug candidate of the Company from the ASTrIA platform, is under clinical development for the treatment of moderate-to-severe cases of Crohn's disease which are refractory to current treatments in December 2014, with the launch of a Phase IIb international multicenter clinical trial named CATS29, the second stage of its development started with the goal to confirm the positive results of the Phase I/IIa study. However, in June 2015, the CATS29 study had to be temporarily suspended because of manufacturing issues at the Company's site in Besançon, France, which has since been closed (see paragraph 6.5.3 of the *Document de Référence*). This suspension has been notified to the health authorities.

Because of these issues, the Company has decided to externalize the manufacturing of Ovasave® to MaSTherCell, a Contract Manufacturing Organization ("CMO"). On July 29, 2015, the Company announced the initiation of the technology transfer to MaSTherCell, which should be achieved in Q2 2016. On the basis of the first validation batches of Ovasave® manufactured by MaSTherCell in compliance with specifications, the Company has submitted an amendment to the clinical protocol of the CATS29 study to the European regulatory authorities via the VHP procedure (Voluntary Harmonized Procedure), including in particular the change of manufacturing site. The Company expects to receive the approval from the European regulatory authorities in Q2 2016. The recruitment of patients for CATS29 study may resume once the Company has received the approval from the European regulatory authorities, once the manufacturing technology transfer to MaSTherCell has been completed, and once the Company has obtained the necessary funds to finance the study.

Additional delays to control the manufacturing, obtain authorizations or recruit doctors or patients could lead to delay of this study and to a material adverse effect on the Company's business, results, financial position and prospects.

The clinical trials are subject to authorizations from regulatory authorities

Biomedical research is subject to a rigorous regulatory framework. In France in particular, clinical studies must obtain a positive opinion from the *Comité de Protection des Personnes* (ethical committee for the protection of the person) ("CPP") and an authorization from the *Agence Nationale de Sécurité du Médicament et des produits de santé* (national agency governing the safety of medicines and healthcare products) ("ANSM"), prior to their launch and if there are substantial amendments made to the study. The organization of clinical studies must identify a site, investigator doctors and patients meeting the inclusion criteria for the needs of the trial and giving their consent to participate, which can be long or difficult and cause delays in the Company's projected timeline.

In accordance with Good Clinical Practices ("GCP"), the Company has established a Data Safety Monitoring Board; given that GCP require the recommendations of the committee to be followed, these recommendations could lead to early terminations or delays in products development. Moreover, depending on the information which may be communicated during the trial, in particular on the

occurrence of serious undesired events, the health authorities could impose the suspension or the early termination of the trial.

Given the manufacturing incidents of Ovasave® experienced by the Company on the Besançon site, and the suspension of the CATS29 clinical trial, the Company has submitted an amendment to the design of the CATS29 trial in order to change the manufacturing site and to focus on the initial goal of the trial, resulting especially in a decrease in the associated costs (for example, by reducing the number of active arms from 4 to 2 and , reducing the number of patients) and in a reduction of the trial's duration. The Company expects to receive the approval from the European regulatory authorities in Q2 2016. It is not certain that these amendments will be accepted by the relevant authorities, which could consider that they are more than simple amendments to the existing clinical trial, therefore requesting a new authorization. If that is the case, it would cause additional delays in the achievement of this study, which would have a material adverse effect on the Company's business, results, financial position and prospects. Moreover, in the context of a future Phase III trial, the relevant authorities could ask the Company to carry out a study with several arms of research on the optimal dosages, which could result in the increase of the cost and of the duration of the clinical trial.

Furthermore, although the CATS29 study is a European clinical study, the Company benefits from an IND allowing it to expand the trial to the United States. Given the amendment to the CATS29 study, it cannot be excluded that the U.S. authorities will review their position regarding the IND granted for CATS29, which, in such event, will result in additional delays to the clinical trials conducted for authorization purposes in the United States.

The clinical trials are submitted to continuous monitoring from the regulatory authorities

At each stage of development, the Company presents the results of its clinical studies to authorities in different countries according to its development plan. In particular, insofar as the regulatory framework applicable to cell therapy is still being developed (please refer to paragraph 4.2.3 of the *Document de Référence*), additional requirements may be necessary regarding, for example, study protocols, patient characteristics, length of treatment, post-treatment follow-up or discrepancies in the interpretation of results by local regulatory agencies and, where applicable, could lead to requests for additional studies. Any decision by the health authorities to request further trials or examinations would be likely to delay or interrupt the development of the therapeutic products in question.

Therefore, the Company cannot guarantee that, following the results of the Phase IIb study of Ovasave® and even if those results are positive, the regulatory authorities will not demand that a research study for optimal dosage in Phase III be conducted, especially since the Company does not have dosage comparative data for the amended CATS29 trial.

Moreover, the occurrence of side effects which are currently not identifiable could delay or interrupt the development of the products concerned. Finally, since clinical trials are necessarily of a limited duration, the Company cannot guarantee the efficacy of any product over a long period. If the effects of its products, and hence its effectiveness on patients, decrease over time, additional studies may be required.

If after obtaining a Marketing Authorization ("MA"), the therapeutic products of the Company cause unacceptable side effects or side effects that are undetected during the clinical trial phase, it will become impossible for the Company to continue to market it for all or part of the targeted indications, which would have a material adverse effect on the Company's business, prospects, financial position, results and development.

To date, the Company therefore cannot guarantee that the development of drug candidates, now or in the future, will be successful, or that *a fortiori* it will happen within a timeframe compatible with the requirements of the market. Any failure or delay in the development of products could have a material adverse effect on the Company's business, results, financial position and prospects.

The Company has limited experience in the clinical development of products

In addition to date, the Company does not have any strategic partner, which would enable it to benefit from its clinical development experience. The Company therefore intends to develop its products, Ovasave® in particular, either on its own, or through future partnerships. These partnerships would be sources of funding and could in addition allow the Company to benefit from a leading player in the pharmaceutical or in the biotechnology sector with a clinical development experience if need be.

However, it is possible that the Company will not be able to engage in a development partnership on financially reasonable terms or to develop the product on its own. Such an event could have a negative effect on the timetable for the development of these products, Ovasave® in particular, as well as on the Company's results and prospects.

The development of a new type of cell therapy generates many uncertainties

At the date of the *Document de Référence*, there are only a few cell therapy products with marketing authorization. The work carried out by the Company as part of the development of its drug candidates is based on T lymphocyte cells (Tregs). These drug candidates have an effect on patients' immune systems, an area in which there are still many unknowns.

Therefore, the preclinical and clinical data on the safety and efficacy of the treatments developed by the Company is still limited. Not only are tests on animals not necessarily indicative of the results which could be obtained on humans, but potential positive results recorded in early clinical phases and obtained on a limited number of patients might not be confirmed by subsequent phases involving a larger number of patients. This would have a significant impact on the Company's business, results, financial position, development and prospects.

4.1.2 Risks related to the manufacturing process for products developed by the Company

The transfer of the manufacturing of Ovasave® could cause additional delays to the CATS29 clinical trials

The manufacturing process of the Company's product is long and costly. Due to the manufacturing issues at the Besançon site, in 2015 the Company decided to review its manufacturing strategy. Manufacturing is now outsourced to a CMO, MaSTherCell, as part of a 5-year exclusive agreement in Europe for products from the ASTrIA platform. The manufacturing technology transfer of this product is ongoing and constitutes a risk that the technology will not be sufficiently mastered by MaSTherCell, which could have an impact on the quality and timing of the manufacturing.

The results obtained after implementing the new, optimized production process may be different from results previously obtained. The Company may be required to conduct additional studies which would lead to additional expenses or even delay the Phase III clinical trials and the future marketing of Ovasave®.

The optimization of the manufacturing process is necessary to the financial viability of the products of the Company

The manufacturing process currently used by the Company for its clinical trials includes numerous improvements compared to the manufacturing process which allowed the achievement of the CATS1 trial, the first clinical trial conducted by the Company with Ovasave®. However, the process remains complex, long (10 to 12 weeks) and costly (please refer to paragraph 6.5.1 of the *Document de Référence*).

Given the prospect of advanced clinical trials and of the future launch of its products on the market, and of Ovasave® in particular, the Company intends to develop, internally and in partnership with subcontractors, the manufacture of these products based on an automated and optimized production process. Such standardization is an essential part of the economic liability of the Company's products' (time required to release the product in compliance with medical practice and increased production

volumes) and financial strategy (decrease of production costs per patient). Given the complexity of the manufacturing process in cell therapy, the Company cannot guarantee that all of the manufactured products will meet the required specifications and that they will be cleared for their administration to the patient. In such case, the manufacturing process for that patient would have to be restarted, which would have a material adverse effect on the duration of the trial and on the financial prospects of the Company. Moreover, despite the Company's efforts regarding the quality control of its products, the Company cannot guarantee that the products meeting the required specifications and therefore administered to the patient, will have the expected effects. Thus, the Company is developing a new biological test that will monitor the performance of its Ovasave® products manufactured by MaSTherCell. This test will notably allow to ensure that the products used all possess the qualities required to have the expected impact while offering a good safety profile to the patients. This test could prove to be inadequate or inefficient with a material adverse effect on the Company, its business and its reputation. Since the strategy of the Company is to outsource its present and future manufacturing activities, it will have to ensure that its subcontractors be granted or have been granted all necessary authorizations and approvals and that they comply with current regulations, in particular on asepsis (please refer to paragraph 4.1.5 of the *Document de Référence*). In addition, an adjustment period will be necessary in order for the Company's subcontractors to apply these optimized processes to their own production processes.

These factors could result in a delay in the implementation of the required automated processes or the need for additional investment.

Any of these events would have a negative impact on the Company's development, strategy, prospects and financial position.

> *The Company's drug candidates are biologics and their manufacture is complex. The Company may encounter difficulties in production, particularly with respect to process development or scaling-out of manufacturing capabilities. If the Company or any of its CMOs encounter such difficulties, its ability to provide supply of its drug candidates for clinical trials could be delayed or stopped, or the Company may be unable to maintain a commercially viable cost structure.*

The Company's drug candidates are biologics and the process of manufacturing them is complex, highly-regulated and subject to multiple risks. The manufacture of these drug candidates in cellular therapy involves complex processes, including harvesting T cells from patients, selecting antigen-specific regulatory T cells (Ag-Treg), multiplying the T cells to obtain the desired dose, and ultimately infusing the T cells back into each patient's body.

As a result of these complexities, the cost to manufacture products of cellular therapy in general, and the drug candidates of the Company in particular, is generally higher than traditional molecule chemical compounds. In addition, the manufacturing process is less reliable and is more difficult to reproduce.

The Company's manufacturing process is susceptible to product loss or failure due to:

- logistical issues associated with the collection of white blood cells, or starting material, from the patient, shipping such material to the manufacturing site, shipping the final product back to the patient, and infusing the patient with the product, or
- manufacturing issues associated with the differences and unique character of patient-specific starting materials, time required for and interruptions in the manufacturing process, contamination, equipment or reagent failure, improper installation or operation of equipment, supplier or sub-contractor error, inconsistency in cell growth, and variability in product characteristics.

Even minor deviations from normal manufacturing processes could result in reduced production yields, product defects, and other supply disruptions. If for any reason the Company loses a patient's starting material or later-developed product at any point in the process, the manufacturing process for that patient will need to be restarted and the resulting delay may adversely affect that patient's outcome. If microbial, viral, or other contaminations are discovered in its drug candidates or in the manufacturing facilities in which its drug candidates are made, such manufacturing facilities may need to be closed for an extended

period of time to investigate and remedy the contamination. Because its drug candidates are manufactured for each particular patient, the Company will be required to maintain a chain of identity with respect to materials as they move from the patient to the manufacturing facility, through the manufacturing process, and back to the patient.

Maintaining such a chain of identity is difficult and complex, and failure to do so could result in adverse patient outcomes, loss of product, or regulatory action including withdrawal of authorizations to conduct clinical trials. Further, as drug candidates are developed through preclinical to late stage clinical trials towards approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods, are altered along the way in an effort to optimize processes and results. Such changes carry the risk that they will not achieve these intended objectives, and any of these changes could cause the drug candidates to perform differently and affect the results of planned clinical trials or other future clinical trials.

Although the Company is working to develop commercially viable processes, doing so is a difficult and uncertain task, and there are risks associated with scaling to the level required for advanced clinical trials and commercialization, including, among others, cost overruns, potential problems with process scale-out, process reproducibility, stability issues, lot consistency, and timely availability of reagents or raw materials. The Company may ultimately be unable to reduce the manufacturing cost of drug candidates to levels that will allow for an attractive return on investment if and when those drug candidates are commercialized, which would have a material adverse effect on the Company's financial position and its prospects.

4.1.3 Risks associated with the technology platform

All products that are at a development stage are based on the same technology platform ASTrIA, which is owned by the Company. If studies conducted on any of these products were to reveal issues relating to safety and/or therapeutic efficacy, it could call into question the operating of the technology platform, require new R&D efforts to attempt to address the difficulties and extend or even call into question product development. This would have a material adverse effect on the Company's business, prospects, development, financial position and results.

In 2015, the Company diversified its technology basis by developing a second technology platform ENTrIA (please refer to paragraph 6.3.3 of the *Document de Référence*) which could result in a decrease of this risk. Whereas the ASTrIA platform is based on the therapeutical use of type 1 preexisting T lymphocyte cells not genetically modified, the ENTrIA platform proposes cell immunotherapy products based on the use of genetically engineered FoxP3+ regulatory cells (CAR-Tregs). In this context, the Company has entered into an option agreement with Yeda Research Development Co. Ltd. to obtain an exclusive license right for patent applications regarding the regulator T cells modified by genetic engineering (please refer to paragraph 11.3.3 of the *Document de Référence*). If these patent applications are not delivered, if the patents once granted are voided or if the Company does not succeed in obtaining an exclusive license on the patent applications, competition might appear, which could have an adverse effect on the Company's business, prospects, financial position, results and development.

4.1.4 Risks associated with the market and competition

The Company could be dependent on its most advanced product, Ovasave®, because its other products are at less advanced stage of development

Ovasave® – intended for the treatment of Crohn's disease – is the Company's most advanced product in terms of development and marketing process. Regarding the second most advanced drug candidate, Col-Treg, the Company has already fulfilled the last preclinical requirements before the next step which will be the undertaking of a first clinical trial.

In addition to the fact that the development of alternative products would require significant research and development efforts and substantial financial investment, the Company cannot guarantee that it will develop a diverse product portfolio.

This situation would cause the Company to be dependent on Ovasave®, which could have a negative impact on its development prospects.

In 2015, the Company diversified its technology basis by developing ENTrIA, a second technology platform (please refer to paragraph 6.3.3 of the *Document de Référence*) which could result mitigate this risk. Indeed, similarly to ASTrIA, the ENTrIA platform has the capacity to produce numerous drug candidates and could lead to the development of an additional pipeline of therapeutic products. The differences in the mechanisms of action between the type 1 Tregs and the FoxP3+ Tregs will enable the Company to adapt its therapeutic approach to the physiopathology of the targeted indication. The ENTrIA and the ASTrIA platforms are, from this standpoint, extremely complementary in theory, allowing the Company to target a large number of chronic autoimmune and inflammatory pathologies. Nonetheless, given the early development stage of this second platform, it is possible that the Company will not succeed in the development of products from this technology and therefore in the diversification of its products portfolio, which could have an adverse effect on the Company's prospects, development, financial position and results.

Market competition in the treatment of diseases targeted by the Company is intense

Many entities, pharmaceutical companies, biotechnology companies, institutions, universities and other research organizations are actively committed to the discovery, research, development and marketing of therapeutic remedies to treat chronic autoimmune and inflammatory diseases. The market for treating these diseases is characterized by intense competition. In view of their size and their well-established technologies used to develop drugs for treating chronic autoimmune and inflammatory diseases, the Company's main competitors have access to significantly greater resources and experience in clinical development, management, manufacturing, marketing and research than the Company.

However, the Company believes that its product, Ovasave®, will be an alternative to treatments currently prescribed for Crohn's disease. Despite this positioning, the Company cannot guarantee that its competitors will not develop, concurrently or subsequently, alternative therapeutic solutions, which will cause those currently under development by the Company to be less attractive or even obsolete, or which would be preferred by medical centers, doctors or patients.

Finally, given the particularly competitive environment of the pharmaceutical industry, the Company cannot guarantee that its partners and/or employees will not over time join or work with competing structures, or that its competitors will not be favored by medical centers, doctors or patients.

Such events could have a material adverse effect on the Company's business, results, financial position and development prospects.

The commercial success of the Company's products cannot be guaranteed

Even if the Company obtains an MA to market its therapeutic products, it may however not receive the immediate support of the medical community, prescribing physicians and third-party payors which may be reluctant to adopt these products.

Due to the innovative nature of the drug candidates developed by the Company, the development prospects of products arising from these treatments, their safety, efficacy and acceptance by patients, doctors and third-party payors are uncertain.

The degree of acceptance by the market of each of the Company's products depends on several factors, in particular:

- the perception of the therapeutic benefit of the product by prescribing physicians;
- the possible occurrence of undesirable side effects not detected during the clinical trials once the MA has been obtained, making it impossible to market it for all or some of the indications in question;

- the ease of use of the product (particularly in terms of its method of administration), stability of the product initially manufactured and how long the treatment remains effective, on average;
- the cost of treatment;
- the reimbursement policies in different countries and, more generally, of public or private payors;
- the effective implementation of a scientific publication strategy; and
- the development of one or more competing products for the same indication.

The duration of the treatment, and therefore the degree of acceptance by each patient will also have a significant impact on the Company's business. The Company's business model differs in this respect from business models of conventional autologous products (characterized by low margins mainly due to the necessity of a specific production for each treatment administration and for occasional treatments), since the production costs are incurred only once (in a one-time manner), regardless of the length of treatment (please refer to paragraph 6.4.1.1.8 of the *Document de Référence*) and as the products are directed to patients suffering from chronic diseases for which the treatment is by definition chronic as well.

While the Company believes that its products will provide a therapeutic response to a currently unmet need, poor market penetration resulting from one or more of the factors described above could have an adverse effect on the Company's business, prospects, financial position, results and development.

4.1.5 Risks associated with the Company's business and strategic development

Obtaining marketing authorizations and other certifications prior to any marketing may be uncertain

In Europe, the United States, and Asia, as well as in many other countries, access to the drug market is controlled and marketing must be authorized by a regulatory authority.

While the Company does not at present have any particular MA application in process, an MA file is elaborated over the duration of a drug candidate’s development. The Company therefore seeks to ensure that it always complies with good practice so as not to jeopardize its chances of obtaining future MAs on good terms.

The Company's obtaining of a marketing authorization for each of its therapeutic products requires compliance with stringent standards imposed by the regulatory authorities and the reporting to the authorities of a considerable amount of information on the new product regarding its toxicity, dosage, quality, effectiveness and safety. While the process for obtaining the authorization involves substantial investment, the outcome is uncertain.

The grant to the Company of an MA for each of its therapeutic products will depend on several factors, and in particular:

- the possibility to pursue the development of its products currently in preliminary clinical phases or to move the products currently in a preclinical development phase to a clinical phase or from a clinical phase to the next phase;
- the ability of the Company or its subcontractors to complete the requested clinical trials within the time limits and with the human, technical and financial resources initially planned.

If the Company fails to obtain an MA, it would not be able to manufacture or market any products. In addition, it is possible that a product may not obtain an MA for a given geographic area, which could significantly restrict the marketing thereof. Finally, even once granted in accordance with the relevant procedures, an MA may be suspended, especially when an adverse effect is subsequently discovered.

4.1.6 Risk of dependence on third parties

The Company could encounter a dependency situation vis-à-vis subcontractors to which it will outsource the manufacturing of the products it develops

The Company does not operate any manufacturing or logistics unit. It outsources the manufacturing and the packaging of its products to subcontractors (such as MaSTherCell, exclusive subcontractor in Europe for the products from the ASTrIA platform – please refer to paragraph 22.6 of the *Document de Référence*) with a strong expertise in the manufacturing of products in the scope of cell therapies and which are selected by the Company after careful assessment of the performances of their quality department and of the traceability of their operations. The Company has submitted an amendment to the clinical protocol of the CATS29 study to the European regulatory authorities via the VHP procedure (Voluntary Harmonized Procedure), including in particular the replacement of TxCell's manufactunring site in Besançon by the site of the company MaSTherCell. The Company expects to receive the approval from the European regulatory authorities in Q2 2016.

The manufacture of the Company's products is particularly complex and demanding, especially due to the regulations and the requirement specifications applicable to the trials and for the MA should the Company, in the future, succeed in the marketing of a product. In the event the Company would need to change a critical subcontractor for the manufacturing of its products, tests and additional validations could be required to maintain any authorizations granted for its clinical trials. These procedures could be costly, time-consuming and require the attention of the most qualified personnel of the Company. Should any clinical studies be interrupted, the Company may be constrained to search for another subcontractor, which could delay the development, the manufacturing and the marketing of its products and increase the manufacturing costs. Such a transfer of the manufacturing process implies to find a new subcontractor within the few companies with the required expertise and usually takes 12 months.

Moreover, problems could occur during the manufacturing and the distribution of the Company's products, which could cause delays and even a total halt of the deliveries. This could lead to a delay in the clinical trials or, at a marketing phase, to a decrease in the sales combined with a deterioration of the relationship with customers. Such events could also result in an increase of costs and, in some cases, the recall of products, damaging its reputation, and increasing the risk for the Company to be held legally responsible. In case of non-compliance of the products manufactured by these third parties with regulatory standards, sanctions could be imposed on the Company including fines, injunctions, judgments to pay damages, the suspension or the withdrawal of the authorizations granted or the cancellation of licenses. Thus, the Company is developing a new biological test that will monitor the performance of its Ovasave® products manufactured by MaSTherCell. This test will notably allow to ensure that the products used all possess the qualities required to have the expected impact while offering a good safety profile for patients. This test could prove to be inadequate or inefficient with a material adverse effect on the Company, its business and its reputation. Furthermore, the Company cannot guarantee that its partners will strictly respect the manufacturing designs and the tests it has defined which are aimed at ensuring the quality of the manufactured products. Such failure from its partners would be likely to have a material adverse effect on the Company, its business, its financial position and its reputation.

Finally, in case of a break down or deterioration of its relationship with its subcontractors or in case of expansion in its activity, the Company may have to seek new subcontractors. It cannot guarantee that it will be able to enter into new contracts in the desired time frames and on acceptable commercial terms, given the limited number of specialized companies with the infrastructure, experience, as well as the necessary authorizations and approvals for the manufacturing of the medical products developed by the Company.

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

The supply of specific raw materials and products needed to conduct clinical trials and manufacture the Company's products is not guaranteed

The Company is dependent on third parties for the supply of various materials and chemical or biological products necessary to manufacture both the experimental cell drugs used in its clinical trials and future drugs developed by the Company.

Supply to the Company of any of these materials and products could be cut back or interrupted. In this event, the Company could be unable to source other suppliers of materials or chemical or biological products of satisfactory quality, in the appropriate quantities and at an acceptable cost. If its key suppliers or manufacturers were to default or if the supply of products and materials were cut back or interrupted, it is possible that the Company would not be able to continue to develop, produce and market its products in a timely and competitive manner. Given that authorizations are granted by health authorities for specific manufacturing procedures and named suppliers, any amendment requires a new review by the authorities, which could cause delays and additional costs.

In addition, these materials and products are subject to stringent manufacturing requirements and rigorous testing. Delays in the completion and validation of the plants and the manufacturing process for these materials and products by the Company's suppliers could affect the Company's ability to complete clinical trials and to market its products profitably and within a reasonable timeframe.

To prevent such situations, the Company has introduced with certain suppliers of crucial raw materials the implementation of contractual terms (e.g., supply agreements, and outsourced production of batches) in order to secure supply. Furthermore, for most raw materials and products which are considered as critical, the Company has identified alternative sources of supply satisfying these quality criteria.

If the Company encountered difficulties in the supply of these materials, chemical or biological products, or was not able to maintain its existing supply agreements or establish new agreements in order to develop and manufacture its products in the future, its business, prospects, financial position, results and development could be materially affected.

The Company could find itself in a situation where it is dependent on the subcontractors to whom it outsources its clinical trials

The Company does not have at this stage of development, sufficient infrastructures and resources to conduct the clinical trials essential for developing the drugs it designs. Such trials are therefore assigned to specialized medical care establishments or companies specialized in clinical trial management (Contract Research Organizations ("CRO"s)) such as SGS (please refer to paragraph 22.4 of the *Document de Référence*). The subcontracting of clinical trials generates risks relating to the selection of such establishments. Operational difficulties could also occur, especially due to the remoteness or geographical dispersion of these clinical study centers.

Any failure by the Company's subcontractors could affect the timetable, or even the continuation of clinical studies, as well as the quality of data obtained – which must meet strict standards (Good Manufacturing Practice ("GMP"), GCP or other international standards) imposed by the regulatory authorities – and thus delay the marketing of products. Such events could have a material adverse effect on the Company's business, prospects, financial position, results and development.

4.2 Regulatory and legal risk

4.2.1 Risks associated with the Company's intellectual property rights

Protection of the Company's patents, patents applications and other intellectual property rights is uncertain

The Company's business plan depends notably on its ability to obtain, maintain and guarantee the protection, *vis-à-vis* third parties, of its patents, trademarks and related applications together with other intellectual property or similar rights (such as, in particular, its trade secrets, business secrets and know-how) or those it is permitted to use within the scope of its activities. It is also important for the success

of its business that the Company is able to receive similar protection for all its other intellectual property rights in Europe, the United States, Asia and other key countries. The protection by the Company of its intellectual property rights constitutes a significant cost due to, among others, fees relating to filings, the patent office proceedings and the renewal of patents and the management of its other intellectual property rights. The Company, which devotes significant financial and human resources in this regard, intends to pursue its protection policy by filing new patent and trademark applications, as and when it deems appropriate. To the best of its knowledge, its technology is, to date, effectively protected by patents and patent applications it has filed or for which it holds an exclusive license.

However, it is possible that the Company might not be able to continue to protect its intellectual property rights, in which case it might lose its technological and competitive advantage.

Firstly, the Company's intellectual property rights provide protection for a period which can vary from one jurisdiction to another (this period may be, for example, 20 years from the date of filing a patent application in France and in Europe, while it may be extended for up to an additional 5 years when a supplementary protection certificate has been filed).

Secondly, the Company could experience difficulties in connection with the examination of some of its applications for patent, trademark or other intellectual property right currently being reviewed and/or registered. For example, at the time of filing a patent or a trademark application, other filings of patents or trademarks previously constituted but not yet published may be enforceable. Despite the prior art searches and monitoring it performs, the Company therefore cannot be certain that it is the first to have conceived an invention and to file a related patent application; it is important to note that in particular with regard to patents, in most countries, the publication of patent applications occurs 18 months after such filings and that findings are sometimes not published or do not become the subject of a patent application until months and often even years later. Similarly, when registering trademarks in a particular country, the Company could find that the trademark in question is not available in that country. A new trademark would have to be found for that particular country or an agreement negotiated with the owner of the pre-existing trademark. There is therefore no certainty that current and future applications with regard to the Company's patents, trademarks and other intellectual property rights will lead to registration.

Thirdly, the simple granting of a patent, trademark or other intellectual property rights does not guarantee their validity or enforceability. Indeed, the Company's competitors may at any time challenge the validity or enforceability of the Company's patents, trademarks or applications relating thereto before a court or under other specific procedures, which, depending on the outcome of said challenges, could reduce their scope, cause them to become invalid or allow them to be circumvented by competitors. In addition, developments, changes or differences in interpretation of the legal framework governing intellectual property in Europe, the United States or other countries could allow competitors to use the Company's inventions or intellectual property rights, or to develop or market the Company's products or technology without paying it any financial compensation. This applies not only to patents or patent applications which are owned or jointly owned by the Company, but also to those for which it benefits from or could benefit from a license. For example, the Company does not have a patent covering its ENTrIA platform. Indeed, it currently benefits only from an exclusive option agreement enabling the Company to negotiate the terms of an exclusive worldwide license over the family of patent applications regarding redirected genetically engineered regulator T cells and their use for the treatment of autoimmune pathology which is owned by the company Yeda Research and Development Company Ltd. ("Yeda") (please refer to paragraph 22.3 of the *Document de Référence*). A Letter of Intention was signed on October 28, 2015 to define the main terms of the license agreement, should it be concluded, following the possible exercise of the option by the Company within the period provided. However, to date, the Company does not have a license right authorizing it to use the invention subject to such patent applications. The Company cannot guarantee that it will achieve final conclusion of this agreement and obtain an exclusive license right on favorable terms. The rights to these patent applications could then be granted to Company's competitors who could prevent the Company from using them. Furthermore, although the coverage of the patent applications owned by Yeda is rather broad at this stage, the Company will not enjoy a worldwide monopoly over the exploitation but only over the territories indicated by the patent applications and subject to the grant, for each of these territories, of the corresponding rights. The European patent application number EP2126054 (covering in substance

redirected genetically modified regulator T cells and their use in the ending of autoimmune and inflammatory diseases) has received a notification of intention to grant by the European Patent Office, on April 25, 2016. Nonetheless, the U.S. patent application number 12525270, covering in substance the same invention is still under review: an official letter has been issued on December 29, 2015 for which a reply must be sent by June 29, 2016.

Indeed, the question of the patentability of drugs and medical devices is very complex and raises legal, scientifical and factual issues: uncertainties remain as to the interpretation of the impact of the claims which could be granted, which is still at a domestic law issue. Evolutions or changes in the interpretation of the laws applicable to intellectual property in Europe, the United States or in any other country may modify the legal framework and the situation of the Company compared to its competitors. In addition, there are still some countries that do not protect intellectual property rights in the same way as do Europe and the United States; effective procedures and rules necessary to protect the Company's rights may not exist in such countries. There is therefore no guarantee that the Company's existing and future patents, trademarks and other intellectual property rights will not be challenged, invalidated or circumvented, or that they will provide effective protection against the competition and third-party patents covering similar inventions.

In addition, the Company cannot guarantee that it will indefinitely benefit from the license rights which are granted to date, such as, *inter-alia*, rights to certain patents and/or patent applications which are owned by or jointly owned with the French National Public Health and Medical Research Institute (*Institut National de la Santé et de la Recherche Médicale* or "INSERM"). Should the licenses granted expire or be terminated, it cannot be excluded that the Company will find itself in a situation of dependence *vis-à-vis* the patents and/or the patent applications, or may not be in a position to continue their exploitation or find a suitable alternative.

Consequently, the Company's rights over its patents, trademarks, related applications and other intellectual property rights might not give the expected protection against competitors. The Company cannot therefore guarantee with any certainty that:

- applications for patents, trademarks and other intellectual property rights under examination will actually result in the granting of registered patents, trademarks or other intellectual property rights;
- it will succeed in obtaining the rights on the Yeda patent which cover its ENTrIA platform;
- patents, trademarks or other intellectual property rights granted to the Company will not be challenged, invalidated or circumvented;
- the scope of protection afforded by the Company's patents, trademarks and intellectual property rights is and will remain sufficient to protect it against competitors and third-party patents, trademarks and intellectual property rights covering similar devices, products, technologies, developments or similar signs;
- that it will manage to develop new inventions which might generate an application for, or the granting of a patent nor that it will have the necessary resources to ensure and maintain, in the countries in which it foresees to use such inventions, an efficient protection.

Such contingencies, should they occur, could have negative effects on the Company and its development.

The Company benefits from certain intellectual property rights through joint ownership or licenses

The Company also takes part in research and development jointly conducted with scholars at academic institutions or other public or private entities. Such research can lead to the creation of inventions, for which the right (patent or patent application) could be jointly owned between the Company and the entity with which the work was undertaken. In these situations, the Company could be brought to sign a joint ownership agreement to define the terms of the joint owners' relationship, as it has been the case regarding patents and application patents for families PTXC1 and PTXC5 with INSERM (please refer to paragraph 22.1). When no agreement exists or has been concluded (as is the case for the patents and

application patents for families PTXC11 resulting from a partnership with the University of Montpellier) (please refer to paragraph 11.2.2), the general legal regime on joint ownership of patents/patent applications provided by Articles L. 613-39 et seq. of the French Intellectual Property Code, should apply. The Company could find itself in a situation of dependence *vis-à-vis* these patents and not be able to renew its long-term agreements on reasonable financial terms or find an alternative to these partnerships.

The Company, following the terms of contractual agreements, also granted among other things an option enabling Trizell Holding SA ("Trizell") (which was substituted for Ferring International Center ("Ferring")) to obtain, in case of the exercise of the option, an exclusive sublicense on the PTXC1 and PTXC5 patent families and on the related know-how solely or jointly owned by INSERM with the Company. In addition, Trizell has transferred to the Company intellectual property rights which it (or Ferring) could have developed within the scope of the contractual agreements mentioned above (please refer to paragraph 22.2).

Such contracts also expose the Company to the risk of having third parties (i) claim the benefits of the intellectual property rights on the inventions or other intellectual property rights of the Company, (ii) breach the confidentiality of innovations or non-patented improvements as well as confidential information and know-how of the Company, (iii) disclose the Company's commercial secrets to competitors or develop independently commercial secrets and/or (iv) violate such contracts, without the Company having appropriate recourse against such violations.

The Company cannot guarantee that it will not infringe intellectual property rights or that its own rights will not be infringed

The Company's commercial success will also depend on its ability to develop products and technologies that do not infringe patents or other third-party rights. It is important for the success of its business, that the Company be able to freely exploit its products without them infringing patents or other third-party intellectual property rights and without third parties infringing the Company's rights, in particular its intellectual property rights.

As it has done to date, the Company continues to conduct preliminary studies it deems necessary, in the context of the above-mentioned risks, before making investments to develop its various products and technologies. With the help of its intellectual property lawyers, it keeps a watch on its competitors' activities, particularly in terms of patent applications.

However, monitoring the unauthorized use of the Company's products and technology and therefore the infringement of its rights is difficult.

The Company cannot guarantee with any certainty that:

- it will be able to prevent, punish and obtain compensation for the misappropriation or the unauthorized use of its products and technology, particularly in foreign countries where its rights would be less well protected due to the territorial scope of industrial property rights;
- there are no prior patents or other third-party rights (particularly over intellectual property), likely to cover certain Company products, processes, technologies, results or activities and, consequently, that third parties will not sue the Company for patent infringement or infringement of their rights in order to obtain damages and/or termination of manufacturing and/or marketing activities of the Company for the relevant products, processes and other identified technologies;
- no prior third-party trademark rights or other rights likely to lead to an infringement or liability action against the Company exist; and/or
- the Company's domain names will not be the subject of a Uniform Dispute Resolution Policy (UDRP) procedure, or a similar procedure, or an infringement action by a third party having prior rights (e.g. trademark rights).

In the event of a dispute regarding intellectual property, the Company could be required to:

- stop developing, selling or using the product or products to which the disputed intellectual property rights relate;
- obtain a license from the holder of the intellectual property rights, it being possible that this license might be unobtainable or only obtainable on terms which are financially unfavorable to the Company;
- redesign some of its products and/or technologies or, in the case of trademark applications, rename its products to avoid infringing third-party intellectual property rights, which may be impossible or require a lengthy and expensive process, and could, consequently, impact its marketing efforts.

Moreover, third parties (even Company employees) could use or attempt to use parts of the Company's technology protected by an intellectual property right, which would be harmful to the Company. The Company could therefore be forced to initiate judicial or administrative proceedings against these third parties in order to enforce its rights, particularly intellectual property rights, (patents, trademarks, drawings, models and domain names) before the courts.

Regardless of the outcome, any dispute or litigation could result in substantial costs, affect the Company's reputation, adversely affect its results and financial position and not provide the required protection or lead to the sanction sought. Some competitors with access to greater resources than the Company may be in a better position to bear the costs of litigation.

However, on the date of the *Document de Référence*, the Company has not found itself in any of these situations and has not been involved in any litigation, whether as claimant or defendant, regarding its own rights, particularly intellectual property rights, or those of a third party.

The Company may not be able to prevent the disclosure to third parties of confidential information likely to have an impact, in particular on its future intellectual property rights

It is also important for the Company to protect itself against unauthorized use and disclosure of its confidential information, know-how and trade secrets. Indeed, unpatented and/or unpatentable technologies, processes, methods, know-how and proprietary data are considered trade secrets which the Company seeks to protect, partly through confidentiality agreements. Moreover, the rules of transfer to the Company of inventions that its employees have or could make, and the related remuneration arrangements, are governed by Article L. 611-7 of the French Intellectual Property Code, which is considered public policy in France.

The Company enters into diverse collaboration, partnership and research agreements or other types of cooperation between it and researchers with academic institutions and other public or private entities, subcontractors etc., such as MaSTherCell for the exclusive outsourcing of the manufacturing of products from the ASTrIA platform (Ovasave® included) in Europe (please refer to paragraph 22.6) or SGS Belgium NV, for the operational conduct of the Ovasave® Phase IIb trial (please refer to paragraph 22.4). Under these agreements, various types of information and/or products may be entrusted to Company’s counterparty in order for it to perform certain tests and clinical trials. In such cases, the Company requires a confidentiality agreement to be signed.

It cannot be guaranteed that the agreements put in place to protect the Company's technology and trade secrets and/or the expertise that it has developed will provide the required protection or that such agreements will not be breached by subcontractors of the Company or by other third parties, that the Company will have appropriate solutions to counter such violations, or that trade secrets will not be disclosed to its competitors or independently developed by them. Within the scope of the agreements the Company concludes with third parties, it at times takes the precaution of stipulating that the latter are not allowed to use the services of third parties or that they can do so only with the Company's prior approval. Nevertheless, it still cannot guarantee that some of its contractual counterparties will not use third parties. In this event, the Company has no control over the conditions under which its subcontractors protect their confidential information, regardless of the fact that the Company stipulates in its agreements with co-contractors that they pass on such confidentiality obligations to their own contractual counterparties.

Consequently, the Company's rights over its confidential information, trade secrets and know-how may not give the protection it expects against its competitors and the Company cannot guarantee with any certainty that:

- its know-how and trade secrets will not be acquired, usurped, circumvented, disclosed or used without its permission;
- the Company's competitors have not already developed technologies, products or devices similar or comparable in nature or purpose to those of the Company;
- another contractual counterparty will not claim the right to use all or part of the Company's intellectual property rights to inventions, knowledge or results that it owns individually or jointly, or in respect of which it could be granted a license;
- employees of the Company will not claim rights or the payment of additional compensation, or a price, for the inventions that they have helped to develop.

Any one or more of these risks could have a material adverse effect on the Company's business, prospects, financial position, results and development.

4.2.2 Risks associated with product liability

The Company may be exposed to risks involving liability during the clinical development of its products, in particular product liability relating to the testing and manufacturing of therapeutic products for humans and animals. It could, for instance, be held liable *vis-à-vis* patients taking part in clinical trials in the context of the development of the therapeutic products being tested for unexpected side effects resulting from the administration of such products.

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

The Company cannot guarantee that its insurance policies (please refer to paragraph 4.8 of the *Document de Référence*) or that contractual undertaking for damages, contractually capped where applicable, agreed to by its subcontractors (please refer to chapter 22 of the *Document de Référence*) will be sufficient to cover any liability claims that may be brought against it.

If its liability or that of its partners, licensees or subcontractors were thus engaged, or if the Company or its partners, licensees or subcontractors were not able to obtain and maintain adequate insurance cover at an acceptable cost, or if the Company was unable to protect itself in any manner against liability claims, this would result in the Company's marketing of its products being seriously affected and, more generally, would harm its business, results, financial position and development prospects.

4.2.3 Risks associated with a restrictive and evolving regulatory framework

All over the world, the pharmaceutical industry faces constant changes in its regulatory environment and its increased monitoring by competent regulatory authorities, notably the ANSM in France, the European Medicines Agency ("EMA"), and the Food and Drug Administration ("FDA") in the United States. Accordingly, the public is requiring more guarantees vis-à-vis the safety and effectiveness of drugs.

Health authorities – particularly the ANSM, EMA and FDA – have imposed increasingly stringent requirements in terms of the volume of data required to demonstrate the efficacy and safety of a product. Products already on the market are also subject to a periodic reassessment of their benefit/risk ratio after authorization. The late discovery of problems not detected during the research phase can lead to marketing restrictions, suspension or withdrawal of the product and an increased risk of litigation.

Furthermore, as the cell therapy treatment developed by the Company is very innovative, and regulations on the subject are still being drawn up, additional requirements may become applicable.

Insofar as new regulations would increase the cost of obtaining and maintaining product marketing authorizations or limit the economic value of a new product for its inventor, the growth prospects of the pharmaceutical industry and the Company could be reduced.

Occurrence of any one or more of these risks could have a material adverse effect on the Company's business, prospects, financial position, results and development.

4.2.4 Risks associated with the Company's status as a pharmaceutical company or its manufacturers

In France, the manufacture, import, export and wholesale distribution of drugs and the manufacture, import and distribution of investigational medicines may only be carried out in pharmaceutical companies.

Obtaining pharmaceutical company status and/or the GMP certificate requires an application file to be submitted to the ANSM who will only grant authorization after examining the file, usually after verifying that the Company has adequate premises, the necessary personnel (including a head pharmacist in charge) and the appropriate organization with satisfactory procedures to carry out the planned pharmaceutical activities. The ANSM will thereafter conduct regular checks on the pharmaceutical company to verify its compliance with applicable regulations. If the ANSM notices significant disparities regarding the GMP, it can decide to suspend the Company's pharmaceutical company status and its GMP certificate.

The present strategy of the Company is to outsource its manufacturing activities to specialist manufacturers (CMO). In this perspective, it must ensure that its subcontractors have the required regulatory authorizations, and in particular the GMP certificate for the countries in which they perform. The loss by one of its subcontractors of one of these authorizations, in particular in case of non-compliance with manufacturing rules, could cause delay in the manufacturing of the products developed by the Company.

The Company could, in addition and depending on the situation, produce the drugs it develops itself for use in clinical trial or in the marketing phase. Under these circumstances, the Company cannot guarantee that the pharmaceutical company status and/or the GMP certificate for one of its sites will be granted, nor can it guarantee that they will not be partially or fully suspended or revoked afterwards. One of these events would affect the Company's products manufacturing and marketing deadlines.

The materialization of one or several of these risks may have a material adverse effect on the business, prospects, financial position, results and development of the Company.

4.3 Risks associated with the Company's organization

4.3.1 The Company could lose key employees and not be able to attract other qualified personnel

The Company's success depends largely on the work and expertise of its management team and its Chief Executive Officer. To date, the Company has not taken out any so-called key person insurance (permanent disability/death insurance policy). The temporary or permanent unavailability of such individuals could impair the Company's ability to achieve its objectives, in particular by depriving it of their know-how and technical capabilities.

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

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

4.3.2 The Company's development will depend on its ability to manage growth

As part of its growth strategy, the Company will likely be required to develop its operational capacity, which could use a significant amount of its internal resources.

Accordingly, the Company will notably have to:

- anticipate the spending associated with this growth as well as the related funding requirements;
- anticipate the demand for its products and the income they are likely to generate;
- recruit, train, manage, motivate and retain a growing number of employees;
- increase the capacity of its existing operational IT, financial and management systems; and
- manage the outsourcing of the manufacturing of its drugs developed via its present subcontractors and, if need be, to new subcontractors.

The Company's inability to manage growth or unexpected difficulties encountered during its expansion could have a material adverse effect on its business, results, financial position, development and prospects.

4.4 Industrial risks

The Company's operations involve the handling of biological and chemical materials during research and manufacturing, which exposes it to health risks (i.e., occupational diseases).

Although the Company believes that the safety measures it adopts in terms of handling such materials meet the standards prescribed by rules and regulations in force and allow its employees to carry out their activities under good environmental, health and safety conditions, the risk of accidental contamination or occupational disease cannot be ruled out completely. In the event of an accident, the Company could be held liable for any damage resulting therefrom and such liability could exceed the caps specified in the insurance policies taken out by the Company, or not be covered by such insurance.

4.5 Risks related to information systems

The main risks regarding the Company’s information systems are related to the safety and the availability of the system, as well as the integrity and the confidentiality of the data (including patients' personal data or R&D information).

In order to preserve the safety of the information systems and to protect users, the Company has formalized rules governing their use (in particular in employment contracts or in certain internal control procedures) to set forth precautions and recommendations that all user must comply with when using the information systems within the Company.

However, the Company cannot guarantee that the users will comply with these rules and that they are sufficient to avoid risks of cyber-attacks, losses of sensitive data, discontinuation in the operation and risks for the Company to be held liable for loss or damage. These risks could, if they occur, have a material adverse effect on the business, the financial position, the results, the reputation or the development of the Company.

For example, any loss of scientific data could cause delays in the development of the Company's products and in the granting of regulatory authorizations and thus have a material adverse effect on its business, results, financial position and prospects.

4.6 Financial risks

The accounting data mentioned in this section is produced from the Company's annual financial statements restated under IFRS accounting rules for the 2014 and 2015 financial years. The reader is also invited to refer to Note 25 "Financial Risk Management", relating to such financial statements, and appearing in paragraph 20.1 of the *Document de Référence*.

4.6.1 Risks associated with historical and future losses

Since its creation in 2001, the Company has recorded operating losses every year. The net loss for the year ended December 31, 2015 amounted to € 10.1 million, mainly due to the following expenditures:

- launch of the Phase IIb clinical trial of Ovasave®;
- introduction of the development and industrial manufacturing process program for the ASTrIA platform products;
- technology transfer for the manufacture of Ovasave® to MaSTherCell; and
- research on the ENTrIA platform.

In the near future, the Company is expected to incur higher operating losses than in the past, particularly due to:

- its planned preclinical and clinical programs;
- the need to conduct new preclinical and clinical trials in order to address new market segments;
- all of the procedures that need to be followed in order to obtain marketing authorizations and the files required to apply for products to be admitted for reimbursement;
- additional regulatory requirements governing the manufacture of its products;
- sales and marketing expenses which may be incurred depending on the stage of completion of product development;
- the pursuit of an active research and development policy that may, where applicable, require the acquisition of new technologies, products or licenses.

Moreover, after the termination of the partnership between Trizell and the Company, the latter will have to seek an alternative to the financing provided by Trizell of the development, manufacturing and marketing of Ovasave®. The Company cannot guarantee that the terms proposed by any new partner would be on the same terms, or otherwise financially acceptable.

4.6.2 Risks relating to the business model

Owing to the autologous nature of T cell immunotherapies developed by the Company (product intended for the donor himself), the duration of treatment will vary depending on each patient and according to their response to the treatment (lack of response after the first injection/gradual loss of response/sustained tolerance). Depending on the duration of treatment, the Company's revenues and margins could therefore vary from patient to patient, given that production costs are concentrated on the manufacturing phase of the personalized product, regardless of the length of the treatment (please refer to paragraph 6.4.1.1.8 of the *Document de Référence*). A large gap between the Company's expectations and the average length of treatment could have a negative impact on its development, strategy, prospects and financial position.

4.6.3 Risk associated with research tax credit

To finance its activities, the Company has also opted since 2001 for the *Crédit d'Impôt Recherche* (research tax credit) ("CIR"), which involves the State granting a tax credit to companies that invest significantly in research and development. The research expenditure eligible for the CIR includes, in particular, wages and salaries, depreciation expense on research equipment, the supply of services outsourced to approved research organizations (public or private) and intellectual property expenses.

On October 2, 2015, the *Direction Générale des Finances Publiques* (General Directorate of Public Finances) notified the Company of an accounting audit regarding the CIR accounted for in the years ended December 31, 2011, 2012, 2013 and 2014. This procedure ended without any adjustments imposed.

However, the Company cannot exclude the possibility that the tax authorities may challenge the methods used by the Company for calculating research and development expenditure or of the CIR being called into question (for past or future financial years) pursuant to a regulatory change, or of it being challenged by the tax authorities even though the Company complies with the requirements in respect of documentation and eligibility of expenditures. If such a situation arose, it could have an adverse effect on the Company's results, financial position and prospects.

4.6.4 Risks associated with loss carryforwards in the future

At December 31, 2015, taking into account the net loss recorded during the year, the Company had a loss carryforward of € 67.6 million. As of today, this loss can be carried forward indefinitely and applied to future profits.

In France, allocation of these losses is capped at 50% of taxable profits for the year, and this limit applies to any profits in excess of €1 million. The unused balance of losses can be carried forward to following financial years, and allocated under the same conditions with no time limit.

The Company cannot rule out the possibility that regulatory or legislative developments regarding corporation tax will call into question, in whole or in part, the possible offsetting of these prior losses against future profits, or impose a time limit on such offsetting.

4.6.5 Risks related to access to public grants and advances

The Company has received and continues to receive various grants, particularly in the context of:

- the development of autologous cell therapy to treat juvenile idiopathic arthritis and rheumatoid polyarthritis (project entitled "CellArthrix");
- the search for Ovasave® efficacy biomarkers (project entitled "Femtokine");
- the development and the implementation of a procedure to automate the first step of the manufacture process of Ovasave® (project entitled "POSITIVE");
- the clinical development of Ovasave® for refractory Crohn’s disease (project entitled "CATS");
- the development of the manufacturing and clinical development process of Col-Treg for the treatment of autoimmune uveitis (project entitled "TRUST");
- aid for the recruitment of young PhD candidates;
- supporting economic development in the priority areas.

In the future, the Company intends to continue to seek grants in order to accelerate its development.

In the event that it does not comply with the contractual conditions set out in innovation grant agreements entered into (or if early repayment conditions where to be met regarding the Zero-Interest Loan for Innovation granted by Bpifrance Financement (the French public investment bank) on November 28, 2014), the Company may be required to repay any advances early. This could deprive the Company of some of the financial resources needed to successfully carry out its research and development projects.

Although at present, obtaining grants is not essential to the Company's development, it cannot guarantee that it will have the necessary additional financial resources, nor the time or opportunity to replace these financial resources with other financial resources.

4.6.6 Dilution risk

As part of its incentive policy towards executive officers and employees and to attract additional expertise, the Company has allotted or issued stock options, warrants (*bons de souscription d'actions*) and free shares and could also, in the future, issue or allot shares or new financial instruments giving the right to subscribe to the Company's capital.

Furthermore, the Company has established an optional equity financing line (PACEO®) with Société Générale on the issuance of a maximum number of 1,150,000 new shares (i.e. 8.92% of the present share capital) for 24 months starting on January 27, 2016. The Company has no drawing obligations and will use this equity line only if justified by market conditions, and if in the Company's and in the shareholders' best interests.

The board of directors held on May 2, 2016 has granted 600,000 free shares to Mr. Stéphane Boissel and all employees of the Company (see paragraph 21.1.4.3 of the *Document de Référence*). The same board of directors' meeting has issued a plan for 40,000 warrants to the Scientific Advisory Board (SAB) members of the Company (see paragraph 21.1.4.2 of the *Document de Référence*).

At the date of the *Document de Référence*, the full exercise, or as appropriate the full acquisition, of all instruments giving access to capital allotted to date would allow the subscription of 3,220,996 new shares (please refer to paragraph 21.1.4 of the *Document de Référence*), representing approximately 20.00 % of the fully diluted share capital.

Exercise of all instruments giving access to the outstanding capital as well as all new issuances or allotments would lead to a potentially significant dilution for the current and future shareholders of the Company.

4.7 Market risk

4.7.1 Liquidity risk

The Company may need to strengthen its capital base or seek additional funding to ensure its development

Since its creation, the Company has financed its growth by strengthening its capital base through successive capital increases, and by obtaining public grants for CIR, but has never taken out any bank loan. Accordingly, the Company is not exposed to liquidity risk resulting from the implementation of any early repayment clauses in respect of such loans.

The Company has completed a specific review of its liquidity risk and considers at the date of the *Document de Référence* that it is not in a position to meet its upcoming commitments for the twelve next months without changing its current business plan.

As of March 31, 2016, the Company's cash and cash equivalents amounted to € 5 million. This amount includes the payment of € 2 million to Trizell on December 11, 2015 under the signing of the agreement terminating the exclusive licensing and distribution agreement regarding Ovasave® and the receipt of the € 2 million on December 31, 2015 under the 2014 CIR. However, this amount does not include the amount of €3 million due from the 2015 CIR expected to be received by the end of the half year 2016.

Given the contemplated development plan and the operational expenses of the first quarter 2016, the Company's cash available on March 31, 2016, supplemented by the 2015 CIR to be received, will enable the Company to continue its activities until the end of July 2016. Additional financing resources will therefore be necessary.

The Company benefits from a PACEO® optional equity line from Société Générale on 1,150,000 new shares which can be issued during a 24 months period starting on January 27, 2016 by the exercise of warrants (*bons de souscription d'actions*). The operation was the subject of a prospectus rendered available to the public and approved by the AMF under number 16-036 dated January 25, 2016. At the date of the *Document de Référence*, no drawdown on this equity line has been made.

Significant research and development efforts and expense relating to clinical studies have been made and incurred since the Company started to operate, which has generated a negative operating cash flow up to this date. Net cash used by the Company's operating activities amounted respectively to €-10.1 million and €-6.9 million for the financial years ended December 31, 2015 and 2014, respectively.

In the future, the Company will continue to have substantial financing requirements for developing its technology, pursuing its clinical development program and equipping its own R&D sites and, later on, for producing and marketing its products. It is therefore possible that the Company will be unable to finance its growth from operating cash flows, which would lead it to seek other sources of funding, particularly through new capital increases.

The Company is therefore assessing various additional funding sources, in particular by existing shareholders and/or new investors in the prospect, among others, of capital increases, or via potential business partners by entering into development and/or distribution agreements regarding products developed by the Company.

The Company's funding requirements and their future timing depend on factors partly outside the Company's control, such as:

- higher costs and slower progress than anticipated for its research and development programs and clinical studies;
- the cost of preparing, filing, defending and maintaining patents and other intellectual property rights;
- higher costs and longer times than anticipated to obtain regulatory approvals for the marketing of its products, as well as their eligibility for reimbursement, including the time required to prepare application files for the competent authorities;
- the cost of responding to changes in the technology developed by the Company for the manufacture and marketing of all or some of its products; and
- new opportunities for developing new products or for the acquisition of technologies, products or companies.

It is possible that the Company may not be able to raise additional capital when it needs to, or that capital may not be available on financial terms acceptable to the Company. If funds were not available, the Company may need to:

- delay, reduce or eliminate the number or the scope of its preclinical and clinical trials;
- license its technology to partners or third parties; or
- enter into new collaboration agreements on less favorable terms than it would have obtained in a different context.

In addition, if the Company raises capital by issuing new shares, the holdings of its shareholders could be diluted. Debt financing, insofar as it might be available, could also include restrictive conditions for the Company and its shareholders.

Any one or more of these risks could have a material adverse effect on the Company, its business, financial position, results, development and prospects.

4.7.2 Foreign exchange rate risk

At the date of the *Document de Référence*, the Company considers that it is not exposed to foreign currency exchange risks because only a small portion of its supplies are obtained outside the euro zone and invoiced in foreign currencies, mainly in U.S. Dollars, in G.B. Pounds Sterling and in Swiss Francs.

In view of these insignificant amounts in currency positions, at this stage of development of its business, the Company has not made any hedging arrangements to protect its business against fluctuations in exchange rates.

4.7.3 Credit risk

The Company manages its liquid assets in a conservative manner. Liquid assets and equivalents include cash and short-term financial instruments held by the Company (only UCITS classified as "short-term money market").

In addition, credit risk relating to liquid assets, equivalents and short-term financial instruments is not significant in view of the quality of the financial institution counterparties.

4.7.4 Interest rate risk

The only exposure to interest rate risk relates to the investment of cash in cash equivalents (please refer to paragraph 4.7.3 of the *Document de Référence*). Given the current low rate of return on this type of investment, the Company believes that any 1% increase or decrease would have no material effect on its net income in light of the losses generated by its operating activities.

The Company does not have any variable-rate debt. Its debt repayments are not subject to interest rate risk.

4.7.5 Equity risk

The Company considers that it is not exposed to any risk associated with equities or other financial instruments, given that it does not hold any interest or securities in listed companies.

4.8 Insurance and risk cover

The Company has implemented a policy to cover the main insurable risks for amounts that it considers compatible with the nature of its business.

Given the specific nature of its business, which at this stage is focused on research and development of innovative technology in the field of cell therapy, in the absence of a direct loss or loss indicators for its industry, the quantification of potential risks makes it difficult to determine an insurable amount, particularly with regard to civil liability, but the Company believes that the insurance policies described below adequately cover the risks inherent in its activities and that its insurance policy is consistent with industry practices. The Company does not foresee any particular difficulties in maintaining adequate insurance levels in the future, subject to market conditions and capacity.

The main policies subscribed to by the Company are the following:

- “Property damage – operating and financial losses” policy, which covers risks of fire, water, theft, electrical damages, breakdown machinery damages, loss of goods and any damage other than those named that are not excluded. It also covers within the same limits, losses in research and development incomes as well as financial losses following a change in the controlled environment. Given the lack of significant gross sales of the Company, this guarantee aims at enabling it to resume on-going work which would have been destroyed by an accident and to

bear the general and operating expenses for this period. The policy covers the production sites of Valbonne and Besançon with a maximum coverage of € 10 million.

- "Civil liability" policy, which covers on the one hand the operating risks for a maximum coverage of € 5 million per accident with a sub-limit of € 2 million per accident for successive material and intangible damages caused by third-parties, and on the other hand professional civil liability for a coverage amount of € 1 million per year insured.

The liability of the Company because of clinical trials is covered by specific policies which are connected to the "civil liability" policy and for which the pricing system and the covered amounts depend on the domestic regulation applicable to the clinical investigation center involved, as it is the case for France, where the Public Health Code provides for mandatory insurance of clinical trial sponsors as well as the terms of this insurance. The global amount of insurance premiums and subscribed guarantees for the trials therefore depends on the number of trials, of their geographical localization and of the projected number of patients to include in the trial.

The Company has also subscribed a policy to cover its executive officers' civil liability when it might be engaged while performing their duties, with a global annual cap coverage of € 5 million.

The occurrence of one or all of the risks covered by the aforementioned policies could, inspite of the policies subscribed, have a material adverse effete on its business, results, financial position and development of the Company.

4.9 Significant events and legal action

With the exception of an adjustment notice for a non-material amount (€12 thousand), fully paid to this date, relating to an URSSAF (*Unions de Recouvrement des Cotisations de Sécurité Sociale et d'Allocations Familiales* – federal organisation for the payment of social security and family allowance contributions) inspection for the 2009 and 2010 financial years, which the Company has decided to challenge before the courts, there are no other governmental, judicial or arbitration proceedings, including any that the Company is aware of, pending or possible, and likely to have, or which have had, a material impact on the Company's financial position or profitability during the last 12 months.

5. COMPANY INFORMATION

5.1 Company history and development

5.1.1 Company name and trade name

The name of the Company is TxCell.

5.1.2 Place of registration and registration number of the Company

The Company is registered with the Grasse trade and companies register under SIREN number 435 361 209.

Its French classification of activities' code (*code NAF*) is 7211 Z, which corresponds to biotechnology research and development.

5.1.3 Date of incorporation and company term

The Company was incorporated on April 12, 2001 for a 99-year period from the date of registration with the trade and companies register, i.e. until April 11, 2100, except in the event of extension or early dissolution.

5.1.4 Head office of the Company, legal form and laws governing its activities

The Company is a limited liability company (*société anonyme*) governed by French law, whose operation is primarly subject to Articles L. 225-1 et seq. of the French commercial code.

The Company's head office is located at Les Cardoulines, Allée de la Nertière, 06560 Valbonne-Sophia Antipolis, France.

The Company's contact details are as follows:

Telephone: +33 (0) 497 218 300

Email: contact@txcell.com

Website: www.txcell.com

The Company is a French limited liability company (*société anonyme*) with a board of directors (*conseil d'administration*) incorporated under French law, governed by the rules and regulations in force in France (and, in particular, the provisions of Book II of the French commercial code) and by its own bylaws.

The Company also has a second establishment located Besançon: Bâtiment IBFC - 6, rue Docteur Jean-François-Xavier Girod - 25000 Besançon.

On October 14, 2015, the Company announced the revision of its production strategy and its decision to outsource all its current and future production activities, in order to focus on its high value-added activities, namely research, clinical development and strategic partnerships. As a result of this reorganization, the manufacturing site in Besançon was closed. Therefore, the secondary establishment is expected to be removed from the trade and companies register in 2016.

5.1.5 Significant events in the development of the Company's activities

Hervé Groux and Françoise Cottrez founded the Company, but they no longer hold any executive office within the Company and are no longer shareholders.

Significant events in the development of the Company's activities:

2001 Creation of the Company through a spin-off from the National Institute of Health and Medical Research (*Institut National de la Santé et de la Recherche Médicale* – "INSERM").

2003 First preclinical proof of concept of the type 1 regulatory T lymphocyte (Treg) based on the ovalbumin antigen, on inflammatory colitis on animals (Foussat et al., J. Immunol, 2003).

2004 Fund raising of €10.5 million in several tranches from financial investors: Auriga Partners, AXA Private Equity, Bioam Gestion, CDC Innovation and Seventure.

2007 Authorization from the French Agency for the Safety of Healthcare Products (*Agence Française pour la Sécurité Sanitaire des Produits de la Santé* – "AFSSAPS") to initiate clinical testing of Ovasave® for the treatment of Crohn's disease.

2008 Raising of €9.8 million in several tranches from past investors: Auriga Partners, AXA Private Equity, Bioam Gestion, CDC Innovation and Seventure.

Launch of the Phase I/IIa clinical study of refractory Crohn's disease (CATS1) with Ovasave®.

2010 Appointment of Miguel Forte as Chief Medical Officer.

Positive preliminary results of the Phase I/IIa (CATS1) clinical study with Ovasave®.

Successful preclinical studies for TX-RAD in inflammatory arthritis.

Fund raising of €3.5 million from existing financial investors (Auriga Partners, Seventure and CDC Entreprises).

2011 Appointment of François Meyer as Chairman of the board of directors.

Authorization from the AFSSAPS to extend CATS1.

Presentation of positive CATS1 results at the European Gastroenterology Conference in Stockholm.

2012 Presentation of the positive CATS1 results at the 7th Congress of the European Crohn's and Colitis Organisation.

Fund raising of €12.4 million[1] in several tranches from past investors (such as Auriga Partners and Seventure) and an initial equity investment by Innobio.

2013 Obtaining of the pharmaceutical establishment status from the National Health Products Safety Agency (*Agence Nationale de la Sécurité du Médicament* – "ANSM") for the Besançon manufacturing site.

Signing of a partnership agreement with Ferring/Trizell regarding Ovasave®.

2014 Launch of the development of Col-Treg for the treatment of autoimmune uveitis.

Initial public offering in Compartment C of the Euronext Paris regulated market for a gross amount of €16.2 million, a simultaneous €3.5 million bond conversion, followed by an additional fund raising of €1.5 million from major shareholders.

Obtaining of the Good Manufacturing Pratice (GMP) compliance certificate from ANSM for the Besançon manufacturing site.

Obtaining of the Advance Therapy Medicinal Products (ATMP) classification from the European Medications Agency (EMA) and, then the orphan drug designation for Col-Treg in Europe.

Presentation of positive preclinical results for Col-Treg in autoimmune uveitis.

Launch of the Phase IIb (CATS29) study of refractory Crohn's disease (CATS-1) with Ovasave®.

2015 Launch of a program to develop and industrialize the production process.

Appointment of Stéphane Boissel as Chief Executive Officer and Miguel Forte as Chief Operating Officer.

Besançon manufacturing site closed and patient recruiting suspended for CATS29.

[1] This round of fund-raising included a capital increase for €6.5 million, the conversion of convertible bonds for €2.9 million and the exercise of Tranche 2 warrants for €3 million.

Capital increase by way of private placement of €7.9 million gross mostly from international and healthcare investors.

Review of the Company's production strategy to outsource all existing and future production activities in order to focus on R&D and strategic partnerships, and signature of an exclusivity contract with MaSTherCell for the production in Europe of cellular therapy products coming from the ASTrlA platform.

Investigational New Drug (IND) request to extend CATS29 to the United States approved by the US Food and Drug Administration (FDA), and "fast track" designation for Ovasave® obtained from the FDA.

Obtaining exclusive rights on key patent filing for CAR-Tregs through an option agreement with Yeda.

Obtaining of the orphan drug designation for Col-Treg in the United States.

Termination of the partnership agreement and waiver by Trizell of its option to obtain an exclusive worldwide license covering the developing, the manufacturing and the commercialization of Ovasave®.

2016 Successful production of the first test batches of Ovasave® by MaSTherCell.

Launch of a new laboratory specializing in the development of manufacturing processes and of an academy dedicated to technology transfers.

Appointment of a new Scientific Advisory Board (SAB) chaired by Professor Zelig Eshhar

Signing of a strategic collaboration agreement mainly dedicated to research and development on CAR-Tregs with Ospedale San Raffaele (OSR)

5.2 Investments

Investments made in the last two financial years:

In €k	12/31/2015	12/31/2014
Intangible assets		
Acquisition	(5,902)	(8)
Sale	0	0
Change in intangible assets supplier account	3,905	0
Other eliminations of intangible items with no impact on cash and cash equivalents	(3)	0
Net cash from intangible assets	**(2,000)**	**(8)**
Property, plant and equipment		
Acquisition	(214)	(582)
Sale	23	17
Change in property, plant and equipment supplier account	(83)	0
Net cash from property, plant and equipment	**(274)**	**(566)**
Financial assets		
Acquisition	(3)	(84)
Sale	3	2
Net cash from financial assets	**(0)**	**(82)**
Net cash from investing activities	**(2,274)**	**(656)**

The financial year ended December 31, 2015 includes net cash flow from investment in intangible assets of €2 million (see Notes 3 and 14.2 of paragraph 20.1 of the *Document de Référence*).

This amount equals the first payment made to Trizell on signing the agreement that terminated the collaboration, development, option and license agreement between Trizell and the Company on December 2, 2015. Under this agreement the Company recovered all Trizell's rights over Ovasave® in return for paying amounts which could reach €15 million, €6 million of which is fixed and €9 million of which is conditional by the future revenues generated by Ovasave®.

The acquisition cost of these rights, whose amount and maturity can be estimated with certainty, was recognized in assets at €6 million. These acquisition costs were discounted in accordance with IAS 38. The 10-year French Government bond rate (*taux OAT*) as at December 31, 2015 of 0.995% was used as the discount rate. The repurchase of the rights therefore amounts to €5.9 million on a discounted basis.

When the termination agreement was signed, €2 million of the original debt of €6 million had been repaid. The balance is due on December 2, 2017 for €2 million and on December 2, 2018, for €2 million, for a total of €3.9 million on a discounted basis.

For the financial year 2015 capital expenditures mainly concerned the purchase of laboratory equipment as part of the program to develop and industrialize the Ovasave® production process. In 2014, capital expenditures mainly concerned the purchase of laboratory equipment necessary to conduct the Phase IIb clinical study.

5.2.1 Main investments in progress

Since the start of the financial year 2016 the Company has acquired laboratory equipment as part of opening its new specialized laboratory for developing its manufacturing processes.

5.2.2 Main future investments

The capital expenditures planned for 2016 and 2017 will mainly aim to equip the Company's R&D facilities, in particular the new laboratory, with a view to improving and automating the manufacturing process for products from the ASTrlA platform and for developing the manufacturing process for products from the new ENTrIA platform.

6. BUSINESS OVERVIEW

6.1 General presentation

6.1.1 Generalities

The development of cellular immunotherapy is identified today as a major breakthrough in medical research and personalized treatments. This innovative technological approach represents a real opportunity for patients in therapeutic failure who require therapeutic treatments with more targeted action to provide a new treatment option.

Cellular immunotherapy can be defined as a treatment based on immune cell administration to patients with the goal of stimulating their immune system to kill off cancer cells, or inhibiting their immune system as a way to suppress inflammation. These cellular immunotherapy treatments can be personalized by the use of patient's own cells, strengthening the treatment tolerability due to their autologous nature while targeting the patient's disease.

TxCell (the "Company") was founded in 2001 as a spin-off from the INSERM. Up until 2015, the Company's technology was based exclusively on the pioneering work of the founding scientist who in 1997 co-discovered the type 1 regulatory T lymphocytes (Type 1 Tregs)[2]. These cells play an important role in the immune system by suppressing undesired immune responses to environmental antigens that are normally tolerated (ingested, contact, inhaled, etc.) and several tissue-specific self-antigens. These antigen-specific Type 1 Treg cells (Ag-Tregs) have the potential to treat autoimmune and chronic inflammatory diseases. The Company's developments on this lymphocytic population have been consolidated onto a single product platform called ASTrIA (Antigen-Specific Tregs for Inflammation and Autoimmunity).

In 2015, the Company diversified its technological base by addressing other regulatory T lymphocytes such as the cells known as FoxP3+. Work on FoxP3+ Treg cells has been consolidated on a single platform called ENTrIA (Engineered Tregs for Inflammation and Autoimmunity). Like Type 1 Tregs, FoxP3+ T regulatory cells (FoxP3+ Tregs) play a key role in controlling autoimmunity and hypersensitivity mechanisms to our environment. This population of regulatory cells is known for constitutively expressing the intercellular factor FoxP3, a deficiency of which in humans results in a widespread fatal autoimmune syndrome. Numerous studies have also revealed that FoxP3+ Tregs could treat inflammatory diseases.

The two populations, FoxP3+ Tregs and Type 1 Tregs, have different origins as well as differing mechanisms of action. Whereas the ASTrIA platform is based on the therapeutic use of pre-existing, non-genetically modified Type 1 Tregs, the ENTrIA platform offers cellular immunotherapy products based on the use of genetically modified FoxP3+ regulatory cells (CAR-Tregs).

Using these two platforms, the Company has targeted its strategy on severe chronic inflammatory and autoimmune diseases, which present significant unmet medical needs. The drug candidates developed by the Company are currently generated *ex vivo* from the patient's own peripheral blood in a proprietary manufacturing process. This is known as "autologous" therapy. The Company could later conduct research to validate the concept of taking Treg cells from a third-party donor as opposed to taking them from the patient. This is known as "allogenic" therapy.

Ovasave®, the Company's lead drug candidate produced on the ASTrIA platform, is in clinical development to treat patients with active, moderate-to-severe, refractory Crohn's disease. In 2011, the Company successfully completed Phase I/IIa clinical trials in which Ovasave® was administered to patients at this stage of Crohn's disease. This study, known as CATS1 (Crohn's And Treg Cells Study, study 1), showed promising results in terms of Ovasave®'s safety and efficacy. In December 2014, the program's second stage was introduced with the launch of an international and multi-centric Phase IIb clinical trial, called CATS29, to confirm the positive results of the Phase I/IIa study.

[2] A CD4+ T-cell subset inhibits antigen-specific T-cell responses and prevents colitis. Groux H, O'Garra A, Bigler M, Rouleau M, Antonenko S, de Vries JE, Roncarolo MG. Nature. 1997 Oct 16;389(6,652):737-42.

The CATS29 study had to be temporarily interrupted in June 2015 due to manufacturing problems at the Company's site in Besançon, which was later permanently closed. Because of these issues, the Company has decided to externalize the manufacturing of Ovasave® to MaSTherCell, a Contract Manufacturing Organization ("CMO"). On July 29, 2015, the Company announced the initiation of the technology transfer to MaSTherCell, which should be achieved in Q2 2016. On the basis of the first validation batches of Ovasave® manufactured by MaSTherCell in compliance with specifications, the Company has submitted an amendment to the CATS29 study to the European regulatory authorities via the VHP procedure (Voluntary Harmonized Procedure), including in particular the change of manufacturing site. The Company expects to receive the approval from the European regulatory authorities in Q2 2016. The recruitment of patients for CATS29 study may resume once the Company has received the approval from the European regulatory authorities, once the manufacturing technology transfer to MaSTherCell has been completed, and once the Company has obtained the necessary funds to finance the study. The first clinical data will be expected within 18 to 21 months following the resumption of the study. The global cost of the study should amount around €15 million.

Furthermore, in June 2015, TxCell obtained from the US Food and Drug Administration (FDA) the Investigational New Drug ("IND"), the approval to extend its clinical development of Ovasave® to the United States. The FDA's "*Fast Track*" designation was obtained in July 2015.

Col-Treg, the Company's second drug candidate produced on the ASTrIA platform, is being developed to treat autoimmune uveitis (or non-infectious uveitis), which is a rare condition that causes chronic swelling of the eye tissue and for which there are very few treatment options. For the treatment of non-infectious uveitis, Col-Treg received EU Orphan Drug Designation in December 2014 and US FDA Orphan Drug Designation in September 2015. Based on the preclinical findings already obtained for Col-Treg in autoimmune uveitis, the Company expects to finalize in 2016 the preclinical development and the regulatory application, which are necessary to start the first clinical study of Col-Treg in non-infectious uveitis. The start date of the study was not set yet.

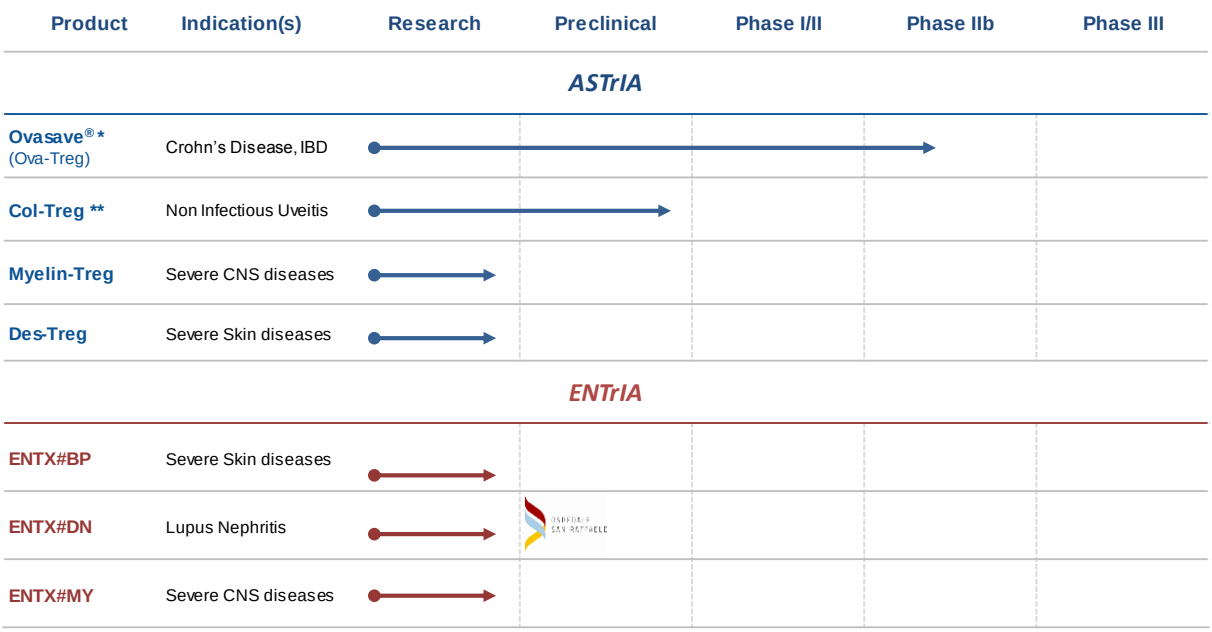
The ASTrIA platform is capable of producing an extensive portfolio of personalized cellular immunotherapy products based on different patient-specific autologous Ag-Tregs. The Company can leverage this platform to build up a sizable product pipeline for treating numerous chronic inflammatory and autoimmune diseases. TxCell has set its sights on expanding these developments beyond its own walls by building strategic partnerships with bio-pharmaceutical groups.

ENTrIA, TxCell's new platform, is also capable of producing numerous drug candidates and could significantly expand the product pipeline developed by the Company.

The differences in the mechanism of action between Type 1 Tregs and FoxP3+ Tregs will help the Company adapt its therapeutic approach to the pathophysiology of the indication under review. From this standpoint, the ENTrIA and ASTrIA platforms are extremely complementary and should be able to target the majority of autoimmune and chronic inflammatory diseases. Moreover, the cell engineering used in producing the ENTrIA cell products will make it possible to specifically target the FoxP3+ Tregs to a given pathology. This targeting occurs naturally in the ASTrIA product pipeline. The cell engineering is also expected to increase the ENTrIA products' efficacy and safety by introducing appropriate genes.

The following table provides an overview of the Company's drug candidates:

Figure 1 : *Product pipeline*



* The Phase IIb study (CATS29) had to be temporarily interrupted in June 2015. The Company has submitted an amendment to the clinical protocol of the CATS29 study to the European regulatory authorities via the VHP procedure (Voluntary Harmonized Procedure), including in particular the change of manufacturing site. The Company expects to receive the approval from the European regulatory authorities in Q2 2016. The recruitment of patients for CATS29 study may resume once the Company has received the approval from the European regulatory authorities, once the manufacturing technology transfer to MaSTherCell has been completed, and once the Company has obtained the necessary funds to finance the study. The first clinical data will be expected within 18 to 21 months following the resumption of the study.

** TxCell expects to finalize in 2016 the preclinical development and the regulatory application, which are necessary to start the first clinical study of Col-Treg in non-infectious uveitis. The start date of the study was not set yet.

The Company has numerous advantages needed to establish itself as a fully-fledged biotech company. These advantages include an attractive business model, two innovative technological platforms and a pipeline of highly-promising drug candidates to treat high-incidence pathologies, such as Crohn's disease, multiple sclerosis and rheumatoid arthritis, as well as rare and orphan diseases, such as non-infectious uveitis. These products could be developed and marketed by the Company itself and/or through strategic partnerships with international bio-pharmaceutical groups.

TxCell's operational priorities are as follows:

- to obtain placebo-controlled clinical data for Ovasave®;
- to obtain compelling preclinical proof of principle for ENTrIA, TxCell's second platform based on CAR-Treg;
- to achieve best efficiency in the manufacturing processes of ASTrIA and ENTrIA products.

Beyond the three operational priorities mentioned above, all other programs and developments, including the development of Col-Treg, are currently second priorities. Any meaningful investment in these programs will be subject to further ad hoc financing, and especially in the form of specific industry partnerships. Furthermore, the Company is no longer actively working on the HSP60-Treg program which no longer appears in the product pipeline.

6.1.2 Immunotherapy: a new model for numerous diseases

Recent years have seen the long held promise of immunotherapy turned into reality. A number of products now on the market or in late development have shown excellent results, notably in oncology

but also in other areas. The first wave of products consists of antibodies directed at key checkpoints in the cellular immune system or at specific antigens expressed on certain types of tumors to have the body's own immune system recognize and attack the tumors. These include anti-CTLA-4 and anti-PD-1 specific monoclonal antibodies and breast cancer specific antigen vaccines.

Cell-based immunotherapies have also shown great promise. Provenge® from Dendreon, consisting of a dendritic T cell vaccine prepared from the patient's own cells, was the first cellular immunotherapy to be approved by the US FDA in 2010 for the treatment of refractory prostate cancer and more recently, in 2013, by the European Medicines Agency (EMA). The Swiss-based Novartis group and the US-based Juno Therapeutics, Inc. (Juno) and Kite Pharma, Inc. (Kite) recently published highly-promising findings on responses to treatment using T lymphocytes expressing chimeric antigen receptors (CAR-T) in patients with acute lymphocytic leukemia (ALL) who had no second-line treatment alternative or a very short life expectancy when they first received this new treatment. Introducing a CAR receptor by genetically modifying the patient's own T cells implies that these cells can recognize a tumor antigen expressed in the lymphomas and leukemia. Initial applications for product licenses for these new cellular immunotherapy products are expected to be submitted in 2017 or 2018 in the United States. These new products could be a major paradigm shift in how certain hematological tumors are treated. Furthermore, the last few years has seen an increasing number of partnerships in cell therapy including major pharmaceuticals companies (such as Novartis, Pfizer and Merck) and top biotech companies (such as Celgene).

There are encouraging signs for the technologies developed by TxCell, such as the clinical breakthroughs with the CAR-T cells in hematology as well the significant investment inflows from the financial markets and industrial players to build up this sector. The Company expects that the CAR-T stakeholders, investors and industrial players will embrace the use of regulatory T cells in autoimmune and inflammatory diseases given the success of these approaches in cancer treatment. The total market could represent more than $100 billion per year with an annual growth of over 5% between 2016 and 2020[3]. For comparison, the oncology market represents approximately $100 billion[4].

For these reasons, TxCell should be able to attract more funding and step up its growth by signing strategic partnerships with leading pharmaceutical and biotech companies.

6.1.3 TxCell: a radically different positioning

Unlike effector T lymphocytes, the discovery that various sub-populations of regulatory T lymphocytes play a key role in preventing autoimmunity (when the body turns against itself) and maintaining immune tolerance is relatively recent. In the 1990s, first Shimon Sakaguchi[5] followed by Hervé Groux[6] respectively identified and characterized the FoxP3+ Tregs and Type 1 Tregs. Over the past two decades, advances have been made in describing these cell types, their differences, their physiologic roles, but most of all in grasping their therapeutic potential, especially in numerous profiles of autoimmune and chronic inflammatory diseases in animals.

In the early 2000s, early-stage clinical trials were conducted with FoxP3+ Tregs primarily in the prevention of Graft versus Host Disease (GVHD) in stem cell transplants in leukemia patients[7]. A few Phase I/II clinical trials were also conducted with FoxP3+ Tregs in type 1 diabetes[8]. These clinical trials

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[3] Source: Company's estimate .

[4] Developments in Cancer Treatments, Market Dynamics, Patient Access and Value: Global Oncology Trend Report 2015. IMS Health 2015.

[5] Takahashi T, Kuniyasu Y, Toda M, Sakaguchi N, Itoh M, Iwata M, Shimizu J, Sakaguchi S. Immunologic self-tolerance maintained by CD25+CD4+ naturally anergic and suppressive T cells: induction of autoimmune disease by breaking their anergic/suppressive state. Int Immunol. 1998 Dec;10(12):1969-80.

[6] Nature 389, 737-742 (October 16, 1997). A CD4+T-cell subset inhibits antigen-specific T-cell responses and prevents colitis. Groux et al.

[7] Brunstein CG, Miller JS, Cao Q, McKenna DH, Hippen KL, Curtsinger J, Defor T, Levine BL, June CH, Rubinstein P, McGlave PB, Blazar BR, Wagner JE. Infusion of ex vivo expanded T regulatory cells in adults transplanted with umbilical cord blood: safety profile and detection kinetics. Blood. 2011 Jan 20; 117(3): 1061–1070.

[8] A Phase I Safety Trial of CD4+CD127lo/-CD25+ Polyclonal Treg Adoptive Immunotherapy for the Treatment of Type 1 Diabetes: T1DM Immunotherapy Using CD4+CD127lo/-CD25+ Polyclonal Tregs (Treg). NCT01210664.

validated not only the feasibility of the FoxP3+ Treg-based therapeutic approach, but also confirmed the appropriate tolerance profile of these cell therapy products after administering them in patients. Other early-stage clinical trials (Phase I-IIb) are ongoing such as on organ transplants using FoxP3+ Tregs cell products called polyclonal (non-specific to a given antigen)[9]. These clinical trials have always been conducted for the most part by the academic world (hospitals or universities).

To date, TxCell is the only industrial player who has led clinical trials on Type 1 Tregs. The Company is also the only one to have developed an extensive platform of cell products based on this regulatory cell sub-population. Moreover, contrary to earlier polyclonal and current FoxP3+ Treg approaches, TxCell is striving to develop on its ENTrIA platform antigen-specific FoxP3+ Treg cell-based products, which are therefore more targeted to the diseases treated.

The Company's autologous antigen-specific products reflect a unique approach in immunotherapy for treating autoimmune and chronic inflammatory diseases. It is a personalized, multi-mechanism approach using the natural properties of the patient's own Treg cells.

Each patient will receive his or her own cells, educated to treat their own disease. From a single blood collection, TxCell can manufacture many doses of product potentially allowing 3 to 5 years of treatment. The autologous nature of the products implies that, upon administration, cells composing the cellular immunotherapy as well as anti-inflammatory molecules secreted by the cells are not rejected by the patient's immune system.

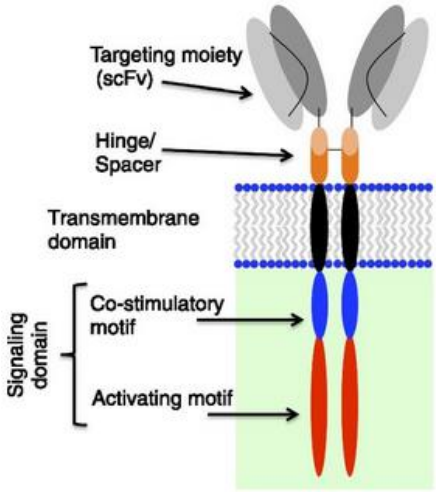
With respect to the ASTrIA platform, Ag-Treg cells are antigen-specific. This means that all cells composing the Ag-Treg products have the capacity to specifically recognize, thanks to a membrane-bound receptor, a pre-determined antigen. This recognition leads to *in vivo* Ag-Treg cell activation and triggering of the anti-inflammatory activity.

The antigen is determined depending on the inflamed tissue to treat and is not dependent on the disease to be treated. As an example, ovalbumin, a food antigen, has been chosen as the specific antigen for Ovasave® (developed for the treatment of Crohn's disease), due to its localization in the inflamed intestine after ingestion. In the same manner, Collagen Type II, a self antigen (expressed by the body's own tissues), has been chosen as the specific antigen for Col-Treg (developed for the treatment of uveitis), due to its localization in the inflamed eye.

On the ENTrIA platform, the antigenic specificity will be induced by introducing into the FoxP3+ cells a gene coding for the chimeric antigen receptor (CAR). This chimeric receptor is made up of: 1) an antigen recognition domain typically derived from a monoclonal antibody, 2) an extracellular domain called a spacer or a hinge enabling the antigen recognition domain to be distant from the membrane, 3) a transmembrane domain, and 4) an intracellular area composed of signalization and co-stimulation domains specific to T lymphocytes. The CAR's recognition of the antigen triggers cell activation by transmitting an intracellular signal through these signalization and co-stimulation domains.

[9] Trzonkowski P, Bacchetta R, Battaglia M, Berglund D, Bohnenkamp HR, ten Brinke A, Bushell A, Cools N, Geissler EK, Gregori S, Marieke van Ham S, Hilkens C, Hutchinson JA, Lombardi G, Madrigal JA, Marek-Trzonkowska N, Martinez-Caceres EM, Roncarolo MG, Sanchez-Ramon S, Saudemont A, Sawitzki B. Hurdles in therapy with regulatory T cells. Sci Transl Med. 2015 Sep 9;7(304):304ps18.

Figure 2 : *Structure of a chimeric antigen receptor (CAR)*[10]



The CAR is chosen in relation to the disease targeted. If the CAR recognizes an antigen whose expression is limited to the inflamed tissue (for example, a specific skin antigen within the context of skin diseases), the activation of the FoxP3+ Treg cells transduced with the CAR (CAR-Tregs) will therefore also be limited to the inflamed tissue, thereby allowing specific and selective action.

6.1.4 Products aimed at significant unmet medical needs

An unmet medical need is Txcell's top criteria in deciding to launch the development of a new drug candidate.

The Company's two leading drug candidates are now in development. The first is being developed for the treatment of Crohn's disease and the second for the treatment of a type uveitis, namely non-infectious uveitis. Both product candidates address a stage of the disease for which no therapeutic option currently exists for the patients.

Crohn's disease

Crohn's disease is a lifelong disease, which is often characterized by chronic diarrhea, abdominal pain, anorexia, fever and musculoskeletal abnormalities. Patients frequently have flares with varying degree of remission. Crohn's disease is extremely debilitating and severely disables patients who are often in the prime of their lives. The disease significantly hinders these young people's social and professional lives.

Conventional therapies for Crohn's disease include amino salicylates, corticosteroids, thiopurines, methotrexate, anti–tumor necrosis factor agents, and anti-integrins[11]. Traditional step-up therapies have been, to a certain degree, replaced by potent top-down therapeutic approaches, in which patients are given aggressive therapy early in the disease course. In any circumstances the therapeutic objective is to induce and maintain remission of the disease by rendering the patient asymptomatic and improving quality of life.

However, a significant proportion of patients become intolerant or resistant to third-line biologics (anti-TNF or anti-integrin), and eventually develop refractory Crohn's not manageable by medication currently available on the market, therefore requiring a switch of biologics. Eventually, after two years, it is

[10] Design taken from Davies and Maher, Blood, July 30, 2015 (126)5.

[11] Gastroenterology 2011;140:1827–1837.

estimated that only one-third of treated patients remain responsive to ongoing, first line or subsequent, biologic treatment.

There are therefore still significant unmet medical needs for treating Crohn's disease. TxCell estimates that there are approximately 74,000 to 100,000 patients resistant to treatment in the eight major pharmaceutical markets (United States, Canada, United Kingdom, France, Germany, Spain, Italy and Japan) in 2016. TxCell considers that this number will probably not decrease even with the emergence of new products such as Vedolizumab (approved in Europe and the United States for treating Crohn's disease) or other integrin or chemokine inhibitors or cytokine inhibitors in addition to the ones already on the market. While these products may offer alternatives in the short term to the existing approved products, it is expected that the same number of patients as today will eventually become refractory. This is mostly due to the fact that the majority of treatments developed represent the same single target and systemic approach. They have the same mechanism of action of the already-available treatments.

Ovasave® is positioned as the last line of treatment for these patients with moderate-to-severe Crohn's disease who have failed on or are not tolerant to existing treatments. Provided Ovasave® confirms the benefits seen to date, it is expected to bring a valuable new treatment option.

Non-infectious uveitis

Uveitis is classified as a rare disease and an orphan indication. It is one of the leading causes of blindness in the developed world. The disease affects about 35-50 out of 100,000 people[12]. Autoimmune uveitis (or non-infectious uveitis) refers to uveitis without an infectious cause and includes idiopathic uveitis.

To date, all approved treatments for non-infectious uveitis are based on steroid compounds. While steroid therapy normally provides fast initial relief of symptoms in uveitis, the effect is limited and insufficient for the more severe cases. Moreover, this therapy is associated with significant local and systemic side effects. Autoimmune uveitis therefore has significant unmet medical needs.

TxCell's upcoming products will be developed to address untreated types of multiple sclerosis, lupus and even bullous pemphigoid (a rare inflammation of the skin) for which no effective treatment exists to date. For each of these targeted diseases, TxCell will strive to provide a therapeutic option for an unmet medical need.

6.1.5 TxCell's leading advantages

6.1.5.1 Intellectual property

At the date of the *Document de Référence*, the ASTrIA platform, the products and derived processes are covered by 13 patent families and more than 125 patents have been granted. This patent portfolio covers four critical aspects of the "Ag-Treg" technology: identification of Type 1 Tregs, the production of Ag-Treg cells, the Ag-Treg cells' mechanism of action, and the clinical applications of various Ag-Treg-based products. Since its foundation, the Company has expended considerable financial and human resources in building this patent portfolio. It will forge ahead with these efforts to ensure that its technology is well protected and that barriers to any new entrants are very high.

For its ENTrIA platform, TxCell signed on June 30, 2015 an option agreement to obtain an exclusive license agreement for patent applications on genetically-engineered regulatory T cells to treat autoimmune diseases. This patent family was registered in 2008 by the Weizmann Institute of Science in Rehovot, Israel. It covers the use of Fox3+ Tregs modified by CAR and therefore all of the future products on the ENTrIA platform. Professor Zelig Eshhar, recognized as the pioneer in CAR-T technology, invented this patent family. His work has spun off a completely new domain in translational medicine, which has already delivered very promising results in oncology. The patent applications in this family have not been granted yet, but they have received a notification of intention to grant by the European Patent Office, and are still under review in the United States. TxCell is working with the Yeda Research and Development Co. Ltd (the technology transfer office of the Weizmann Institute) to ensure that these applications are being processed (see paragraph 22.3 of the *Document de Référence*). The option agreement signed in June 2015

[12] January 21, 2013. EMA/COMP/450332/2012. Committee for Orphan Medicinal Products.

grants TxCell until June 30, 2016 to opt-in at predefined terms. A Memorandum of Understanding was signed on October 28, 2015 to define the main terms of the license agreement. This license agreement will be entered into if the Company opts in.

In addition to this patent family protecting all of the CAR-Treg technology, the Company's strategy seeks to protect under patent families the various products generated on the ENTrIA platform ("product" patents) and certain stages of the manufacturing process ("process" patents). The Company has set its sights on building up its patent portfolio on this new platform to position itself as the leader in CAR-Treg technology.

The description of the Company's portfolio and its intellectual property strategy is presented in chapter 11 of the *Document de Référence*.

6.1.5.2 Industrial know-how

For the ASTrIA platform, the Company has developed the manufacturing process for Ag-Tregs with the goal of achieving a cost-effective, resilient and reproducible process. The key attribute of this manufacturing process is that, from a single sample of a patient's peripheral blood and one processing at TxCell's manufacturing site, multiple years of treatment doses are produced. The doses are stored frozen and thawed at the time of use to treat the patient.

The Company's current manufacturing process for its ongoing and upcoming clinical trials has been upgraded in many ways since the manufacturing process used for the CATS1 study, the Company's first clinical study with Ovasave®. The process nonetheless remains complex, long and costly. Therefore, the Company intends to dedicate a large portion of its capital expenditure on improving this process. Its goal is to achieve an economically viable process by 2018, the tentative launch date of its first registration trials.

Likewise, the Company has launched the development of a manufacturing process for future products on the ENTrIA platform. The Company has set its sights on achieving a viable process by 2018.

The Company's goal is to ultimately generate gross margins on the products manufactured on the ASTrIA and ENTrIA platforms in line with pharma industry standards and especially with biologic products already on the market, such as monoclonal antibodies.

6.1.5.3 The teams

Stéphane Boissel, Chief Executive Officer (CEO), has a proven track record in both investment banking and immunotherapy. He has steered several public offerings and private placements and negotiated many global strategic partnerships during his tenures at Transgene and Innate Pharma.

Miguel Forte, Chief Operating Officer (COO), has worked for leading pharmaceutical laboratories and biotech companies. He is recognized for his in-depth medical and business background in gastro-intestinal diseases. During his tenure at the Belgian laboratory UCB, he played a role in bringing to market a monoclonal antibody for treating Crohn's disease.

Arnaud Foussat, Chief **(**Scientific Officer (CSO**),** worked for INSERM earlier in his career prior to joining TxCell over ten years ago. He is an expert in the biology of regulatory T lymphocytes and cell-based immunotherapy development.

Raphaël Flipo, Chief Financial Officer (CFO), has worked as a financial auditor for a global audit firm and subsequently as a finance manager for a Nasdaq-listed company. He has both legal and financial expertise.

In 2015, the Company significantly strengthened its management team by appointing five new vice-presidents and bringing on-board executives to oversee critical business activities such as process development, regulatory matters, molecular biology and business development.

At March 31, 2016, the Company had 49 employees in total, over 65% with post-graduate qualifications, covering all the necessary areas and competencies required for it to accomplish its mission.

TxCell also has directors and top scientific advisers to round out and support its management and operating teams.

Among these directors are François Meyer, chairman of the board of directors (a doctor in molecular biology with in-depth knowledge of the pharmaceutical industry, notably gene and cellular therapies) and two independent directors, namely David Horn Solomon (a doctor in medical sciences with extensive experience in listed biotech companies, healthcare investing and pharmacology research) and Marie-Yvonne Landel-Meunier (a French CPA specialized in setting up subsidiaries in the United States). These directors provide the management team with ongoing critical counsel in a number of domains such as development, finance and corporate governance.

The members of the Company's board of directors, their biographies and areas of expertise are set forth in chapter 14 of the *Document de Référence*.

The Company also receives counsel and support from several European and US opinion leaders in gastroenterology, such as Professor Colombel (United States), Professor Desreumaux (France) and Professor Sandborn (USA), and in ophthalmology from Professor Bodaghi (France). These experts play an important role in the clinical development of the Company's products. Furthermore, their opinion in the medical community contributes to the growing awareness of the promise of the Company's products, particularly Ovasave® and Col-Treg.

The Company has recently joined forces with top scientific experts and formed a new Scientific Advisory Board ("SAB") for developing treatments with regulatory T lymphocyte cells. This SAB includes Professor Zelig Eshhar (Chairman) of the Weizmann Institute of Science in Rehovot, Israel, and the scientific inventor of CAR-T cells; Professor Chiara Bonini of the *Ospedale San Raffaele* in Milan, Italy, a pioneer in gene and cell therapy; and Professor Bernard Malissen of the *Centre d'Immunologie de Marseille Luminy* in Marseille, France, a member of the French *Académie des Sciences* and an opinion leader in immunology. This SAB will provide TxCell with global expertise to promote the Company's scientific research and the ASTrIA and ENTrIA platforms. The SAB's expertise in genetic engineering will also be a major advantage in developing new genetically engineered products in cellular immunotherapy that are more efficient and better tolerated.

6.2 **Cellular immunotherapy market**

6.2.1 Immune system and immunotherapy

6.2.1.1 The immune system

The immune system is composed of a variety of specialized cells. These cells recognize specific chemical structures called antigens. Foreign antigens trigger an immune response that typically results in resistance to disease-causing agents from the body. The immune system recognizes and generates a strong response to hundreds of thousands of different foreign antigens.

An immune response is triggered by a specialized class of immune system cells called antigen-presenting cells. Antigen-presenting cells take up antigen from their surroundings and process the antigen into fragments that are then displayed on the surface of the antigen- presenting cell. Once displayed, these antigens can be recognized by classes of immune cells called lymphocytes. One category of lymphocytes, cytotoxic T lymphocytes ("T CD8+ cells"), combats disease by killing antigen-bearing cells directly; another class of T lymphocytes, helper T cells ("T CD4+ cells"), coordinates the activities of cells that directly target diseased tissue. Certain of these helper T CD4+ cells are responsible for coordinating defense activities against infectious agents and tumors (effector T CD4+ lymphocytes) while others are responsible for inhibiting unwanted inflammatory responses (regulatory T lymphocytes or Treg). A second category of lymphocytes, B lymphocytes ("B cells"), produce specific antibodies when activated. Each antibody binds to and attacks one particular type of antigen expressed on a cell.

6.2.1.2 Immunotherapy approaches

Immunotherapy is intended to stimulate and enhance the body's natural mechanism. Immunotherapeutic approaches to treat disease can be separated into two broad classes, passive and active, based on their mechanism of action.

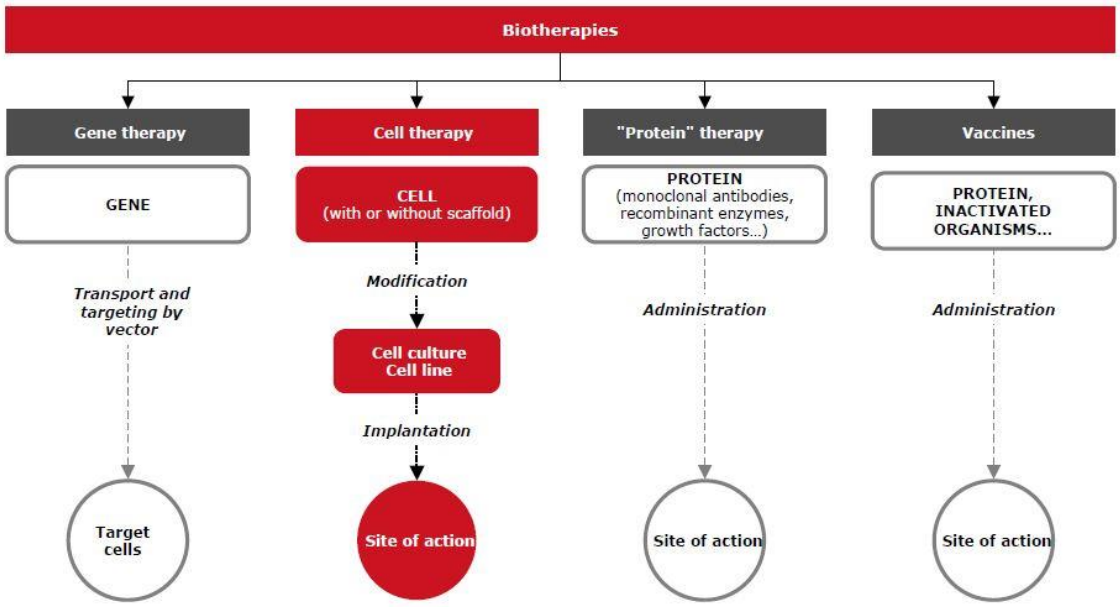
Passive immunotherapy. Passive immunotherapies do not rely on or actively stimulate the body's immune system to initiate the attack on the disease. Instead, the attack is made by the therapy which is manufactured *ex vivo*, or outside of the body. These therapies are not considered to be personalized and consist mainly of monoclonal antibodies directed at a single disease-specific enzyme or protein on the surface of targeted cells. The goal of these passive immunotherapies is to prevent targeted cells from dividing or *to* cause their death.

Active immunotherapy. Active immunotherapies, on the other hand, are designed to trigger or stimulate the body's own immune system to fight the disease. They include both traditional T-cell stimulation with antigen and cell-based immunotherapies. Active immunotherapy is a more specific approach to immunotherapy than passive immunotherapy because active immunotherapies contain a particular antigen or set of antigens that are designed to activate the patient's own immune system to seek out and kill cells that carry the same antigen. Active immunotherapies have no direct therapeutic action, but rather rely on the patient's immune system to recognize and kill the intended target. Most active immunotherapies utilize off-the-shelf antigens, also referred to as defined antigens, rather than antigens that are patient specific, and are frequently paired with adjuvants, which are agents that non-specifically activate the cells of the immune system to enhance tumor-specific immune responses.

6.2.2 Concept of cell therapy

As illustrated here below, cell therapy belongs to the family of biotherapies, alongside gene therapy, protein therapy (monoclonal antibodies, recombinant enzymes, growth factors, etc.) and vaccines. Cell therapy itself has three sub-segments: cellular immunotherapy, regenerative medicine and *ex vivo* therapy - the latter one essentially addressing rare monogenic disorders such as adenosine deaminase deficiency (ADA-SCID), metachromatic leukodistrophy (MLD) or Wiskott-Aldrich syndrome (WAS).

Figure 3 : *Cellular therapy in the context of biological therapies*[13]



Cell therapy products vary with respect to characteristics such as formulation (including combination with a scaffold or other non-cellular component), the genetic relationship of the injected cells to the patient (autologous, allogeneic, xenogeneic), and the cell source.

[13] Cell Therapy Study, Bionest Partners/LEEM, February 2010.

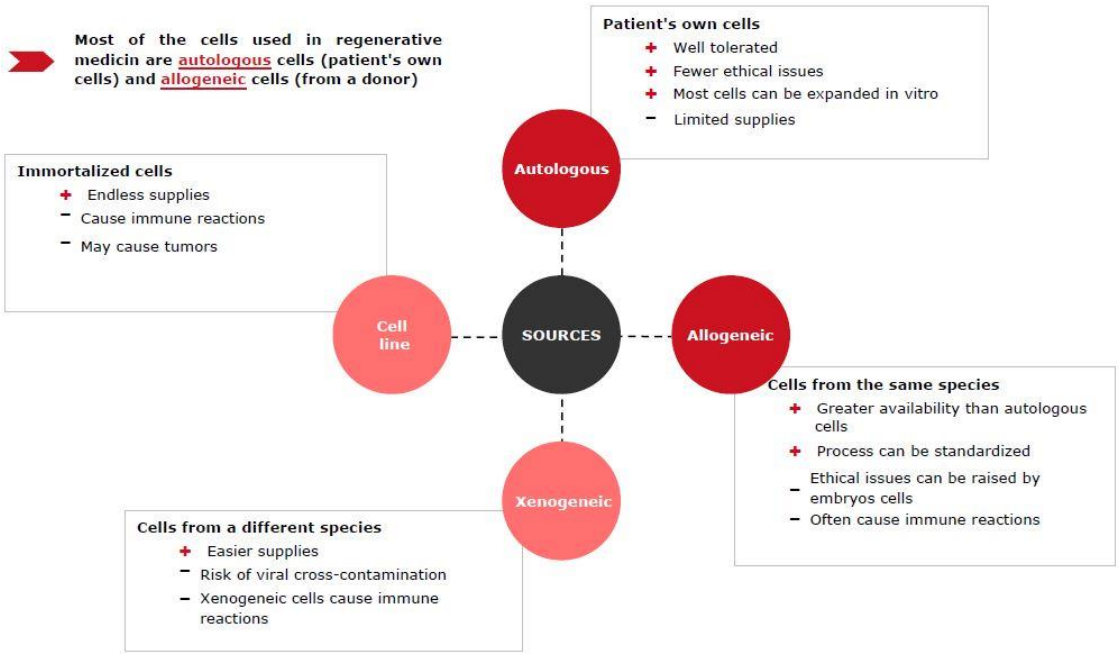
Cell therapy products can generally be classified into two categories: stem cell-derived products or mature/functionally differentiated cell-derived products.

1. Tissue sources of stem cells include: a) adult (e.g., hematopoietic, neural, mesenchymal, cardiac, adipose, skin); b) perinatal (e.g., placental, umbilical cord blood); c) foetal (e.g., amniotic fluid, neural); and d) embryonic.

   Stem cell-derived products are characterized by a variable capacity for self-renewing replication through cycles of cell division and the capacity for differentiation into a variety of cell types with specialized properties/functions. Such differentiation and replication are primarily controlled by the physiologic milieu of the host in which the cells reside following *in vivo* administration.

2. Functionally differentiated tissue-derived cell therapy products may be obtained from adult human donors (autologous or allogeneic) or from animal sources (xenogeneic) as shown on the next chart. Source cells can include chondrocytes, pancreatic islet cells, hepatocytes, neuronal cells, and various immune cells. Cell therapy products derived from functionally mature tissues typically do not possess the property of self-renewing proliferation and the capacity to differentiate into multiple cell types; however, they may retain some cellular characteristics of their tissue of origin. Additionally, their characteristics may change after *in vivo* administration, based on specific extracellular cues.

Figure 4 : *Different sources of cells for cellular therapy*[14]



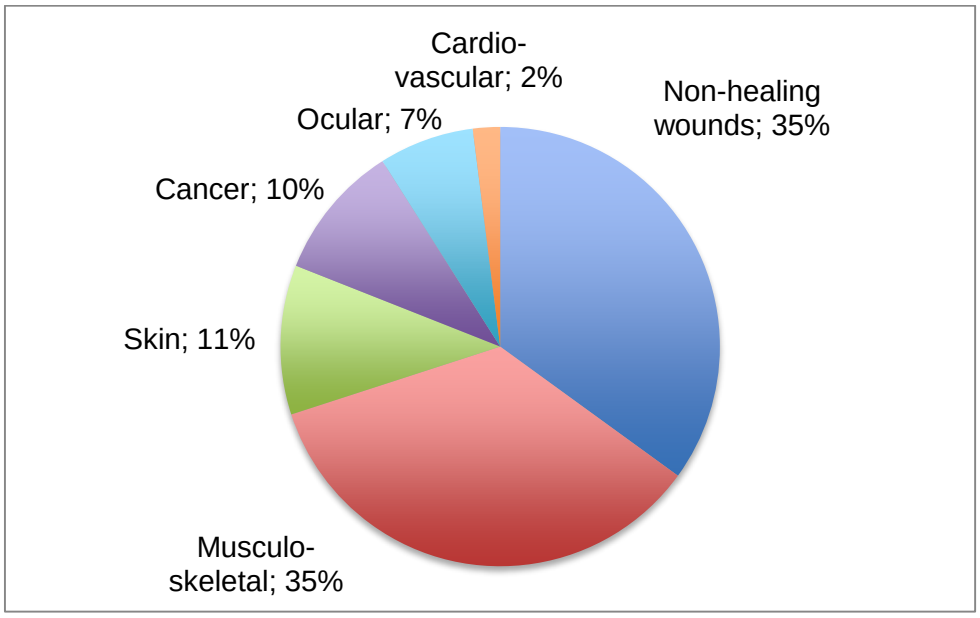
6.2.3 Strong growth on the global cell therapy market

In 2012, there were approximately 40 cell therapy products commercially distributed in regulated markets according to the Alliance for Regenerative Medicine[15]. While no cell therapy was approved by any regulatory agency from 2002 to 2008, in the past five years there have been 12 approvals.

[14] Cell Therapy Study, Bionest Partners/LEEM, February 2010.

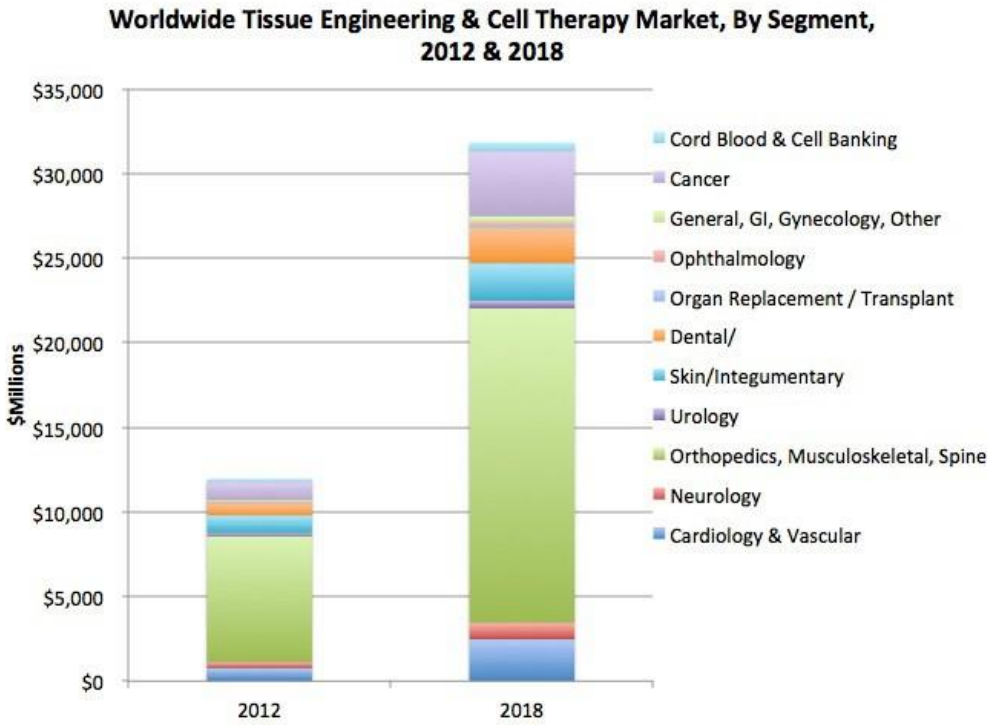
[15] ARM Annual Report 2012-2013.

Figure 5 : *Cell therapy products on the market: Over 40 cell therapy products commercially available, primarily in regenerative medicine* [16]



The registered cell therapy products include for the most part regenerative medicine products.

Figure 6 : *Strong growth on the global cell therapy market*[17]



Revenues generated by the top 20 cell therapy products were estimated to be $900 million in 2012 vs. $730 million in 2011 and $460 million in 2010[18]. Cell therapy products currently generate rather low revenues compared to all biotherapies combined, including monoclonal antibodies. The growth outlook

[16] ARM Annual Report 2012-2013.

[17] MedMarket Diligence "Tissue Engineering, Cell Therapy and Transplantation: Products, Technologies & Market Opportunities, Worldwide, 2009-2018", Report #S520; February 2010.

[18] ARM Annual Report 2012-2013.

for the cell therapy market is based mainly on the fact that there are currently 630 cell-based therapy clinical trials being performed around the world [19].

Dendreon's Provenge® (T-sipuleucel) is the first and only cellular immunotherapy approved both in the United States and Europe. The latter was approved by the FDA in April 2010 as the first active immunotherapy for the treatment of cancer. Sipuleucel-T is a partially personalized cellular immunotherapy that consists of taking white blood cells from the patient and combining them with a fusion protein consisting of two parts: the antigen prostatic acid phosphatase, which is present in many prostate cancer cells, and an adjuvant, granulocyte-macrophage colony stimulating factor (GM-CSF).

A large number of cell immunotherapy projects are in the pipelines of products in development in the emerging cell therapy industry. Many of the first-generation products were based on interleukins, cytokines, chemokines, etc., but an emerging, more sophisticated class is primarily based on T lymphocytes, macrophages, dendritic cells, and natural killer cells. Some are autologous, some are allogeneic, and some are both. Some products are not genetically modified, some are genetically modified.

6.2.4 The increasing strategic interest of the bio-pharmaceutical industry

The pharmaceutical industry, which was not really involved in cell therapy a few years ago, is becoming increasingly interested in this sector. Some have invested in cell therapy by creating their own individual departments (e.g. Pfizer or Novartis), whereas others have invested in biotech companies or research centers (e.g. GSK, Roche, AstraZeneca, Johnson & Johnson).

Provenge®'s success in the final clinical stages and its approval have triggered a significant resurgence in the field of immunotherapy and bolstered support for both cell-based therapies and autologous cell therapies in particular. More recently, prominent pharmaceutical companies became even more enthusiastic about cell immunotherapy when in 2011 Novartis and the University of Pennsylvania obtained outstanding initial clinical data for the treatment of acute lymphocytic leukemia (ALL) with a CAR-T. Amgen, Pfizer and GSK have gained a foothold in the cell immunotherapy sector by signing R&D contracts with biotech companies or universities working on cancer treatments based on genetically-modified T lymphocytes.

Genzyme, a member of the Sanofi Group, has been active on this market as it has been selling cell therapy products (Epicel and Carticel) for more than ten years. It has also invested in a wide range of biotech companies. Celgene, another leading biotech company, also ventured into cell therapy ten years ago and has considerably built up its influence in this sector through strategic agreements with BlueBird Bio, Inc. (BlueBird) and Juno signed in 2013 and 2015, respectively. The agreement with Juno in 2015 is particularly meaningful as it provides insight into the sector's new growth trajectory: Celgene paid Juno $1 billion to secure a 10-year R&D collaboration with this biotech startup, founded as recently as 2013. This collaboration will initially focus on CAR-T cells in the treatment of cancer and autoimmune diseases.

Figure 7 : *A sample of recently-signed partnerships in cell therapy*

Date	Seller		Buyer		Object
Feb-16	US	Precision Biosciences	US	Baxalta (Shire)	Co-development option for up to 6 targets based on Precision's technology
Feb-16	UK	Adaptimmune Ltd	UK	GlaxoSmithKline Plc	Expansion of the 2014 agreement
Nov-15	FR	Servier	US	Pfizer	US Licence on UCART19
Nov-15	FR	Cellectis	US	Servier	Early opt-in on UCART19

[19] ARM Annual Report 2015.

Jun-15	US	Juno Therapeutics Inc	US	Celgene Corp	Collaboration for the development and commercialization for up to 3 targets of Juno
Jun-15	US	Kite Pharma Inc	US	Bluebird Bio Inc	Co-development collaboration on TCR programs in oncology directed against HPV
Mar-15	US	Intrexon	DE	Merck kGaA	Licensing of Intrexon's "Sleeping Beauty" technology for the development of up to 2 targets in oncology
Jan-15	US	Kite Pharma Inc	US	Amgen	Research collaboration with targets and technology share
Nov-14	US	Transposagen Biopharmaceuticals	US	Janssen Biotech Inc	Collaboration for allogeneic CAR-T targets based on Transposagen's technology
Jun-14	UK	Adaptimmune Ltd	UK	GlaxoSmithKline Plc	Exclusive license agreement on TCR programs in oncology
Jun-14	FR	Cellectis SA	US	Pfizer Inc	Collaboration for up to 15 allogeneic CAR-T targets
Feb-14	FR	Cellectis SA	FR	Servier	Collaboration for up to 6 allogeneic CAR-T targets, including UCART19

6.3 **Scientific foundations of TxCell's cellular immunotherapy**

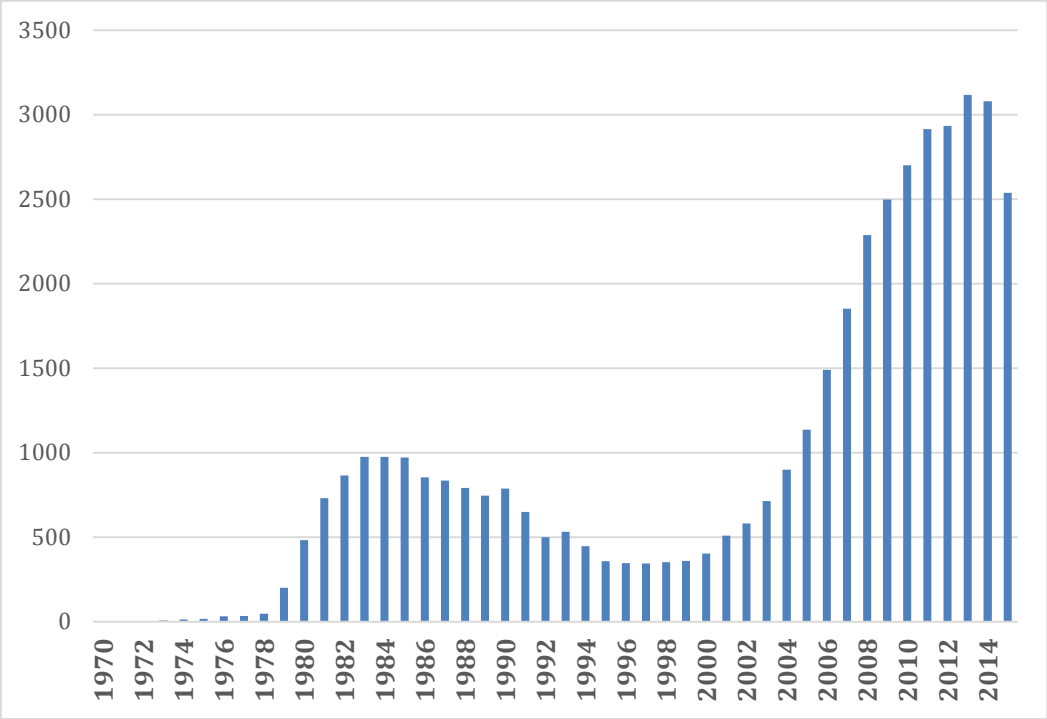
6.3.1 Introduction

Regulatory T cells (Treg) are naturally occurring circulating lymphocytes. They can modulate immune responses and inhibit inflammatory processes *in vivo*. The natural role of Treg cells is to maintain homeostasis of the immune system, preventing unwanted immune activation to self-antigens (autoimmunity) or to antigens that are normally tolerated (dietary antigens, inhaled antigens, contact antigens and bacterial flora antigens). A strong relationship exists between alteration of the Treg compartment and the development of uncontrolled inflammation. Such alterations of their function or in their numbers have been widely associated with the development of autoimmune diseases and chronic inflammation. Individuals lacking Tregs or molecules implicated in Treg functions suffer from major inflammatory diseases[20]. In 1997, the founders of TxCell discovered a subpopulation of Treg cells, known as Type 1 Treg (published in *Nature*, 1997)[21]. This Treg subpopulation displays anti-inflammatory properties upon in-vivo administration in animal models of chronic colitis. This therapeutic efficacy was taken as the basis to develop cell therapy products based on the anti-inflammatory activity of this new Treg cell subpopulation.

[20] Torgerson TR, Ochs HD. Immune dysregulation, polyendocrinopathy, enteropathy, X-linked: forkhead box protein 3 mutations and lack of regulatory T cells. J Allergy Clin Immunol. 2007 Oct;120(4):744-50; 751-2.

[21]Nature 389, 737-742 (October 16, 1997). A CD4+T-cell subset inhibits antigen-specific T-cell responses and prevents colitis. Groux et al.

Figure 8 : *Publications on Treg cells*[22]



TxCell's core expertise is developing cellular immunotherapy products based on the anti-inflammatory properties of regulatory T lymphocytes, first with antigen-specific regulatory Type 1 Treg cells (Ag-Treg) and more recently with FoxP3+ Tregs. TxCell has the first-mover advantage in this field and has gained a competitive edge by leveraging its expertise and vast intellectual property portfolio. Between 2004 and 2007, the ASTrIA platform was developed to generate Ag-Treg drug candidates from the technology patented by the Company for the treatment of chronic inflammation and autoimmunity.

6.3.2 ASTrIA platform

Type 1 regulatory T cells were first described in 1997[23] by one of TxCell's founders. In this first report, murine Type 1 Treg cells were educated *in vitro* to recognize a food antigen, ovalbumin, giving rise to an ovalbumin-specific Treg (Ova-Treg) cell population, displaying the capacity to secrete high amounts of the anti-inflammatory cytokine IL-10, and low amounts of pro-inflammatory cytokines. *In vivo* transfer of murine Ova-Treg inhibited the development of chronic inflammatory colitis in mice. In this first report, authors also described the potential to generate cells with Type 1 Treg cell properties from human peripheral blood lymphocytes. Between 2000 and 2003, several publications described the potential of antigen-specific Type 1 Tregs in inhibiting the development of allergic diseases (Cottrez et al., J. Immunol, 2000) [24], vascular inflammation (Mallat et al., circulation, 2003)[25] and skin inflammation (Foussat et al., J. Immunol, 2003[26]).

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[22] "Treg cell" research on PubMed, Medline extraction.

[23] Nature 389, 737-742 (October 16, 1997). A CD4+T-cell subset inhibits antigen-specific T-cell responses and prevents colitis. Groux et al.

[24] Cottrez F, Hurst SD, Coffman RL, Groux H.T Regulatory Cells 1 Inhibit A Th2-Specific Response In Vivo. J Immunol. 2000 Nov 1;165(9):4848-53.

[25] Mallat Z, Gojova A, Brun V, Esposito B, Fournier N, Cottrez F, Tedgui A, Groux H. Induction Of A Regulatory T Cell Type 1 Response Reduces The Development Of Atherosclerosis In Apolipoprotein E-Knockout Mice. Circulation. 2003 Sep 9;108(10):1232-7.

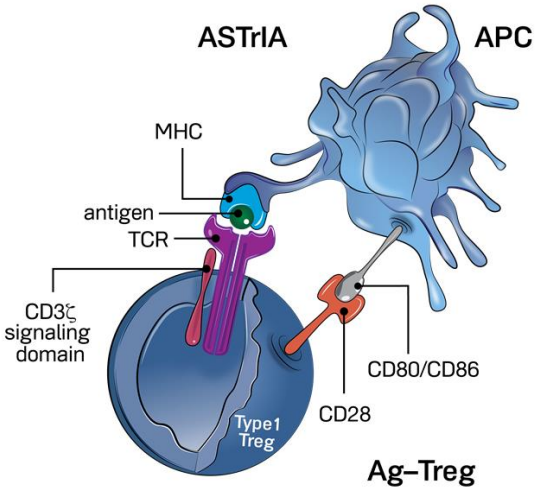
[26] Foussat A, Cottrez F, Brun V, Fournier N, Breittmayer JP, Groux H. A Comparative Study Between T Regulatory Type 1 And CD4+CD25+ T Cells In The Control Of Inflammation. J Immunol. 2003 Nov 15;171(10):5018-26.

The first preclinical proof-of-concept of Type 1 Treg therapeutic efficacy was obtained in 2003 (Foussat et al., J. Immunol, 2003[27]) using murine Ova-Treg cells in animal models of inflammatory colitis. Instead of injecting Ova-Treg at the start of the inflammatory process to inhibit disease evolution, the cell administration was performed at a time when mice already developed inflammation of the colon. Ova-Treg therapeutic administration was shown effective, allowing inhibition of gut tissue inflammation, local infiltration with proinflammatory cells and restoration of tissue integrity only three weeks after the treatment. Ova-Treg cells were efficient only when mice were given ovalbumin in the drinking water, confirming that both the cellular administration of Ag-Treg cells and the presence of the specific antigen in the inflamed tissue are required for Ova-Treg therapeutic efficacy.

Type 1 Treg cells are recognized as a key regulatory population for the control of chronic inflammation. Dysfunction of Type 1 Treg cells has been implicated in human inflammatory diseases such as multiple sclerosis, pemphigus vulgaris and allergies in general. Preclinical proof of efficacy of Type 1 Treg administration has been obtained in a large panel of chronic inflammatory diseases in the animal (please refer to above). The therapeutic potential of Type 1 Treg cells is largely recognized for treating human inflammatory diseases in connection with autoimmunity and transplantation (notably for the prevention of Graft versus Host Disease in patients who have received a bone marrow transplant 28). Research performed by TxCell and others have elucidated certain important anti-inflammatory mechanisms of action that add to IL-10 secretion, further increasing the therapeutic potential of Type 1 Tregs (discussed below for Ag-Treg products).

The ASTrIA platform for producing Ag-Treg has been developed to generate cellular immunotherapy drug candidates based on the regulatory properties of Type 1 Treg cells and using the technology patented by TxCell.

Figure 9 : *ASTrIA platform –Ag-Treg cells*

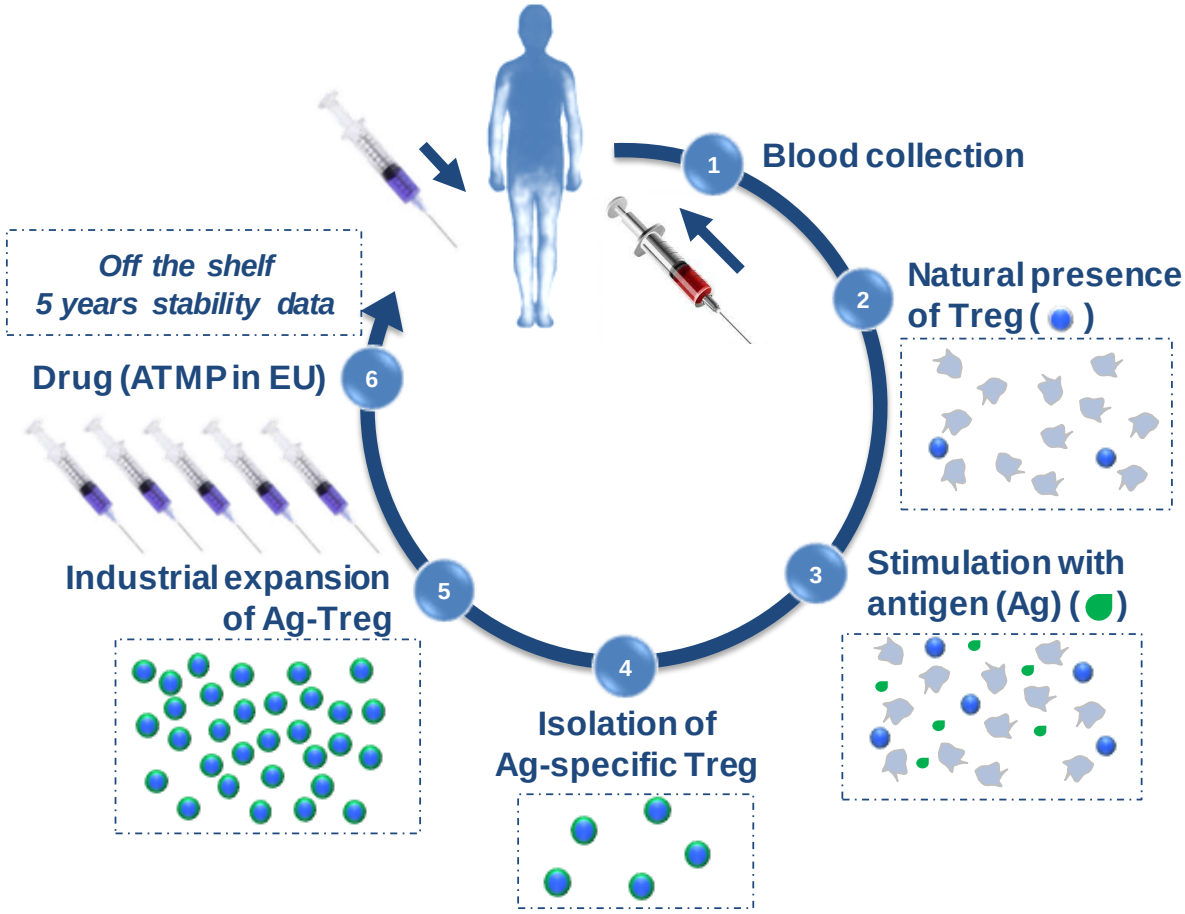


[27] Foussat A, Cottrez F, Brun V, Fournier N, Breittmayer JP, Groux H. A Comparative Study Between T Regulatory Type 1 And CD4+CD25+ T Cells In The Control Of Inflammation. J Immunol. 2003 Nov 15;171(10):5018-26.

[28] Gregori S, Bacchetta R, Roncarolo MG. Tr1 cells: from discovery to their clinical application. Semin Immunol. 2006 Apr;18(2):120-7.

The technology of TxCell to produce Ag-Treg cells can be summarized in six distinct steps:

Figure 10 : *TxCell's ASTrIA platform educates the patient's own cells to treat their disease*



Production *ex vivo* of therapeutic products via the ASTrIA platform:

1. Blood sampling of a patients.
2. T lymphocytes are naturally present in the sample.
3. Stimulation of white blood cells a selected antigen.
4. Isolation of the desired antigen-specific Treg cells.
5. Mass production of Ag-Treg cells and storage of Ag-Treg cells as individual doses.
6. Intravenous injection of medicinal product to the same patient.

- **Autologous cell immunotherapy products**

Each patient will receive his or her own cells, educated to treat their own disease. From a single blood collection, TxCell can manufacture several doses of autologous Ag-Treg product potentially allowing three to five years of treatment. The autologous nature of the Ag-Treg products implies that, upon administration, cells composing the cellular immunotherapy as well as anti-inflammatory molecules

secreted by the cells are not rejected by the patient's immune system, a known issue with allogeneic (non-self or non-autologous) cell therapies[29].

- **Antigen-specificity**

Ag-Treg cells are antigen-specific. This means that all cells composing the Ag-Treg products are able to specifically recognize a pre-determined antigen thanks to a membrane-bound receptor. This recognition leads to Ag-Treg cell activation and triggering of the anti-inflammatory activity.

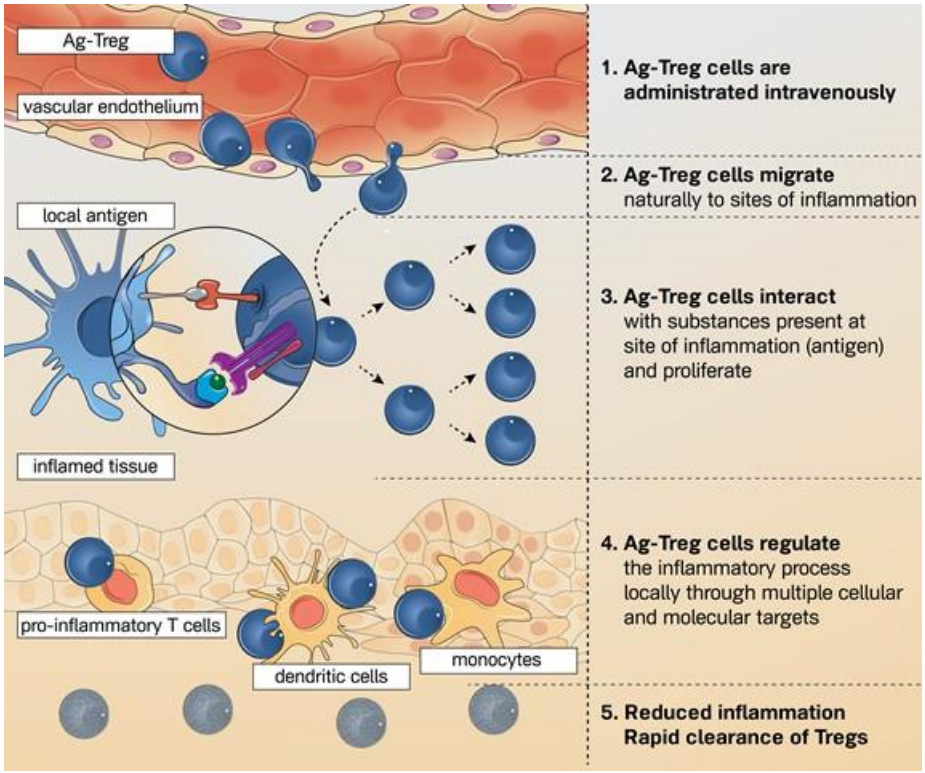
The choice of the antigen depends on the inflamed tissue to treat. It may be, but does not have to be, a disease-associated antigen. It may also be co-located at the site of inflammation. For instance, ovalbumin has been chosen as the specific antigen for Ova-Treg (Ovasave®) developed for the treatment of Crohn's disease, due to its localization in the inflamed intestine after ingestion. In the same manner, Collagen type II has been chosen as the specific antigen for Col-Treg, developed for the treatment of uveitis, due to its localization in the inflamed eye.

- **Type 1 Treg**

During the manufacturing process, Ag-Treg cells are selected on the basis of Type 1 Treg cytokine secretion profile that includes a high production of Interleukin-10 as a key identification factor. An identity test for the different Ag-Tregs ensures at the end of the manufacturing process the identity of the product.

Ag-Treg's putative mechanism of action largely differs from that of conventional drugs developed for the treatment of chronic inflammation: Ag-Tregs have multiple mechanisms of action as well as targets. Ag-Tregs actually have a specific tropism for the tissue to treat and impact multiple molecular and cellular targets. The putative mechanism of action of Ag-Treg cells can be summarized in four different steps.

Figure 11 : *Putative mechanism of action of Ag-Treg products*



1. *Ag-Tregs are administered intravenously*

[29] Blood. 2005 Dec 15;106(13):4057-65. Epub 2005 Aug 23. Allogeneic marrow stromal cells are immune rejected by MHC class I- and class II-mismatched recipient mice. Eliopoulos N et all.

Ag-Tregs are systemically administered regardless of the disease being treated (such as Crohn's disease and non-infectious uveitis) or the targeted inflamed tissue. The Ag-Tregs' ability to migrate toward inflamed tissues (known as "homing") implies that this mode of administration is minimally invasive compared to local injections).

2. *Preferential migration of Ag-Treg cells to inflamed tissues after intravenous administration*

Ag-Treg cells express at the cell membrane homing molecules known as integrins and chemokine receptors that are implicated in the preferential migration of lymphocytes to inflamed tissues. After intravenous injection, TxCell has demonstrated in murine inflammatory colitis models that Ova-Treg cells are found in the inflamed intestinal tissue. Similarly, Col-Treg cells have been shown to migrate to the inflamed tissues in animal models for chronic eye inflammation. This particular tropism allows for preferred distribution of the therapeutic cells in the area to treat and restrict the anti-inflammatory activity of the Ag-Treg cells to this location.

3. *Local antigen-specific activation of Ag-Treg cells*

After Ag-Treg infiltration of inflamed tissues, Ag-Tregs must encounter their specific antigen to deliver their therapeutic effect. Antigens are usually presented by specialized Antigen-Presenting cells (APC) such as dendritic cells in the context of the Major Histocompatibility Complex (MHC) under the form of peptides. Upon contact of Ag-Tregs and APC, antigen presentation and recognition by the Ag-Treg specific membrane receptor leads to Ag-Treg cell activation.

Local antigen presentation is a crucial step of the therapeutic efficacy of Ag-Treg cells. It has been confirmed that the absence of the antigen (ovalbumin) abolishes the activity of Ova-Treg in a murine model of inflammatory colitis. Furthermore, it is important to note that local antigen-specific activation restricts the anti-inflammatory activity of Ag-Treg cells to the desired area to treat.

4. *Suppression of the local pro-inflammatory response*

The antigen-specific activation of Ag-Treg cells leads to de novo gene expression showing suppressive activities. Whereas it is difficult to assess the main mode of action of these cells in patients, *in vitro* gene expression and functional studies have shown that Ag-Treg cells express a range of suppressive molecules with differential activities on the extracellular milieu and on different pro-inflammatory cell types. The table below summarizes the expression of suppressive molecules by Ag-Treg cells and their main cellular and/or molecular targets.

The anti-inflammatory and immuno-suppressive activities confer to Ag-Treg cells a synergistic effect, acting on the one side on the cellular components of the pro-inflammatory immune response and on the other side on the extracellular milieu.

Figure 12 : *Main known Ag-Treg suppressive molecules expression and targets*[30]

Expressed Molecule	Main suppressive Activity	Cell targets
IL-10	Inhibition of activation, proliferation and cytokine production Inhibition of Dendritic cell maturation and antigen presentation	Pro-inflammatory T cells Pro-inflammatory Monocytes Dendritic cells B lymphocytes
IL-13	Inhibition of cytokine production and proliferation	Pro-inflammatory T cells Pro-inflammatory Monocytes
IFN-γ	Acts in synergy with IL-10	Pro-inflammatory T cells Pro-inflammatory Monocytes
Cytotoxic granules (Granzyme B)	Cell contact cytotoxicity	Pro-inflammatory Monocytes Dendritic cells
GITR	Inhibition of cell activation and cytokine production	Pro-inflammatory T cells B lymphocytes
CD39/CD73	Inhibition of extracellular inflammation by degradation of ATP and production of Adenosine	Extracellular ATP

5. *Ag-Treg clearance*

Pharmacokinetic data suggest that once the effect has been delivered in the inflamed tissue, Ag-Treg cells population is reduced and become undetectable. This observation correlates with the limited survival capacity of Ova-Treg cells *in vitro*, which showed that upon chronic stimulation the cells died after an average survival length of eight weeks in responder patients. This Ag-Treg characteristic assures a limited life span and prevents unlimited proliferation of Ag-Treg cells after intravenous administration, which is reassuring from a safety viewpoint. This limited lifespan also suggests that as a chronic treatment Ag-Treg may need to be administered at least every eight weeks.

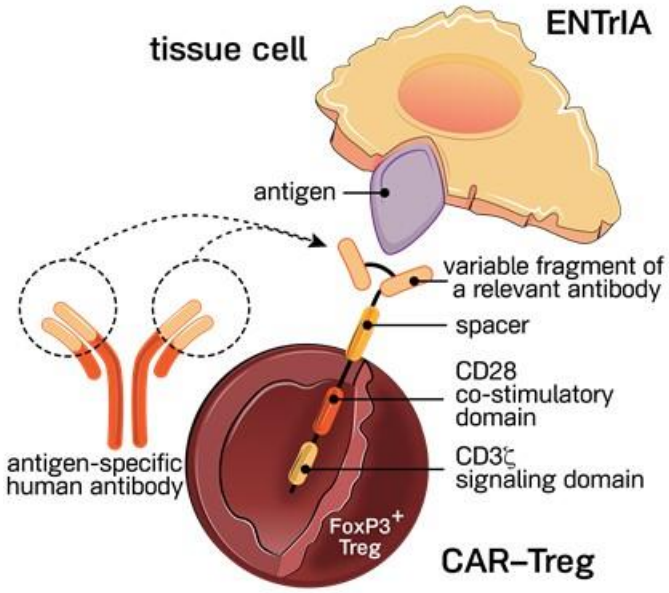
6.3.3 ENTrIA platform

The ENTrIA platform is made up of FoxP3+ Tregs that constitutively express several surface markers (CD25, CD62L, CTLA-4) and the FoxP3 transcription factor (see figure below). This intercellular factor is absolutely necessary for this cell type's differentiation and function and therefore for its role in the body. A mutation of FoxP3 in humans actually leads to a fatal autoimmune disorder known as IPEX (Immune dysregulation, Polyendocrinopathy, and Enteropathy, X-linked). This clinical observation has demonstrated the key role of FoxP3+ Tregs in the maintenance of the immune system's homeostasis and in immune tolerance induction[31].

[30] Source: Company.

[31] Piccirillo CA, d'Hennezel E, Sgouroudis E, Yurchenko E. CD4+Foxp3+ regulatory T cells in the control of autoimmunity: in vivo veritas. Curr Opin Immunol. 2008 Dec;20(6):655-62.

Figure 13 : *ENTrIA platform – CAR-Treg cells*



Since FoxP3+ Tregs were discovered in the 1990s[32], numerous studies have indicated that mutations in this cell population, either in number, its antigenic specificity or its immunomodulatory function, are present in the majority of autoimmune and chronic inflammatory diseases. A corollary to these observations is that FoxP3+ Tregs demonstrate therapeutic activity in numerous animal models for chronic inflammation. The published data clearly shows that this population is at the core of the pathophysiology of many chronic inflammatory diseases. It also demonstrates that a therapeutic approach to restore an effective FoxP3+ Treg population in patients is justifiable from both a scientific and clinical standpoint[33].

The first clinical tests on the therapeutic activity of FoxP3+ Tregs were performed within the context of preventing Graft versus Host Disease in stem cell transplants in leukemia patients. A few Phase I/II clinical trials were also conducted with FoxP3+ Tregs in Type 1 diabetes[34]. These clinical trials validated not only the feasibility of the FoxP3+ Treg-based therapeutic approach, but also confirmed the excellent tolerance profile of these cell therapy products after administering them in patients. Other early-stage clinical trials (Phase I-IIb) are ongoing, such as on organ transplants, but still with cell products called polyclonal (non-specific to a given antigen) and FoxP3+ Tregs. These clinical trials have always been conducted for the most part by the academic world (hospitals and universities).

The "CAR-Treg" approach consists of introducing a coding gene in the FoxP3+ Treg cells for the chimeric antigen receptor. It was started in 2008 by Professor Zelig Eshhar of the Weizmann Institute of Sciences in Rehovot, Israel. With this new property, FoxP3+ Tregs can zero in on a given antigen in relation to the CAR's selected design and therefore target closely a pathology in which an antigen recognized by the CAR is expressed in the inflamed tissue. For example, Professor Eshhar's team demonstrated the therapeutic efficacy of a CAR-Treg product for which the CAR specifically recognizes an antigen present in the colon of an animal with inflammatory colitis. In this model, although inducing an inhibition to the pathology, a polyclonal FoxP3+ Treg population (without CAR) demonstrates a

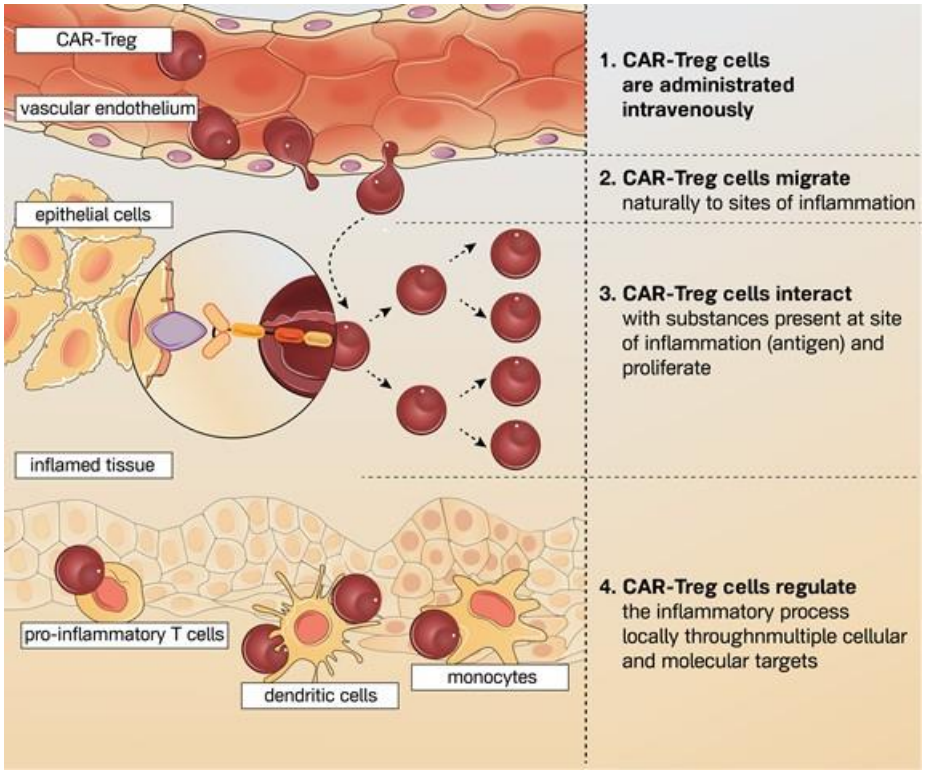
[32] Sakaguchi S, Sakaguchi N, Asano M, Itoh M, Toda M. Immunologic self-tolerance maintained by activated T cells expressing IL-2 receptor alpha-chains (CD25). Breakdown of a single mechanism of self-tolerance causes various autoimmune diseases. J Immunol. 1995 Aug 1;155(3):1151-64.

[33] Spence A, Klementowicz JE, Bluestone JA, Tang Q. Targeting Treg signaling for the treatment of autoimmune diseases. Curr Opin Immunol. 2015 Dec;37:11-20.

[34] Trzonkowski P, Bacchetta R, Battaglia M, Berglund D, Bohnenkamp HR, ten Brinke A, Bushell A, Cools N, Geissler EK, Gregori S, Marieke van Ham S, Hilkens C, Hutchinson JA, Lombardi G, Madrigal JA, Marek-Trzonkowska N, Martinez-Caceres EM, Roncarolo MG, Sanchez-Ramon S, Saudemont A, Sawitzki B. Hurdles in therapy with regulatory T cells. Sci Transl Med. 2015 Sep 9;7(304):304ps18.

significantly lower therapeutic potential than the injected CAR-Tregs[35]. The same approach was taken by Professor A. Loskog's team[36] and revealed therapeutic activity of the myelin antigen-specific CAR-Tregs in a model of multiple sclerosis in mice. In this study, the expression of the myelin (antigen recognized by the CAR) is restricted to the brains of the sick mice. As a final example, Dr. Levings's team established proof of the therapeutic activity of CAR-Treg in which the CAR is specifically targeted against the graft's antigen in connection with the prevention of Graft versus Host Disease. This approach was the first to use human Tregs and proved to be much more efficient than using non-antigen-specific Tregs[37].

Figure 14 : *Putative mechanism of action of CAR-Treg products from the ENTrIA platform*



The ENTrIA platform is capable of generating many drug candidates using a shared production method. Similar to the ASTrIA platform, the first generations of products on the ENTrIA platform are autologous. They are produced as follows:

1. isolation of the donor's FoxP3+ Tregs;
2. transduction by the desired genes and particularly the gene coding for the CAR;
3. expansion of the transduced cells;
4. selection of CAR-Tregs and formulation.

Other genes are expected to be transduced in addition to the introduction of the CAR-coding gene in the FoxP3+ Treg cells. These genes will optimize the efficiency, the migratory properties and even the safety of the CAR-Treg products, by using suicide genes for example. These suicide genes (e.g. HSVTK, iCas9 and CD20) code for proteins which, acting with the pharmacological compounds ingested orally by the patient, become cytotoxic for the cells that produce them. Introducing a suicide gene in the CAR-

[35] Blat D, Zigmond E, Alteber Z, Waks T, Eshhar Z. Suppression of murine colitis and its associated cancer by carcinoembryonic antigen-specific regulatory T cells. Mol Ther. 2014 May;22(5):1018-28.

[36] Fransson M, Piras E, Burman J, Nilsson B, Essand M, Lu B, Harris RA, Magnusson PU, Brittebo E, Loskog AS. CAR/FoxP3-engineered T regulatory cells target the CNS and suppress EAE upon intranasal delivery. J Neuroinflammation. 2012 May 30;9:112.

[37] MacDonald KG, Hoeppli RE, Huang Q, Gillies J, Luciani DS, Orban PC, Broady R, Levings MK. Alloantigen-specific regulatory T cells generated with a chimeric antigen receptor. J Clin Invest. 2016, in press. http://dx.doi.org/10.1172/JCI82771.

Treg will therefore increase the safety of these products as they can be quickly eliminated by the injected patients' bodies in the event of serious adverse effects from the injected cell product.

The mode of action of the FoxP3+ Treg cells is extensively documented in scientific studies. Similar to Type 1 Tregs, this mode of action breaks down into several immune-regulatory activities. The most documented ones are presented in the table below:

Figure 15 : *Main known FoxP3+ suppressive molecules expression and targets*[38]

Expressed Molecule	Main suppressive Activity	Cell targets
CTLA-4	Inhibition of antigen presentation, inducing production of the anti-inflammatory IDO molecule	Dendritic cells
TGF-beta membrane	Inhibition of proliferation, induction of Treg	Pro-inflammatory T cells, Dendritic cells
CD25 (IL-2Rα)	Deprivation of IL-2 from the extracellular domain	Pro-inflammatory T cells
Cytotoxic granules (Granzyme A and B)	Cell contact cytotoxicity	Pro-inflammatory T cells
CD39/CD73	Inhibition of extracellular inflammation by degradation of ATP and production of Adenosine	Extracellular ATP

The ability of FoxP3+ Tregs in inhibiting pro-inflammatory processes is based on several mechanisms working together on cell and molecule targets. Certain mechanisms of action also express CTLA-4 and membrane-bound TGFbeta and are not found in Type 1 Tregs. Other mechanisms of action on top of the FoxP3+ Treg extensive immune-regulatory range have also been documented. This makes them a forerunner therapeutic approach in treating chronic inflammatory diseases.

6.4 First TxCell cell immunotherapy products

6.4.1 Ovasave®, a new approach to the treatment of Crohn's disease

6.4.1.1 Inflammatory bowel disease and Crohn's disease

Crohn's disease ("CD") and hemorrhagic rectocolitis ("HR") represent the two major forms of inflammatory bowel diseases ("IBD"). The clinical course of these diseases frequently exhibits a relapsing-remitting clinical course. Crohn's disease can affect the entire gastrointestinal tract from mouth to anus, while hemorrhagic rectocolitis normally involves only the large intestine. Extra-intestinal manifestations can be associated with these pathologies.

The incidence and prevalence of inflammatory bowel diseases have increased in the past 50 years. Today, hemorrhagic rectocolitis newly occurs in 8 to 14 people per 100,000 per year (incidence), and about 120 to 200 people per 100,000 are affected (prevalence). For Crohn's disease, the incidence is 6 to 15 newly diagnosed cases per 100,000 and 50 to 200 people affected per 100,000[39].

The increase in incidence of Crohn's disease coupled with low mortality rates will result in an increase in the prevalence population.

[38] Source: Company.

[39] Gastroenterology. Volume 140, Issue 6, Pages 1785-1794.e4, May 2011. Epidemiology and Natural History of Inflammatory Bowel Diseases. Cosnes et al.

TxCell has chosen to primarily focus on the Crohn's disease because of the continued unmet medical need.

6.4.1.1.1 Etiology of Crohn's disease

Although the etiology of Crohn's disease is not fully elucidated, it tends to occur in genetically predisposed people. It is mediated by T lymphocytes as a result of a breakdown in the regulatory restraint on mucosal immune responses to enteric bacteria. It is a lifelong disease, which is often characterized by chronic diarrhea, abdominal pain, anorexia, fever and musculoskeletal abnormalities. Patients frequently have flares with varying degrees of remission. Crohn's disease can be a severe disease and is usually complicated by fistulas. It affects males and females equally and occurs typically between the ages of 15 and 35 years. The most commonly affected areas are the terminal ileum (35%), the ileocecal region (40%) and the colon region (20%)[40]. The perianal region can be also affected with fistulizing disease and associated complications. In 2012, GlobalData considered that there were more than 1.3 million patients suffering from Crohn's disease worldwide[41]. On the 10 main global pharmaceutical markets[42], the incidence and prevalence of Crohn's disease is expected to increase with an annual growth rate of 1.32% between 2012 and 2022, with the number of new annual cases increasing from 124,216 in 2012 to 140,561 in 2022[43].

6.4.1.1.2 Diagnosis and assessment

The diagnosis of Crohn's disease rests on the clinical anamnesis, laboratory evidence of inflammation and medical imaging. The gold standard for the diagnosis rests in the endoscopic evidence of the disease, even though recent advances in ultrasound and MRI allow for the use of these tools in complementing the diagnosis (ECCO guidelines)[44].

Although the assessment of the degree of disease activity can be made with different tools, the most common one is the Crohn's Disease Activity Index (CDAI). This index is based on a full week assessment on number of stools, abdominal pain, general well-being, extra-intestinal symptoms, use of antidiarrheal medication, and presence of abnormal mass, hematocrit and body weight. Higher scores correspond to more active disease while lower scores translate less symptomatic disease. Indeed, clinical active and symptomatic disease is normally grouped into mild, moderate or severe according mainly to CDAI (table below).

The CDAI score is frequently used in the context of clinical trials to assess the clinical evolution and the impact of the medication under study. In fact, the regulatory authorities require this score as the primary assessment tool, even though additional evidence, namely with inflammatory markers, are regularly used to contribute to this assessment. A clinical response corresponds to a decrease of 100 points of the CDAI score. The patient is in clinical remission if the CDAI is lower than or equal to 150 points.

Figure 16 : *Grading of disease activity in Crohn's disease*[45]

Mild	Moderate	Severe
Equivalent to a CDAI of 150-220	Equivalent to a CDAI of 220-450	Equivalent to a CDAI of > 450

[40] Globaldata report: Crohn's Disease (CD) Therapeutics - Pipeline Assessment and Market Forecasts to 2018. Reference Code: GDHC406PRT. Publication Date: December 2011.

[41] Crohn's Disease – Global Drug Forecast and Market Analysis to 2022. GlobalData 2014.

[42] United States, Canada, France, Germany, Italy, Spain, United Kingdom, Japan, India and China.

[43] Crohn's Disease – Global Drug Forecast and Market Analysis to 2022. GlobalData 2014.

[44] Journal of Crohn's and Colitis (2013) 7, 982–1018 Consensus/Guidelines European evidence based consensus for endoscopy in inflammatory bowel disease Vito Annesea.

[45] ECCO guidelines.

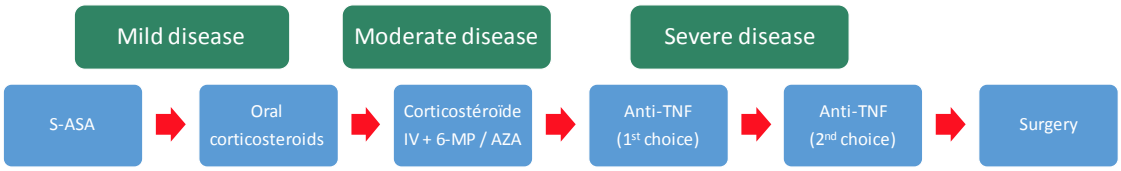
E.g. ambulatory, eating and drinking < 10%	E.g. intermittent vomiting, or weight loss > 10%	E.g. cachexia (BMI < 18 kg m^{-2}), or evidence of obstruction or abscess
No features of obstruction, fever, dehydration, abdominal mass, or tenderness	Treatment for mild disease ineffective, or tend mass. No overt obstruction	Persistent symptoms despite intensive treatment.
CRP usually increased above the upper limit of normal	CRP elevated above the upper limit of normal	CPR increased

In addition to the CDAI score, Crohn's disease activity and response to treatment can also be assessed by laboratory measurements of inflammation. C Reactive Protein, measured in blood, translates the presence of systemic inflammation. The majority of patients, but not all, with active CD have a raised CRP and the normalization of blood CRP is a good indicator of reduction of inflammation and response to treatment. Particularly useful is the reverse, which is the increase of CRP in patients that have previously responded, which corresponds to a worsening of Crohn's disease and thus provides an anticipation or confirmation of a flare. Calprotectin, measured in stool, is a direct measurement of intestinal inflammation and correlates to the local level of neutrophils. Calprotectin appears also particularly relevant to support the assessment of disease response to treatment.

6.4.1.1.3 Treatment

The treatment of CD should take into consideration the degree of activity, the location and behavior of the disease. Conventional therapies for Crohn's disease include aminosalicylates, corticosteroids, thiopurines, methotrexate, anti-tumor necrosis factor agents and anti-integrins[46]. Traditional step-up therapies have been to a certain degree replaced by potent top-down therapeutic approaches. In any circumstances the therapeutic objective is to induce and maintain remission of the disease by rending the patient asymptomatic and improving quality of life.

Figure 17 : *The treatment chain*



There are currently three biologic drugs approved to treat Crohn's disease in Europe: infliximab (Remicade®), adalimumab (Humira®) and vedolizumab (Entyvio®). In the United States, two other products have also been approved in addition to the three above: certolizumab (Cimzia®) and natalizumab (Tysabri®). Infliximab, adalimumab and certolizumab act by blocking the tumor necrosis factor. Natalizumab acts by inhibiting the α4-integrin adhesion molecule while vedolizumab acts by inhibiting the α4β7 integrin. Furthermore, the first anti-TNF biosimilar agent (Inflectra®, biosimilar of infliximab) was approved in 2013 by the European regulatory authorities. The efficacy of these biologic products is clinically significant and similar between them delivering up to 70-80% of induction of response and up to 50-60% of maintenance of effect in first-line therapy[47].

6.4.1.1.4 Unmet medical need

A significant proportion of patients become intolerant or resistant to first biologics, requiring a switch in product, and end up developing refractory Crohn's disease not manageable by currently available medication.

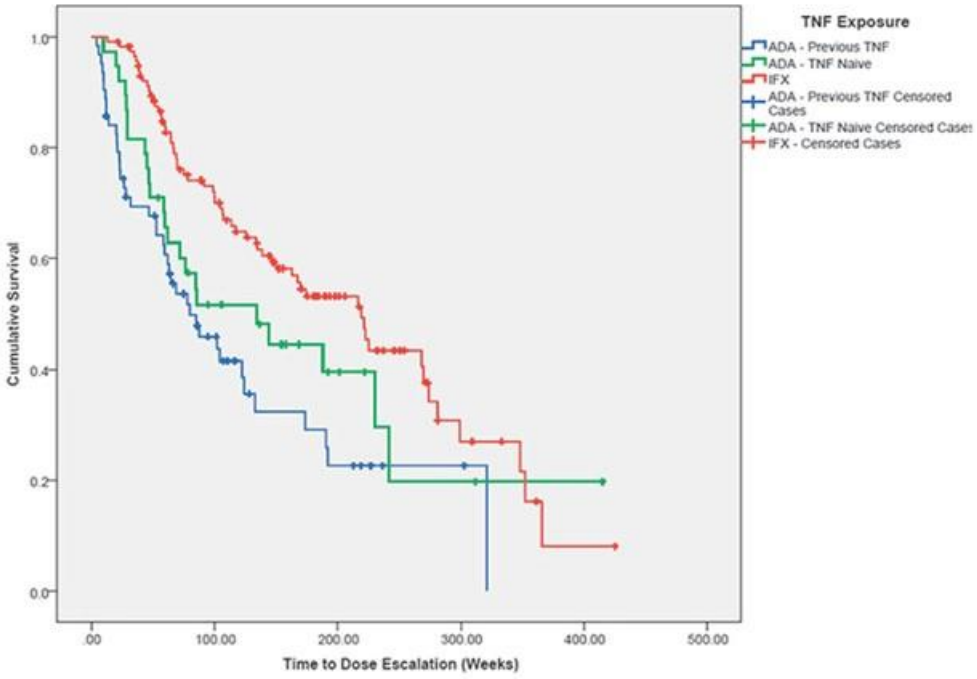
[46] Gastroenterology 2011;140:1827–1837. Conventional Medical Management of Inflammatory Bowel Disease. Daniel Burger Simon Travis. Translational Gastroenterology Unit, John Radcliffe Hospital, Oxford, United Kingdom.

[47] GlobalData report: Crohn's Disease (CD) Therapeutics - Pipeline Assessment and Market Forecasts to 2018. Reference Code: GDHC406PRT. Publication Date: December 2011.

About 10-30% of patients fail to respond to anti-TNF type biologic treatments (primary non-responders) and approximately 23-46% of patients stop responding to these anti-TNF treatments with time (secondary non-responders)[48].

Based on the intensification of doses, it appears that patients present a loss of response to anti-TNF of 13% per year for infliximab and 24% per year for adalumimab. In most cases, the loss of response occurs during the first year of treatment. Consequently, the rate of loss of response after one year of treatment, if it is measured by the intensification of doses, is between 23-46% for patients suffering from Crohn's disease treated by infliximab or adalumimab. When it is measured by the discontinuation of the anti-TNF treatment, this rate drops to approximately 7-25%[49].

Figure 18 : *Curves for secondary loss of response that require an increase in dosage*[50]



Current therapeutic approaches to Crohn's disease are not curative and the approved biologics, even though beneficial to many patients, still present a limited efficacy together with tolerability and resistance issues.

The pipeline of new products for the treatment of Crohn's disease is fairly rich, with products like ustekinumab (Stelara®), another monoclonal antibody, and new approaches such as SMAD7 anti-sense oligonucleotide-based therapies. These approaches are primarily positioned as second- and third-line treatments and are therefore in direct competition with anti-TNF and anti-integrin monoclonal antibodies. Furthermore, unlike cell therapy, these technologies are primarily based on mono-target mechanisms. Preliminary data from clinical tests indicate that a proportion of patients receive a clinical benefit. However, TxCell believes that these products are likely to ultimately lead to resistance, like the currently approved biologic products.

[48] Roda G, Jharap B, Neeraj N, Colombel JF. Loss of Response to Anti-TNFs: Definition, Epidemiology, and Management. Clin Transl Gastroenterol. 2016, in press. doi: 10.1038/ctg.2015.63.

[49] Ben-Horin S, Chowers Y. Tailoring anti-TNF therapy in IBD: drug levels and disease activity. Nature Reviews Gastroenterology & Hepatology 2014 (11): 243–255.

[50] Ma C, Huang V, Fedorak DK, Kroeker KI, Dieleman LA, Halloran BP, Fedorak RN. Crohn's disease outpatients treated with adalimumab have an earlier secondary loss of response and requirement for dose escalation compared to infliximab: a real life cohort study. J Crohns Colitis. 2014 Nov;8(11):1454-63.

It is clear from physician and patient perspectives that the treatment of Crohn's disease at all stages, but in particular for the moderate-to-severe disease and for cases refractory to currently approved products, continues to represent a significant unmet medical need. Crohn's disease even though with limited impact on mortality is a disease with significant morbidity and active and social life limitations. The degree of suffering and quality of life limitation is significant in particular when considered the young adult age of the majority of the patients. In this context, therapeutic options that are tolerable, with a good safety profile and delivering induction and maintenance efficacy, remain in high demand for the management of Crohn's disease.

6.4.1.1.5 Preclinical data obtained with Ovasave®

Pre-clinical data have been generated with Ovasave® in mice models of inflammatory colitis. All pharmacokinetic data highlight the preferential migration of Ova-Treg cells to the site where inflammation is present. Migration of Ova-Treg cells in the context of inflammatory colitis has been observed in the inflamed colon and associated lymph nodes. In terms of efficacy, Ovasave® has shown preventive and therapeutic benefit in mice models of colitis.

Two distinct toxicology studies in mice have been performed with Ovasave® confirming an absence of Ova-Treg related toxicity in two different settings:

- with a single dose injection after nine months follow-up; and
- with a multiple dose regimen (four doses over eight weeks) after three months follow-up.

These toxicology studies have been performed according to Good Laboratory Practices (GLP). Toxicology studies on the human Ova-Treg cells have shown the absence of tumorigenicity and confirmed the limited life span of the cells *in vitro* and *in vivo*.

In 2007, the preclinical Ovasave® data already generated was considered sufficient by the French regulatory authorities for the start of clinical development, leading to a first-in-man clinical study started in 2008.

6.4.1.1.6 Clinical data obtained with Ovasave®

The CATS1 study (*Crohn's And Tr1 Study 1*) was a 12-week, multicenter, open, uncontrolled, dose ranging, Phase I/IIa clinical study to evaluate the safety and efficacy of Ovasave® in patients with Crohn's disease, refractory to standard and biologic treatments. The study was conducted on six sites in France between 2008 and 2011 according to GCP guidelines and followed by an independent Data Monitoring Committee (DMC). The study was published in an international peer-reviewed reference journal, Gastroenterology, in November 2012.

Twenty patients were administered with Ovasave® while monitored for vital signs and were subsequently followed through six subsequent visits until week 12. Patients had a daily intake of ovalbumin as a food supplement in the form of a meringue cake to ensure high levels of ovalbumin in the gut. The study planned for four cohorts of ascending doses of autologous Ova-Tregs (10^6, 10^7, 10^8 or 10^9 cells). Progression from one dose to the next required DMC approval after assessment of safety data.

The study was subsequently amended and extended to allow for additional re-treatment injections:

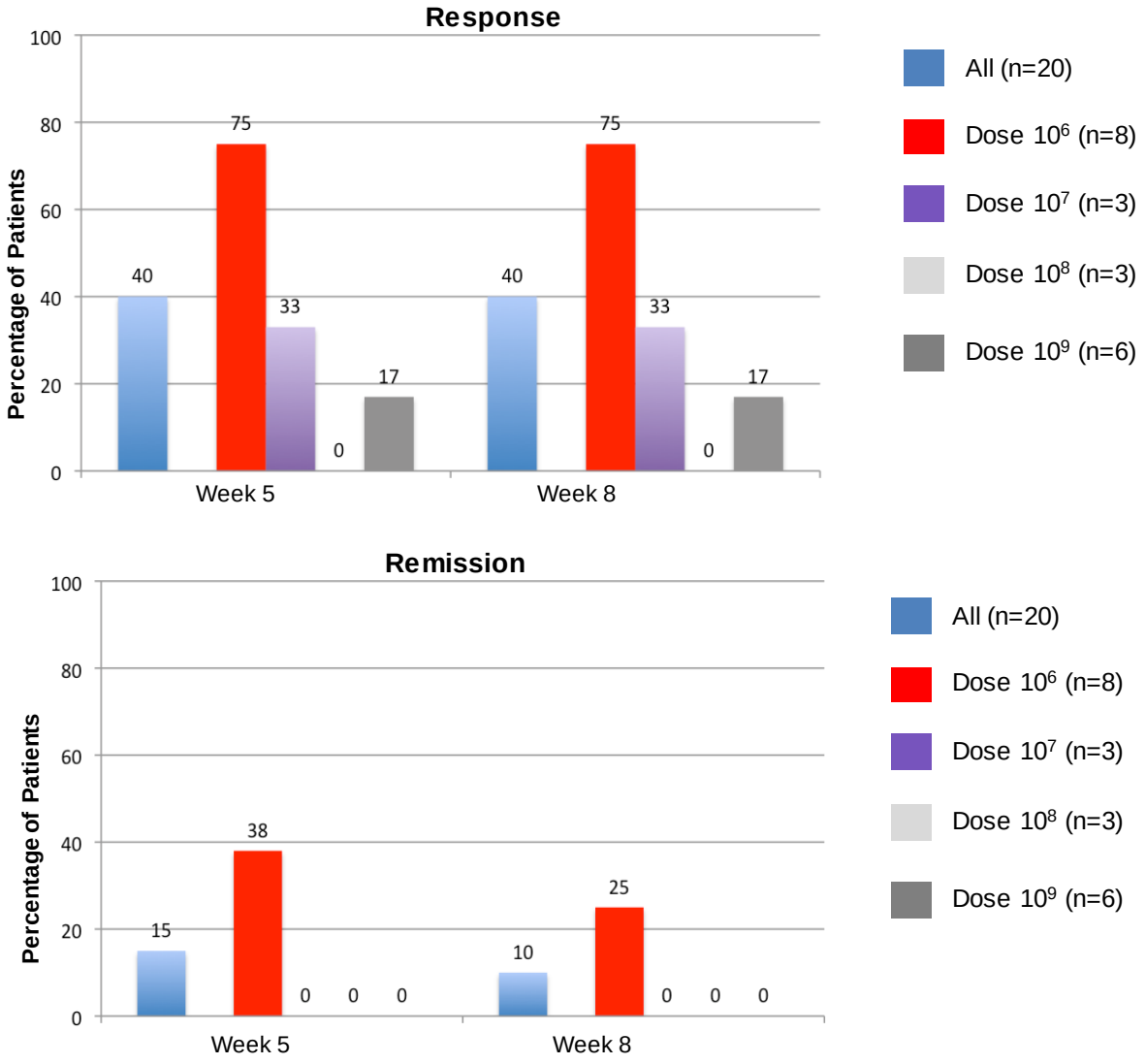
- One initial extension aimed at assessing the safety and tolerability of a second administration of Ova-Treg cells in patients. Seven patients were included in this extension (one patient received a second injection of 10^8 cells and six patients 10^6 cells).
- Another extension concerned multiple injections upon investigator request for patients who presented clinical benefit from the initial injections. Two patients received up to five injections every eight weeks.

Overall, the treatment was well tolerated regardless of the cell dose used. The safety profile of Ovasave®, in the limited human exposure of CATS1, is in line with the context of a first-in-man study in the recruited patient population of moderate-to-severe, refractory Crohn's disease with most of the events

relating to the underlying pathology and conditions. In addition, *ex vivo* experiments using blood samples from CATS1 patients showed that Ovasave® administration does not alter the immune response of patients to infectious pathogens-derived antigens.

In terms of efficacy, 40% of the patients had a clinical response at both weeks 5 and 8 after treatment (see figure below). The 10^6 dose group had the highest percentage of patients in CDAI response (75%) and was the only group with patients in CDAI remission at both weeks 5 and 8 (38% and 25%, respectively). Two patients in the 10^6 dose group were in sustained remission at weeks 5 and 8 after treatment. The assessment of CDAI values as a continue variable (see figure below) shows that the patients were in a stable and active disease with high CDAI values before and at the injection point. Subsequent to the treatment with Ovasave®, the CDAI values dropped significantly. This evolution was observed both in the overall population (p=0.003) and in the patients that received the 10^6 cell dose (p=0.039) where the mean CDAI reduction was larger than the 100 point clinically significant reduction.

Figure 19 : *Percentage of patients in CDAI response (Δ CDAI ≥ 100) or remission at week 5 and Week 8, per dose group*[51]



[51] Desreumaux P, Foussat A, Allez M, Gastroenterology, November 2012.

	CDAI Week -2	CDAI Week 0	CDAI Week 5	Delta CDAI W0 vs. W5	CDAI Week 8	Delta CDAI W0 vs. W8
All (n=20)	377 ± 81.8	363.7 ± 80.	281.5 ± 116.1	-82.2 ± 95.4	292.0 ± 108.1	-63.0 ± 87.9
				p = 0.003		p = 0.006
10^6 (n=8)	400.9 ± 101.2	395.1 ± 91.	251.8 ± 157.9	-143.4 ± 105.0	244.6 ± 130.1	-131.6 ± 65.4
				p = 0.039		p = 0.031

Using the IBDQ (Inflammatory Bowel Disease Questionnaire) relating to quality of life , the 10^6 dose group showed also the best results reaching statistical significance at week 5 for improvement of quality of life and 25% and 37.5% of remission according to IBDQ at week 5 and 8, respectively. A reduction of serum CRP (C-Reactive Protein), a serum surrogate marker of inflammation, was also observed particularly in the 10^6 dose group.

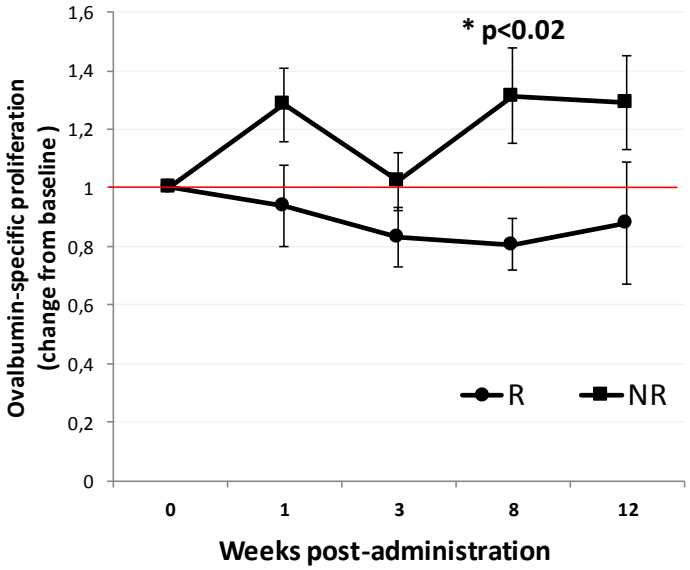
Analysis of patient's blood samples showed that the pro-inflammatory monocyte subpopulation ($CD14^+$ $CD16^+$) was decreased after Ovasave® treatment, particularly in responder patients and in a more sustainable fashion in the 10^6 dose group. This observation suggests that pro-inflammatory monocytes are one of the main cellular targets of Ova-Treg suppressive activity.

The very limited numbers of patients that received a second injection (n=7) and that received multiple injections up to one year (n=2) limit the opportunity of assessing the clinical effect of multiple injections. However, continued administration required presence of perceived benefit by the investigators. Also, in these extension protocols, tolerability of multiple administrations was demonstrated.

During the CATS1 study, the *in vitro* proliferative activity of patient's white blood cells to ovalbumin, the specific antigen of Ova-Treg, was assessed before and after treatment. The starting hypothesis was that Ova-Treg being antigen-specific suppressor cells, the suppression would be firstly targeted to the normal patient's response to ovalbumin.

Proliferative responses of white blood cells from patients to ovalbumin with a clinical response (measured by CDAI decrease) were significantly lower than those of cells from non-responders. Similar to the CDAI reduction, the reduction in ovalbumin-specific proliferative response was more pronounced in the 10^6 dose group. These results suggest that for Ag-Treg cell immunotherapy products, evaluation of the systemic proliferative response to the Ag-Treg specific antigen after treatment can be indicative of a clinical benefit. Such a biomarker of response could be useful in the future to ensure that only responder patients will continue to be treated with Ag-Tregs.

Figure 20 : *Evaluation of proliferative response of Peripheral Blood Mononuclear Cells to ovalbumin in responders (n=8) vs Non-Responders (n=12) (week 5) (Mean (±SEM))* [52]



6.4.1.1.7 Next development stage: resumption of the Phase IIb clinical study (CATS29)

The results from the CATS1 study were the basis for the international Phase IIb study (CATS29) in patients with moderate-to-severe refractory Crohn's disease. The CATS29 study, which started in December 2014, was an international, multicenter, randomized, double-blinded, placebo controlled, multiple dose study to document the efficacy and expand safety information of Ovasave® in patients with refractory Crohn's disease. It is intended to be a controlled proof-of-concept for the ability of Ovasave® to induce response.

CATS29 aims to confirm the induction of a clinically significant CDAI response six weeks after start of treatment with 10^6 Ova-Treg cells versus placebo.

The initial protocol required a total of 144 patients in 4 groups (36 patients per group). The primary objective of CATS29 was the confirmation, controlled versus placebo, of the ability of a single intravenous (IV) injection of a 10^6 cells dose of Ovasave® to induce a CDAI response (CDAI decrease $\geq$ 100 points) six weeks post administration. The sample size calculation was initially based on the assumption of 70% responder patients in the 10^6 cells group versus 35% in the placebo control group. Secondary study objectives include the safety assessment of a first and second IV injection of Ovasave®, assessment of different doses (placebo, 10^4, 10^6 and 10^7 cells) with comparison of the efficacy and the safety between doses, assessment of the safety and efficacy of a second injection at week 8 including remission and steroid-sparing effect at week 14.

However, the CATS29 study had to be temporarily interrupted in June 2015 after the Company encountered production problems on its Besançon site, which was later closed. The health authorities were informed of this interruption.

After these incidents, the Company decided to outsource the production of Ovasave® to MaSTherCell, a Contract Manufacturing Organization (CMO). In February 2016, MaSTherCell successfully produced the validation batches. The successful production of validation batches is a key stage in an industrial technology transfer.

The protocol of the CATS29 study was modified in early 2016 with the aim of focusing in the primary assessment criteria of the study, i.e. to confirm the induction of a clinically significant CDAI response

[52] Desreumaux P, Foussat A, Allez M, Gastroenterology, November 2012.

in a controlled study. The rationale of this decision was to cut down on the study duration and costs while maintaining the study's main assessment criteria. Consequently, the assumption is still to obtain 70% of responder patients in the group treated with Ovasave®, which will be compared with a placebo response rate of 30%. However, the exploration of 10^4 and 10^7 dose cells was abandoned. To minimize the exposure of patients to the placebo, while maintaining a controlled study, the blinded phase of the study was reduced to a single comparative injection between the 10^6 cell dose and the placebo. The study will thus continue to assess the safety of multiple injections and the efficacy through remission and steroid-sparing effect.

The modified protocol provides for the assessment of 56 patients in 29 centers in 6 European countries. For each patient, after the production of the autologous clinical batch (between 10 and 12 weeks), there will be a 32-week treatment period: 8 weeks of blinded study followed by a 24-week open-label trial. The first injection at the beginning of the treatment (week 0) will be blinded (i.e. either a placebo or Ovasave® 10^6). The next three injections (one every eight weeks) will be open-label (Ovasave® 10^6 only).

The Company expects to receive the approval from the European regulatory authorities in Q2 2016. The Company is planning to repeat the clinical study, i.e. recruit new patients, once it has received the approval from the European regulatory authorities, once the manufacturing technology transfer to MaSTherCell has been completed, and once the Company has obtained the necessary funds to finance the study. The first clinical data will be expected within 18 to 21 months following the resumption of the study. The global cost of the study should amount around €15 million.

The reader is invited to read chapter 4 of the *Document de Référence*, and in particular paragraph 4.1.1 that describes the risks associated with clinical development.

6.4.1.1.8 New business model with high added value

The treatment of Crohn's disease has evolved significantly with the introduction of biologics in the late 1990's with the launch of Remicade® (infliximab) the first approved anti-TNF in CD. Before the introduction of biologics and still today as first line the treatment of CD includes steroids, anti-inflammatory drugs and immunosupressors. There is growing evidence in favor of an early treatment start with biologics in order to induce early remission and attempt to change the progression of the disease and therefore treat patients. Nevertheless, a significant proportion of the patients, approximately two-thirds, do not respond or eventually lose response, stressing the fact that the management of Crohn's disease still represents a significant unmet medical need.

Currently, treatment with the biologic therapies described above together with the standard treatment regimens has an annual average cost of at least €22,000[53]. A new product with superior results to the existing products in refractory patients is expected to be sold at a premium price compared with these.

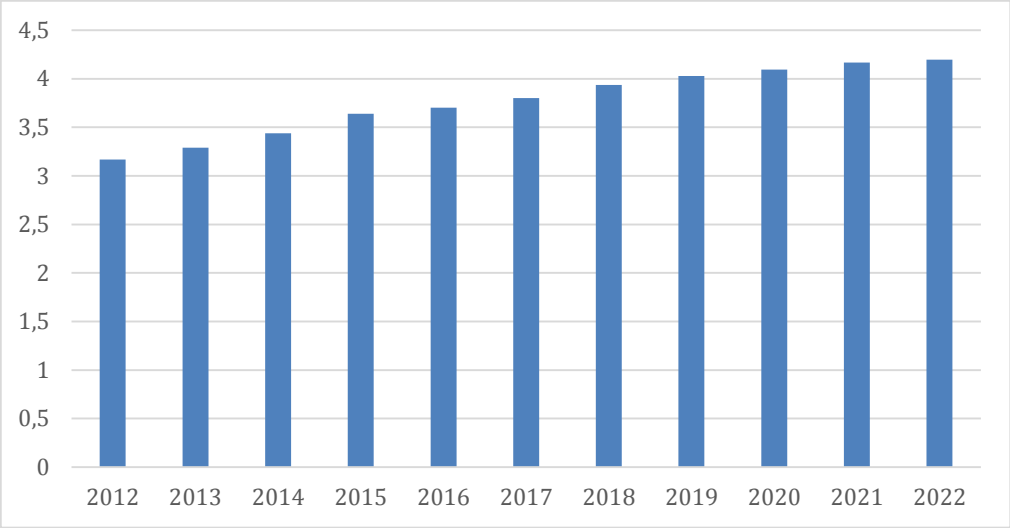
Furthermore, the launch of biologics such as vedolizumab (Entyvio®) in 2014 and the interleukin inhibitor IL-12/IL-23 ustekinumab (Stelara®), which is being developed and which could be marketed in 2016, on condition that the *ad hoc* regulatory authorizations have been obtained, will contribute to increasing income from these treatments for Crohn's disease. In particular, ustekinumab, intended for patients refractory to current anti-TNFs, could have a high launch price and should rapidly generate significant revenue.

In this context, GlobalData estimates that the overall Crohn's disease market will increase from $3.2 billion in 2012 to $4.2 billion in 2022, representing an average annual growth of 2.8% over the period[54] (see figure below). Again, this growth rate reflects shifting competitive dynamics as market growth from emerging agents, such as vedolizumab and ustekinumab, offsets the decline in sales of older, established agents, which will face increasing erosion by biosimilars and declining use.

[53] Crohn's Disease (CD) Therapeutics - Pipeline Assessment and Market Forecasts to 2018, GlobalData 2011.

[54] Crohn's Disease – Global Drug Forecast and Market Analysis to 2022. GlobalData 2014.

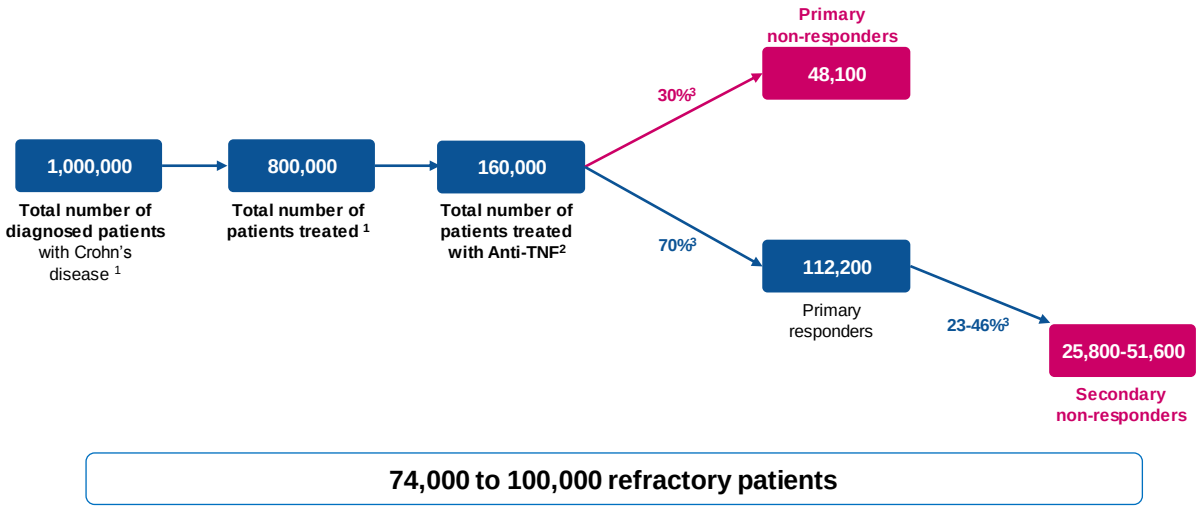
Figure 21 : *Crohn's disease therapeutic market global forecast (billion $), 2012-2022*[55]



The Crohn's disease market in 2022, with its expected value of $4.2 billion, will be distributed among the seven major markets with a significant share in the US (68%) followed by the combined major markets in the EU (11%), Canada (8%) and Japan (7%).

The launch of Ovasave®, assuming confirmation of the preliminary positive strong data seen so far, which aim to show benefit in over 70% of refractory Crohn's disease patients, should result in significant penetration of the approximately 74,000 to 100,000 target patient population (see figure below), where the unmet medical need is greatest.

Figure 22 : *Management of Crohn's disease*[56]



1. Mild Crohn's disease moderate to severe and fistulizing. Estimation for the year 2016 for in the eight major markets (United States, France, Germany, United Kingdom, Spain, Italy, Canada, Japan). GlobalData.
2. Crohn's disease moderate to severe and fistulizing. Estimation for the year 2016 for in the eight major markets (United States, France, Germany, United Kingdom, Spain, Italy, Canada, Japan). GlobalData.
3. Roda G. et al 2016 (In Press. Doi:10.1038/ctg.2015.63)

A successful launch and market penetration needs to consider the unmet medical need being addressed, the value proposition, the compliance with clinical practice and patient expectations and pricing and reimbursement strategies with payers.

[55] Prof A Cortot, Hôpital Huriez, Lille, France; présentation aux investisseurs de Neovacs en 2010.

[56] Source: Company.

Ovasave® development has taken and will take these aspects in consideration in order to deliver a value adding proposition that in addition to the tolerability and efficacy is in line with clinical practice, easy to prescribe and administer from a physician and patient perspective and delivers value to payers.

The target product profile for the Company is as follows:

- An individual treatment produced in five weeks

Ovasave® is an autologous immunocellular therapy aimed at being produced after blood collection. The Company's target is to improve its manufacturing to reduce the current 10-12 week manufacturing time to 4 or 5 weeks. This would be in line with current clinical practice for the regular follow-up of patients suffering from Crohn's disease and for therapy adjustment and treatment change decisions.[57].

- A stable product over several years

The long term stability of multiple frozen Ovasave® vials produced in a single batch from a single blood collection will enable chronic treatment for several years.

Once the first injection of the therapeutic product has been given, all subsequent injections will be available off the shelf as needed. The drug product can be stored for several years and will be distributed to the patient, either directly, through central pharmacies or through especially dedicated storage centers.

- Bedside administration every eight weeks

Ovasave® is produced in vials allowing for easy bedside administration.

Ovasave® treatment requires chronic re-administration, probably every two months which is well in line with current biologic treatment regimens for chronic treatment, particularly some of the less frequently administered ones, resulting in a treatment with a positive impact on the patient's quality of life and daily routine.

- Rapid targeting of patients showing signs of clinical improvement

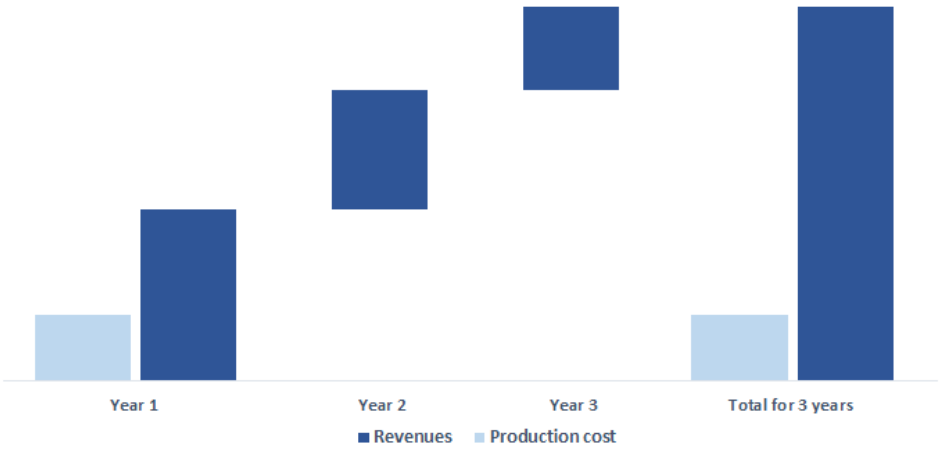
The prospective biomarker of immune response to the Ovasave®-specific antigen, ovalbumin, is expected to allow for personalization of treatment leading to only maintaining treatment in those patients with evidence of improvement. This therapeutic monitoring also benefits paying bodies, who will only be asked to maintain payment for those patients with indication of potential therapeutic benefit.

The Company believes that Ovasave® and its manufacturing process allowing several years of treatment from one patient batch, represents added value through a completely new economic model in the cell therapy field, making it competitive with any other biologic.

Considering the target treatment compliance and the initial single cost of goods for the batch production the model shown below indicates an attractive cumulated return at the end of the third year. The first year would already deliver a strong return with the first six doses. The model is based on a significant reduction in production costs which is necessary to make the business model of Ovasave® viable. The Company considers that this cost reduction target is realistic and is working actively to improve its production process.

[57] Market study conducted by LEK for Ferring and TxCell, conducted in 2012.

Figure 23 : *Model of treatment revenue and cost/patient for three years*



Independent market research into a limited sample of physicians, payers and specialty pharmacies in the US, the UK, France and Germany was performed in 2012 by LEK Consultants on behalf of TxCell. The treatment paradigm and the target product profile (TPP) tested were as presented in this chapter 6:

- Target product profile: payers reacted positively to the TPP, suggesting a minimal acceptable remission delta of approximately 20% to facilitate reimbursement.
- Duration of treatment: the treatment period of one year is considered acceptable (availability of follow-up data) with premium reimbursement for three years.
- Premium pricing: payers indicate that the budget impact of Ovasave® would be minimal, a premium price point in excess of intensified treatment with current biologics is attainable.
- Pricing model: payers viewed the pricing model positively, with availability of a test that makes it possible to pay Ovasave® only when the treatment is effective with patients.

6.4.1.2 Treatments in development for Crohn's disease

As of today, five biologics are approved for Crohn's disease in the US and three in Europe including the first anti-TNF alpha monoclonal antibody biosimilar (Inflectra®). Several new molecules and other biosimilars of anti-TNF antibodies are in late-stage clinical development (see figure below). Mesenchymal stem cells based cell therapy products are also in development for the treatment of Crohn's disease.

Figure 24 : *Main products in late-stage development for moderate-to-severe Crohn's disease*[58]

Compound(s)	Mechanism of action	Company(ies)	Development phase(s)
Ustekinumab	Anti-IL12/23	Johnson & Johnson	Pre-registration (FDA)
Cx-601	Mesenchymal stem cells	Tigenix	Pre-registration (EMA) - Fistulizing Crohn's disease
Prochymal® (remestemcel-L)	Mesenchymal stem cells	Mesoblast	Phase III (first Phase III study failed)
Etrolizumab	Antagonist of integrins α4-β7 and αE- β7	Genentech	Phase III
HMPL-004	Inhibitor of NF-ƙB	Hutchison Medipharma	Phase III

- **Other cellular therapies for Crohn's disease**

Several cell-based therapy approaches have been attempted for the treatment of CD and related complications, in particular in the more severe resistant to current treatment patient population.

The most successful approach has proved to be hematopoietic stem cell therapy which has delivered good efficacy results but at a high cost as a result of infectious side effects. It is currently restricted to extremely severe cases under investigational protocols and represents a limited opportunity for industrialization since it is in fact a bone marrow transplantation procedure that is performed within hospitals. Mesenchymal stem cells (MSCs) have been used in multiple ways to try to address the therapeutic need in refractory CD patients. The regeneration approach in the fistulized form has demonstrated a clinical benefit in Phase III tests. Conversely, the systemic use of allogeneic or autologous mesenchymal stem cells has also been attempted with limited results. Initial reports have clearly been negative but more recent single injection studies with allogeneic mesenchymal stem cells have turned out to be more promising[59]. Nevertheless, it is likely that this allogeneic approach will not be suitable to the chronic treatment required in the context of Crohn's disease since, despite the limited immune-privilege of mesenchymal stem cells, repeated use leads to immunogenicity and rejection. Autologous systemic MSC approaches are being developed and might represent an opportunity. However, the limited stability of mesenchymal stem cells functionality when stored frozen may compromise the development of MSC-based therapeutics to a commercial stage[60].

In this context, Ovasave® represents an opportunity with significant potential in view of the very low immunogenicity, the tolerability, apparent efficacy and ease of administration to patients described so far.

[58] Source: Company.

[59] Clin Gastroenterol Hepatol. 2014 Jan;12(1):64-71. A phase 2 study of allogeneic mesenchymal stromal cells for luminal Crohn's disease refractory to biologic therapy. Forbes GM et al.

Inflamm Bowel Dis. 2013 Mar-Apr;19(4):754-60. Safety and tolerability of human placenta-derived cells (PDA001) in treatment-resistant Crohn's disease: a phase 1 study. Mayer L et al.

[60] François M., Galipeau J. et al. Cryopreserved mesenchymal stromal cells display impaired immunosuppressive properties as a result of heat-shock response and impaired interferon- y licensing. Cytotherapy, 2012; 14: 147–152 .

Figure 25 : *Cellular therapies in development for Crohn's disease*[61]

Technology	HSCT Auto / Allo	MSC Autologous	MSC Allogeneic	MSC Autologous	MSC Allogeneic	Ag-Treg (Ovasave®)*
Source	Peripheral Blood	Bone Marrow	Bone Marrow	Lipoaspirate	Lipoaspirate	Peripheral Blood
Patients	Moderate to severe refractory CD	Moderate to severe refractory CD	Moderate to severe refractory CD	Fistulizing CD	Fistulizing CD	Moderate to severe refractory CD
RoA / Effect	Systemic	Systemic	Systemic	Local	Local	Systemic / Local
Efficacy	High 50-70% remission	Low 30% response	Low - Good 30-80% response	High local 70% healing	NA	High 75% response 30% remission
Tolerability	High toxicity OI, death	Medium	NA Apparently Good	Good	NA	Good
Immuno-genicity	Low in Auto High in Allo	Low 30% response	High in repeated injections	Low	High in repeated injections.	Very low
Source	Academic[62, 63]	Academic[64]	Osiris[65] Forbes[66]	Academic Cellerix[67, 68]	Cellerix	TxCell[69]

RoA: Route of Administration
HSCT: Hematopoietic Stem Cell Transplantation
OI: Opportunistic infection
MSC: Mesenchymal Stem Cells
CD: Crohn's Disease
* based on the CATS1 study.

- **Ovasave®'s positioning: a promising profile for refractory patients**

Currently anti-TNF refractory CD patients have very limited therapeutic options for their disease. These patients were the targets of the CATS1 study, which demonstrated the feasibility, tolerability and relevant clinical efficacy signals.

The postulated benefits of Ovasave® are the high response (>70%) and high remission (>30%) in refractory patients together with a good tolerability profile, low immunogenicity and a local effect. The

[61] Source: Company.

[62] Cassinotti A, Annaloro C, Ardizzone S, et al. Autologous hematopoietic stem cell transplantation without CD34+ cell selection in refractory Crohn's disease. Gut 2008;57:211–7.

[63] Ditschkowski M, Einsele H, Schwerdtfeger R, et al. Improvement of inflammatory bowel disease after allogeneic stem-cell transplantation. Transplantation 2003;75:1745–7.

[64] Duijvestein M, Vos AC, Roelofs H, et al. Autologous bone marrow-derived mesenchymal stromal cell treatment for refractory luminal Crohn's disease: results of a phase I study. Gut 2010;59:1662–9.

[65] Osiris, ACG 2006.

[66] Forbes GM, Stum MJ, Leong RW, Sparrow MP, Segarajasingam D, Cummins AG, Phillips M, Hermann RP. A phase 2 study of allogeneic mesenchymal stromal cells for luminal Crohn's disease refractory to biologic therapy. Clin Gasteroenterol Hepato; 2014 Jan;12(1):64-71. doi: 10.1016/j.cgh.2013.06.021. Epub 2013 Jul 19.

[69] Desreumaux P, Foussat A, Allez M, Gastroenterology, November 2012.

potential biomarker and chronic treatment possibility creates the opportunity to personalize the management of CD and deliver long-term therapy.

The high level of response that was documented in the first Ovasave® study, CATS1, is highly competitive with the efficacy delivered by other approaches, in particular when compared with the results obtained with naive patients using biologics and the effect obtained with Ovasave® in refractory patients (see figure below).

Figure 26 : *Ovasave® compared with other treatments*[70]

Technology platform	Anti-TNF (71, 72, 73, 74)	Kinoïde (75)	MSC Allo. (76, 77)	Ovasave® (78)
Response CDAI (Δ70 or Δ100)	60-70% (Δ100)	60-70% (Δ70)	30-80% (Δ100)	75% (Δ100)
Remission CDAI (≤ 150)	30-40%	30-60%	10-40%	30-40%
Patients inclusion criterias	Patients with moderate CACD* (lower initial CDAI)		Patients with moderate to severe CACD*	Patients with moderate to severe CACD*

* CACD: Chronic Active Crohn's Disease

The Ovasave® mechanism of action actively inhibits inflammation through multiple targets using the natural properties of Ag-Treg cells. This is radically different from the blocking of a single molecule. Thus, the nature of the mechanism of action of Ovasave® distinguishes itself from the activity of monoclonal antibodies in that rather than blocking inflammation (for anti-TNF alpha compounds and ustekinumab) or blocking cell migration (for natalizumab and vedolizumab), Ovasave® induces immuno-modulation with multiple and synergistic effects.

These multiple effector mechanisms inhibit simultaneously multiple proinflammatory immune pathways such as pro-inflammatory cell differentiation, proliferation and pro-inflammatory cytokine production and modulate the antigen presentation capacity of dendritic cells, resulting in an induction of immune tolerance.

In addition, this multiple mechanism of action supports the efficacy in refractory patients as shown in our open-labeled first study (CATS1).

Secondly, Ovasave®, in contrast to the compounds in development, specifically migrates to the inflammatory lesions allowing a localized specific antigen activation, and absence of systemic immuno-suppression.

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[68] Garcia-Olmo D, Herreros D, Pascual I, et al. Expanded adipose-derived stem cells for the treatment of complex perianal fistula: a phase II clinical trial. Dis Colon Rectum 2009;52:79–86.

[69] Desreumaux P, Foussat A, Allez M, Gastroenterology, November 2012.

[70] Source: Company.

[71] Targan SR et al. N Engl J Med. 1997.

[72] Hanauer SB, Gastroenterology 2004.

[73] Schreiber S et al. Gastroenterology 2005.

[74] Sandborn et al. New England J Med 2007.

[75] Neovacs presentation December 2010.

[76] Osiris, ACG 2006.

[77] Forbes et al. Clinical Gastroenterology and Hepatology. S1542-3565(13)01033-1.

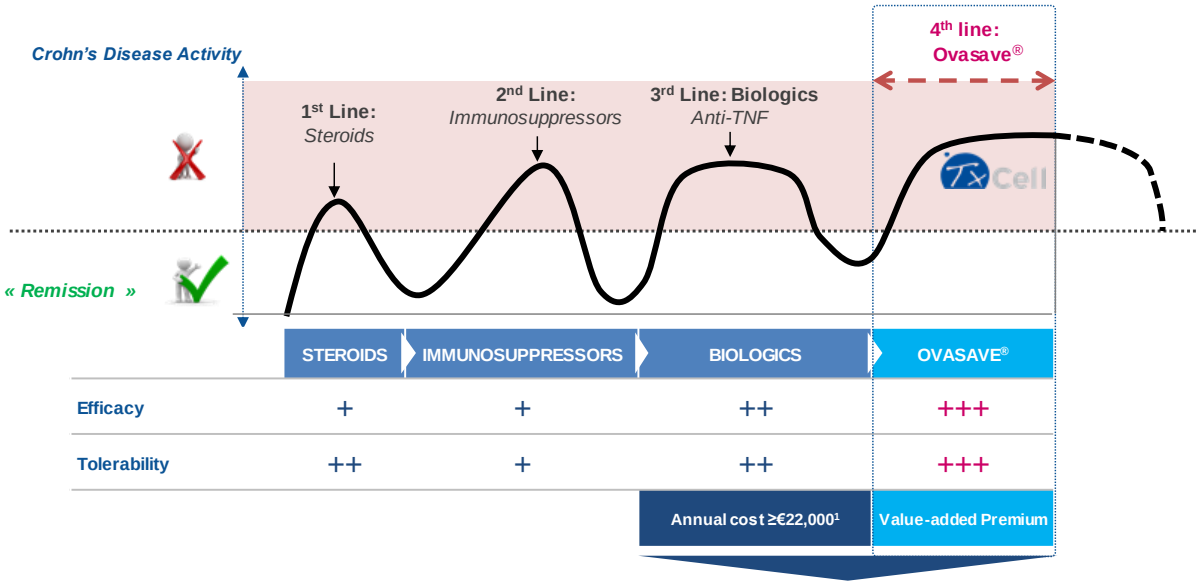
[78] Desreumaux, et al. Gastroenterology, November 2012.

Thirdly, Ovasave® has a good tolerability profile. Because of the autologous nature, we do not expect an immunogenic reaction against the product and the limited proliferative capacity of the Ag-Treg cells renders tumourigenicity unlikely. In view of the lack of immunogenicity and of the multiple target-mediated effects of Ovasave®, the Company believes that an induction of resistance due to escape mechanisms is very unlikely.

Furthermore, this multiple target mechanism of action and the good tolerability profile of Ovasave® allows for the possibility of synergistic concomitant add-on therapies.

In view of the patient population where the current evidence has been generated and where the highest unmet medical need is, Ovasave® is well positioned to add value to patient management as a fourth-line treatment in Crohn's disease patients after failure or intolerance to biologics.

Figure 27 : *Ovasave® positioning in the treatment pathway*



74,000 to 100,000 refractory patients[2] → Potential market estimated at over €2.2bn[3]

1. GlobalData 2014
2. Company estimate for 8 majors markets (US, France, Germany, UK, Spain, Italy Canada, Japan, based on the total number of patients suffering from Crohn's disease and taking anti-TNF drugs (GlobalData 2014) and the rate of patients non-responsive to anti-TNF treatment (Roda G. et al. 2016, in Press, doi:10.1038/ctg.2015.63)
3. Company estimate, based on the estimated number of refractory patients and the selling price of current last line biologic treatments

6.4.2 Col-Treg, a new approach in the treatment of autoimmune uveitis

6.4.2.1 Disease presentation

Uveitis is classified as a rare disease and an orphan indication. It is one of the leading causes of blindness in the developed world. The global annual incidence of uveitis is between 17 to 52 cases per 100,000 in Switzerland and the US respectively, whereas the prevalence is between 38 to 714 cases per 100,000 in France and in India respectively[79]. The disease affects about 35-50 out of 100,000 people[80].

Autoimmune uveitis (or non-infectious uveitis) refers to uveitis without an infectious cause and includes idiopathic uveitis. Anatomically, uveitis is classified by the main site of inflammation as anterior, intermediate, posterior and panuveitis. About 50% of the cases involve the posterior and intermediate

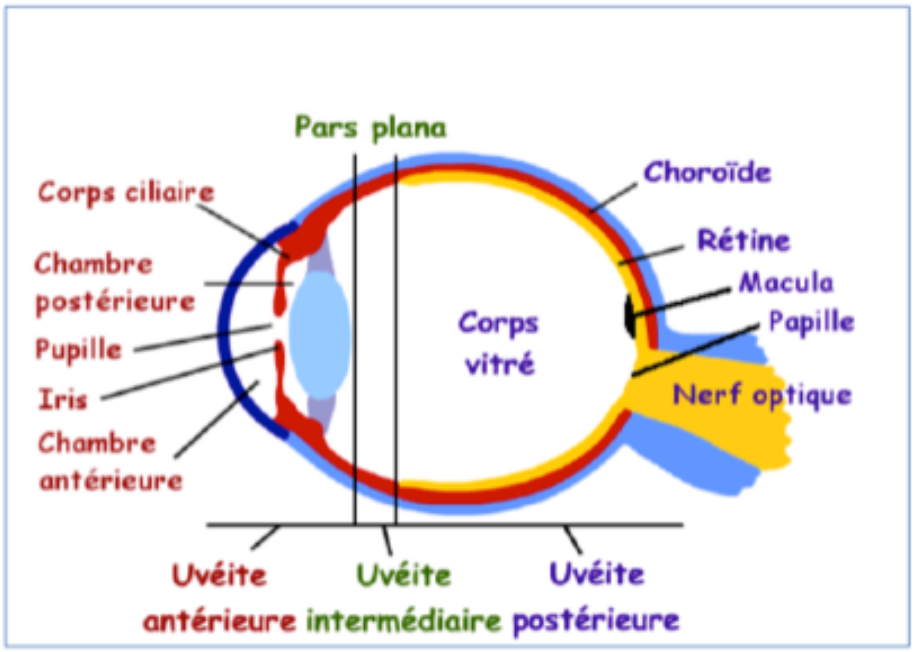
[79] Miserocchi *et al.*, 2013; Wakefield and Chang, 2005.

[80] January 21, 2013. EMA/COMP/450332/2012. Committee for Orphan Medicinal Products.

segments of the eye, where collagen type II can be identified, while the remaining cases tend to be limited to the anterior segment[81].

T cells have been identified to play a significant role in uveitis, either as single manifestation or as part of a systemic autoimmune disease.

Figure 28 : *Uveitis classification*



The diagnosis is generally established by ophthalmologic examination together with local and frequently also systemic laboratory evidence of inflammation. Examination of the vitreous compartment to identify cellular infiltration (vitreous haze) is particularly relevant for the diagnosis as well as to assess disease evolution and response to therapy. Namely, vitreous haze together with visual acuity are frequently included as end-points in clinical trials. The gold standard of uveitis treatment rests, after exclusion of infectious etiologies, on the administration of steroid therapy, locally, intra-lesion and systemically. Most treatments consider a step-wise approach starting with steroids, followed by for this indication unapproved immunosuppressive medication as second line, and finally (also unapproved for this indication) biologics as third line. Intra-ocular steroid therapy is also a therapeutic approach in more severe cases, but associated with significant risk of side effects, in particular an increase in intra-ocular pressure. Most biologics used in the treatment of uveitis are recombinant antibodies that target individual molecules within the inflammatory process. However, there are very limited clinical data available supporting the use of these products in uveitis and their use is "off label" since no biologics have been approved for this condition to date.

The treatment of autoimmune uveitis remains a significant unmet medical need as currently all approved treatments remain steroid based. While steroid therapy normally provides fast initial relief of the symptoms of uveitis, the effect is limited and insufficient for the more severe cases. Furthermore, this therapy is associated with significant local and systemic side effects. The unmet medical need of autoimmune uveitis treatment is particularly relevant considering that this condition represents the first cause of blindness in the western world[82].

[81] Mol Vis. 2013 Jul 20;19:1591-9. Print 2013. Trypsin-mediated enzymatic degradation of type II collagen in the human vitreous. Van Deemter M. GlobalData Report - Opportunity Analyzer: Uveitis – Opportunity Analysis and Forecasts to 2017. GDHC008POA - Dec. 2013.

[82] GlobalData Report - Opportunity Analyzer: Uveitis – Opportunity Analysis and Forecasts to 2017. GDHC008PO - Dec. 2013.

6.4.2.2 Treatments in development for autoimmune uveitis

At the heart of the unmet needs for uveitis treatment is the development of a cure and/or treatment options that are permanently able to control inflammation and prevent a decrease in vision.

The current pipeline of products for the treatment of uveitis has several products but still remains dependent on improvements of steroid or immunosuppressive therapy and mono target biologic approaches. Anti-TNF biologics, in particular adalimumab, are one of the classes of products currently being investigated. Some innovative alternative approaches are being researched but are still in very early stages.

In this context, a new well-tolerated alternative, with a multiple target mechanism of action through an immunomodulatory action could represent a significant added value for the patients and the treatment of autoimmune uveitis.

Figure 29 : *Main products in late-stage development for refractory autoimmune Uveitis*[83]

Compound(s)	**Company**	**Development phase**
Adalimumab	Abbvie	Phase III
Sarilumab (anti-IL6)	Sanofi	Phase II
Secukinumab (anti-IL17)	Alcon	Phase II

6.4.2.3 Col-Treg

Col-Treg is composed of an extended population of autologous collagen-II specific regulatory T lymphocytes. The product is currently being developed by TxCell for the treatment of patients suffering from autoimmune uveitis (or non-infectious uveitis) who have failed to respond to treatment or are intolerant to existing treatments. It is the second Ag-Treg drug candidate from the ASTrIA platform. Col-Treg obtained the status of orphan drug for the treatment of non-infectious uveitis in Europe in December 2014 and in the United States in September 2015.

Collagen-type II expression is found in the vitreous body of the eye and joints. As a consequence, Col-Treg can be developed for the treatment of eye and joint inflammatory diseases. Several pre-clinical experiments have been performed in mouse models of joint inflammation, and TxCell has recently decided to develop Col-Treg for the treatment of autoimmune uveitis as a first indication. Autoimmune uveitis is a pathology that is classified as a rare disease, with insufficient treatment options.

– **Pre-clinical results of Col-Treg against autoimmune uveitis**

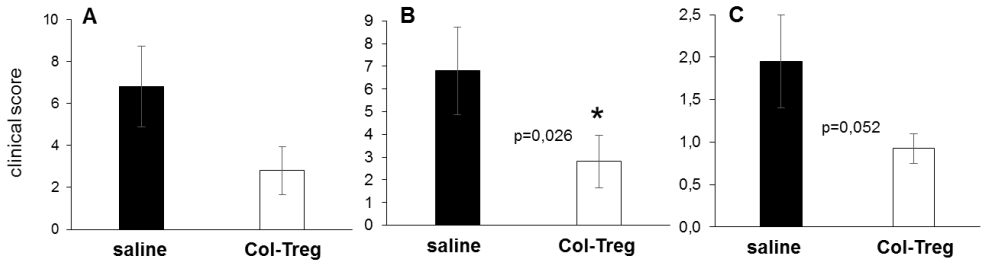
The results of the pre-clinical studies conducted by TxCell were published in October 2015 in Investigative Ophthalmology and Visual Science[84].

The specific migration of Col-Treg cells to the inflammatory eye and not to a healthy eye was demonstrated in vivo using a murine model of autoimmune experimental uveitis. In this autoimmune experimental uveitis model, the Col-Treg cells injected intravenously enabled the inhibition of the eye inflammation. This inhibition was observed not only through ophthalmoscopic measurements (see figure below), but also through histology techniques.

[83] Source: Company.

[84] Asnagli H, Jacquin M, Belmonte N, Gertner-Dardenne J, Hubert MF, Sales A, Fall PB, Ginet C, Marchetti I, Ménard F, Lara G, Bobak N, Foussat A. Inhibition of Non-infectious Uveitis Using Intravenous Administration of Collagen II-Specific Type 1 Regulatory T Cells. Invest Ophthalmol Vis Sci. 2015 Oct 1;56(11):6456-66.

Figure 30 : *Inhibition of clinical signs of autoimmune experimental uveitis by Col-Treg*



Col-Treg was administered intravenously to animals with autoimmune experimental uveitis. Panel A shows the inhibition of total clinical scores in comparison with untreated animals (saline). Panel B shows an inhibition of clinical scores of the anterior segment of the eye. Panel C shows an inhibition of clinical scores of the intermediate and posterior segments of the eye.

The follow-up studies of Col-Treg cells after injection in animals showed that there was no uncontrolled proliferation and tumorigenicity. These results were confirmed *in vitro* with human Col-Treg cells, which also showed that there was no tumorigenic potential. Furthermore, an in vivo toxicology study with Col-Treg conducted on animals according to Good Laboratory Practices (GLP) did not identify any signs of toxicity.

– **Col-Treg production process**

The only significant difference compared with the Ovasave® production process is the use of human type II collagen, instead of ovalbumin, to activate the patient's cells.

– **First Col-Treg clinical test**

Based on the pre-clinical results obtained for Col-Treg in autoimmune uveitis, the Company intends to finalize, in 2016, the pre-clinical development and the regulatory documents required for starting the first clinical study with Col-Treg. The start date of the study was not set yet.

The development of Col-Treg is now approached with a lower priority (regarding operational priorities, please refer to paragraph 6.1.1). Any meaningful investment in these programs will be subject to *ad hoc* financing, and especially in the form of specific industry partnerships.

6.4.3 New products

There are new product candidates currently at the research stage that will enter the pre-clinical development stage in the very near future.

With respect to inflammatory skin diseases, TxCell is developing approaches based on the two platforms ASTrIA (Des-Treg) and ENTrIA. Proof-of-concept studies on animal models of skin inflammation are currently in progress. Interestingly, a few years ago, TxCell published the first demonstration that antigen-specific Type 1 Tregs could inhibit a delayed cutaneous hypersensitivity reaction[85]. TxCell plans to target bullous pemphigoid, a skin disease that is becoming increasingly prevalent and for which there are currently few treatments.

It is also carrying out proof-of-concept studies in pre-clinical models of inflammation of the central nervous system that mimic the characteristics of inflammatory forms of multiple sclerosis. The Company has, in the past, obtained preliminary results that suggest the efficacy of Type 1 Tregs in treating this type of pathology. The CAR-Treg approach has also been validated in the same models by Professor Loskog's team[86]. Myelin-Treg (ASTrIA) and ENTX#MY (ENTrIA) are the two TxCell product candidates for the treatment of inflammatory forms of multiple sclerosis.

Lastly, the development of a product candidate for the treatment of renal lupus has begun on the ENTrIA platform. This development will be conducted as part of a collaboration with San Raffaele hospital in Milan, a reputed institute in gene and cell therapy. The CAR-Treg product developed for lupus will use

[85] Foussat et al., The Journal of Immunology 2003.

[86] Fransson et al., Journal of Neuroinflammation, 2012.

the binding domain of autoimmune antibodies present in lupus patients as a ligand-binding domain of the CAR.

6.5 Manufacturing processes and production sites

In 2015, the Company decided to contract out the current and future production of its products. It will however develop and optimize manufacturing processes in its laboratory based in Sophia Antipolis. Subsequently, these processes will be transferred to the subcontractors chosen by the Company, who will manufacture the products under the conditions defined by the Company.

6.5.1 Manufacturing process for the ASTrIA platform

The manufacturing process of Ag-Treg is a key asset of TxCell with the main process steps being patented. It has been invented and developed by TxCell over the years with a first process version used in the Phase I/IIa CATS1 clinical study and an already improved version for the CATS29 study that started in 2014. The Ag-Tregs cell manufacturing process is an autologous therapy process. It brings important advantages over other cell therapy production approaches. Firstly, the selection method used by TxCell allows the isolation of the desired regulator cells so that the end product is composed of more than 80% of cells with regulatory T lymphocytes. This makes a cell therapy product that is effective at low doses as suggested by the first clinical data (best dose at 10^6 cells). Secondly, the process comprises a therapeutic cells expansion stage that can obtain hundreds of millions of cells. This gives the opportunity to produce with a single blood sample and with a single manufacturing run the number of doses required for several years of a patient's treatment. Importantly, Ag-Treg cells are stable when stored at low temperature with available data showing the stability of Ova-Treg cells for at least five years when stored at -150°C. By producing several years of treatment doses, the overall cost of goods of Ag-Treg product is lowered significantly, rendering this autologous cell therapy product very competitive with more classic therapies, notably for patients suffering from moderate-to-severe Crohn's disease and refractory to existing treatments.

These raw materials are essential for conducting clinical tests and manufacturing the Company's products, in particular certain cytokines (IL-2 or IL-4), the culture medium and the activation balls. For each one of them, the Company sets up contractual tools (supply agreement, batch manufacturing contracts) and identifies alternate suppliers to ensure continuous supply. The Company also looks for alternative raw materials that will enable it to reduce its risk of dependence as well as its production costs.

Optimization of the manufacturing process

The optimization of the manufacturing process remains an important objective for the Company. TxCell continues to work on the optimization of its manufacturing process and will continue to work on it directly and with the help of its subcontractors. The improved processes will then be transferred to the CMOs for the manufacturing of its products.

TxCell has conducted a first optimization of the manufacturing process after the completion of the Phase I/IIa CATS1 clinical study in order to reduce costs and increase its robustness for the Phase IIb CATS29 clinical study.

The first major change was the elimination of a feeder cell line that was used to grow the Ag-Treg cells in culture. Living material used in a manufacturing process introduces a heterogeneity of batches that is not in line with pharmaceutical quality requirements. The feeder cell line has been replaced by inert and fully controlled pharmaceutical grade materials with the same efficiency of Ag-Treg cell expansion rates. Elimination of the feeder cells also increases the safety of Ag-Treg products, eliminating a drug product impurity already identified as a potential immunogenic contamination for the administered patients during the CATS1 study.

The second major improvement in the Ag-Treg manufacturing process is the optimization of the filling and packaging of Ovasave®. For the CATS1 clinical test, Ovasave® doses were formulated manually in single-dose cryopreservation bags. In order to increase the robustness and reduce the cost of the filling process, a semi-automated filling device is now used to fill vials with Ovasave® doses. Although vials

are rarely used in cell therapy, they are convenient and broadly used in the pharmaceutical industry for injectable drugs.

Characterization studies have been performed on Ag-Tregs to delineate key product attributes in terms of function and gene expression. These key product attributes were used to strengthen the manufacturing process robustness. Moreover, several product characteristics have been implemented in new quality controls of the manufacturing process to allow a better control of process steps, intermediate products and of the final drug product. These new control tests ensure that the products used have all the qualities required for obtaining the desired effects and the right safety profile for patients. For example, a measurement of CD71 expression, a marker of T cell activation is now used in the Phase IIb CATS29 process to control the efficient activation of the patient's cells with ovalbumin. Also, evaluation of the expression of the CD127 marker, a membrane bound molecule not expressed by cells from the Treg cell family, is used in the final identity assay of the drug product for its release to ensure there are no non-Treg cells. Lastly, measurement of Interleukin-13, an anti-inflammatory cytokine produced at high levels by Ag-Treg cells, has been implemented for selection of Ova-Treg cells during the manufacturing process.

The manufacturing process optimized for Ovasave® is mostly the same as for Col-Treg. The only difference is with the antigen that activates patient cells (ovalbumin for Ovasave®, and type II collagen or peptides specific to this type of collagen for Col-Treg). Consequently, for its first clinical test, Col-Treg will benefit from a more advanced production process with a quality level approved for a Phase IIb study.

TxCell intends to make regular improvements to the manufacturing process of the ASTrIA platform in order to obtain a process that can be used in Phase III studies as well as commercial production by 2018. A team from TxCell is working with a subcontractor, Cell & Gene Therapy Catapult Services Limited, to this end with the main short-term objectives below:

- **Cell processing and quality control optimization:**

  TxCell has a strong expertise in regulatory T cell processing, in particular the Type 1 sub-population. New tools were recently implemented to increase the robustness of the manufacturing processes and the in-process and quality controls. Areas of focus are: Ag-Treg characterization for more efficient product selection, increasing expansion rate and purification yields.

- **Formulation and storage:**

  As an important area of work, a formulation allowing product stability at higher temperature (-80°C) would simplify the overall logistics even further. A second goal of the process development is to develop a formulation and packaging for Ag-Treg products that would allow a fast and simplified bedside administration such as for example a pre-filled syringe.

- **Automation and industrialization:**

  This is a major focus for the development of Ovasave®. Automation and overall industrialization are key steps that will allow successful and rapid marketing of Ag-Treg products. Robots are already used for cell handling and cell characterization purposes. With the help of specialized engineering companies, TxCell intends to develop automation and closed systems for the manufacturing process in view of Phase II and the potential commercial launch of Ovasave®.

- **Decrease overall cost and time to manufacture:**

  To ensure the commercial success of its products, TxCell must reduce the time and cost of the manufacturing process. For the Ovasave® Phase IIb, the manufacturing process length is 10-12 weeks. The Company plans to reduce this period to a maximum of 4 to 5 weeks before the beginning of the first Phase III study. This will be done by optimizing the cell processing steps and reducing the time from Ovasave® prescription to intravenous injection into patient to a length that is compliant with medical practices. In terms of cost reduction, process length reduction and automation will contribute massively to the overall reduction of cost. In

addition, a dedicated work on the cost of raw materials (such as cytokines) and quality controls testing should be performed to further decrease the process cost, in particular by identifying alternative sources of supply or by developing new methods. The Company's strategy aims at developing a final process with a gross margin per patient in line with that of existing biologics products such as monoclonal antibodies.

Overall, TxCell's strategy is to secure the Ovasave® manufacturing process before Phase III begins, with improved performance and consistency and with an industrialized, automated, competitive and GMP-compliant process, allowing the simultaneous manufacturing of multiple cell therapy batches in parallel for the Phase III clinical study and the commercial launch of the product, if the clinical tests permit and the necessary authorizations are obtained.

6.5.2 Manufacturing process for the ENTrIA platform

In 2016, TxCell started the development of a production process for its ENTrIA platform, with the objective of being able to start an initial clinical test with its new process in 2018.

Contrary to the regulatory T cells of the ASTrIA platform, the regulatory T cells of the ENTrIA platform have surface markers that facilitate their isolation. Once these cells are isolated, after a sample of the patient's blood has been taken, they are transduced in order to express a specific chimeric antigen receptor (CAR) chosen. The transduction of the specific chimeric antigen receptor will be performed via a viral vector, such as a lentivirus, which carries specific transgenes. This transduction will make it possible to insert genes of interest without significantly altering the viability of the patient's normal Treg cells.

At the end of the transformation, these cells will be amplified in order to produce several hundreds of millions of cells that target the pathology. In a manner analogous to the ASTrIA platform, the amplified cells will then be purified and then formulated in a vial before being frozen.

The development of this new manufacturing process will benefit from the knowledge acquired from the ASTrIA process for certain stages, on the one hand, and from the support provided by the use of the latest technological innovations, on the other.

6.5.3 Manufacturing sites

Until 2015, TxCell carried out production with a rationale of vertical integration. The Company had a manufacturing site in Besançon, France. The site was designed specifically for the production of Ovasave® as part of the CATS29 test, and Col-Treg as part of the first test with a theoretical capacity in the region of 100 patients/year. In September 2013, this production site received accreditation for the production of cellular immunotherapy products from the French National Agency for Drug Safety (*Agence Nationale de Sécurité du Médicament* - ANSM). In June 2014, it received the certificate of compliance with Good Manufacturing Practices (GMP) for the Ag-Treg production process.

Following an ANSM inspection in April 2015, which in particular highlighted a risk of microbial contamination, TxCell was obliged to temporarily shut down a section of this site in June 2015. No contamination has however been raised on any of the products manufactured and released from this site.

In the summer of 2015, given the regulatory and capacity constraints, TxCell decided to shut down the site permanently and, for the years to come, to exclusively use subcontractors for the production of the clinical batches of its drug candidates.

For the European market, TxCell has selected MaSTherCell, a company based in Belgium, as its exclusive subcontractor. A transfer of the manufacturing process was initiated as from September 2015 for Ovasave® and should be achieved in Q2 2016. In February 2016, the most important step of the production transfer was taken: MaSTherCell completed the production of validation batches as defined contractually when the transfer agreement was signed. Validation runs are conducted as a test to demonstrate the capacity of a new manufacturing unit to manufacture products according to specifications.

After the transfer of the Ovasave® manufacturing process to MaSTherCell, the Company may start planning the transfer of the Col-Treg manufacturing process.

In March 2016, TxCell signed an agreement with the PCT Contract Manufacturing Organization (CMO) in the United States. The initial relationship could transition to a technology transfer, and to PCT having responsibility for the future manufacturing of TxCell's clinical supply in the US.

Depending on its resources, TxCell is considering a technology transfer to a CMO in Japan in 2017 or 2018.

6.6 Regulatory environment

In the early 1990s medicinal products development evolved from small molecules to more complex molecules, biologics, which despite significant challenges and hurdles in the beginning, particularly in relation to product characterization and manufacturing, significantly contributed to address some of the major unmet medical needs. Currently, biologics are well established in standard clinical practice and in recent years, the first non-intellectual property protected biosimilars have entered the development phase. Some of these have been approved and have recently been introduced in the market.

More recently similar challenges have been identified for a new group of medicinal products, known as advanced therapy medicinal products (ATMP), comprising somatic cell therapy, gene therapy products, drugs derived from cell or tissue engineering, and novel therapy combined products. ATMP cell therapy products are those that undergo considerable manipulation *in vitro* changing the biological characteristics, physiological functions or structural properties and/or that are not intended to perform the same essential functions for the receiver and the donor.

The technical and regulatory challenges linked to these products (advice, assessment, compliance and marketing authorization) have been recognized by health authorities worldwide, in particular by the US Food and Drug Agency (FDA) and the European Medicines Agency (EMA). In 2007, the European Union decided that it was necessary to publish a specific regulation on ATMPs defining the main rules for their development. European directives have been published, specifying for developers the technical requirements relating to the development of ATMPs. To reinforce its expertise, the EMA has created a Committee for Advanced Therapies (CAT) with the mandate to support, advise and prepare the decisions of the Committee for Medicinal Products for Human Use (CHMP) concerning ATMPs. The CHMP is the committee that assesses and authorizes the marketing authorization request, which is then validated by the European Commission. In the case of ATMPs, the Committee for Advanced Therapies covers technical issues on behalf of the CHMP.

In addition to the scientific advice provided by the CAT concerning market authorization requests, the CAT also assesses the classification as an ATMP and participates in the scientific opinions on ATMPs. The CAT also gives a scientific opinion for certification requests. It assesses and certifies the quality and non-clinical data of ATMP products that small and medium-sized enterprises (SMEs) have generated at all the development stages. This enables the SMEs to identify obstacles to the development of the ATMP and to take the right decisions to ensure compliance with the requirements of the marketing authorization.

The products based on TxCell's ASTrIA platform, being cell therapy products, meet the criteria for classification as ATMPs. Ovasave® and Col-Treg have been formally classified as ATMPs by the CAT.

Regulatory requirements for Ovasave®:

Ovasave® is an autologous somatic cell therapy product. Ovasave® has been assessed by the CAT and classified as an ATMP in January 2010. The pre-clinical and clinical evidence generated with Ovasave® supports the importance of its clinical development in the treatment of Crohn's disease. Ovasave® targets the highest unmet medical need in patients suffering from Crohn's disease.

Since 2004, Ovasave® has been the subject of numerous interactions with the regulatory agencies for matters of process development and manufacturing, pre-clinical results, clinical development and study design as well as the creation of the Clinical Trial Application (CTA) specific to these studies. These interactions have taken place within the framework of the opinion procedure of the EMA's Scientific Committee, a pre-investigational new drug (IND) meeting with the FDA, and clinical test applications to the competent national authorities in Europe.

TxCell's regulatory strategy for the development of Ovasave® is to interact as best as possible with the regulatory agencies to validate the stages and key milestones of the development, to take advantage of the advice given by the regulatory agencies about ATMP development, and to engage the health authorities in order to tailor the development of the products to their expectations, all while raising their awareness to the benefits and challenges that these products represent.

These interactions have contributed to the definition of the pre-clinical program. The scientific opinion relating to Ovasave® production led to changes in the production process and the presentation and validation of the current improved manufacturing process. The scientific opinion also concerned the study design of the clinical development program and provided specific clinical study design suggestions. The suggestions of the EMA and the FDA during the pre-IND meeting held in 2012 (see below) were taken into account in the CATS29 Phase IIb study design. In addition, in view of the process development improvements and the opinion of the agencies received pertaining to the quality aspects of Ovasave®, a request for ATMP certification will be submitted to the CAT in 2017 or 2018.

In July 2015, Ovasave® was granted "Fast Track" designation by the FDA. The Fast Track status is a designation obtained after the FDA has assessed the products developed for severe therapeutic indications for which there is a strong unmet medical need. This status is a procedure that facilitates the development of such products and steps up the examination and review of applications.

TxCell intends to conduct the clinical development of Ovasave® as a priority in Europe and the United States, and later to extend it to Japan, Canada and Asia, if relevant in collaboration with a future partner.

As part of the clinical developments for Crohn's disease, regulatory agencies, in particular the EMA, have clear guidance on the evidence to be generated to support the assessment and eventual market introduction of new products for the treatment of Crohn's disease. These data are based on the induction and maintenance of a therapeutic effect. Induction of remission supplemented by one-year maintenance of effect remains the guideline requirement for regulatory authorities. The FDA also requires, even though in a broader way, similar evidence for induction of response and maintenance of effect for the labeling of CD treatment.

Regulatory requirements for Col-Treg:

Autoimmune uveitis is a chronic, orphan disease with significant unmet medical need.

Col-Treg is an autologous somatic cell therapy product currently being developed for the treatment of autoimmune uveitis. Col-Treg was classified as an Advanced Therapy Medicinal Product (ATMP) by the European Medicines Agency (EMA) in May 2014. After performing the required pre-clinical studies, Col-Treg was granted the status of orphan drug in December 2014 in Europe by the European Commission and by the US FDA in September 2015 for the treatment of non-infectious uveitis.

The EMA has indicated guidance on the generation of evidence to support the use of a product for the treatment of autoimmune uveitis through comparative studies versus an active product (steroid), or in some circumstances versus placebo, mainly through a primary endpoint assessing the vitreous haze in active forms or the rate of recurrences in inactive forms of uveitis. There are multiple additional secondary endpoints like visual acuity, quality of life, fundoscopic assessments and steroid sparing that can be used as supportive complementary evidence in clinical studies.

As with Ovasave®, Col-Treg has been the subject of numerous interactions between TxCell and health authorities, in particular in Europe, to present and obtain their opinion about the quality and pre-clinical aspects relating to the development of Col-Treg.

6.7 Intellectual property

6.7.1 Patents and patent applications

See paragraph 11.2 of the *Document de Référence*.

6.7.2 Freedom to operate searches

The Company has carried out "freedom to operate" type searches to determine whether a particular business activity, such as the licensing, testing or marketing of its products or processes, was feasible without infringing valid third-party intellectual property rights.

In 2007, the Company commissioned the patent and trademark attorneys Plasseraud (France) to perform freedom to operate searches for pharmaceutical compositions containing type-1 regulatory T cells. Searches were performed in respect of published patent applications (PCT, EP, US, FR, GB, DE). One document was identified as being relevant. The results of this study were taken into account and were rigorously followed up in order to monitor the examination procedure for this patent application. This application was abandoned in April 2011.

In 2012, the Company commissioned the patent and trademark attorneys Icosa (France) and Young & Thompson (USA) to perform freedom to operate searches regarding the use, in Europe and the United States, of pharmaceutical compositions containing type-1 regulatory T cells to treat inflammatory bowel disease, in particular Crohn's disease. No document identified was considered relevant and likely to restrict TxCell's freedom to operate and use its pharmaceutical compositions for treating Crohn's disease.

To date, no suit for patent infringement has been filed against TxCell, nor has TxCell filed a suit for patent infringement against any third party. It is the Company's policy to commission freedom to operate searches taking into account the stage of development of its drug candidates. No other full, official, freedom to operate searches have been performed. To the best of its knowledge, the Company has not wrongfully used know-how or privileged information relating to its pharmaceutical technologies in a way likely to lead to a breach of contract or other intellectual property rights. The Company will initiate proceedings against any third-party product or process, whether patented or not, likely to be deemed an infringement, and will do everything possible to protect its intellectual property rights.

6.7.3 Trademarks

See paragraph 11.4 of the *Document de Référence*.

6.7.4 Trade secrets

The inventions developed and owned by the Company are based on its know-how in the field of type-1 regulatory T cells. They involve the use of cell isolation and culture techniques that in some cases make use of only ordinary tools and methods, such as isolation by immuno-affinity or by cell sorting, as well as the culture of T regulatory cells in the presence of growth factors and antibody activators. The Company has developed isolation protocols, culture conditions, and expansion protocols, specific to the products, which constitute proprietary know-how. It may not be desirable to file a patent application (which would be published) for some of these techniques. Procedures to protect the confidentiality of this know-how are in place. Thus, the Company ensures that all researchers and partners must enter into a confidentiality agreement with the Company. In addition, the know-how in question is fragmented among different people in order to optimize the protection of secrets.

7. ORGANIZATIONAL CHART

7.1 Company organization

As at December 31, 2015, the Company has no subsidiaries.

7.2 List of subsidiaries, branches and secondary establishments

TxCell's main place of business and head office are located in Valbonne, at Les Cardoulines – Allée de la Nertière – 06560 Valbonne Sophia Antipolis - France. The Company is registered with the Grasse trade and companies register under number 435 361 209.

TxCell has a second establishment located at Bâtiment IBFC – 6, rue Docteur Jean-François-Xavier Girod – 25000 Besançon – France and registered with the Besançon trade and companies register under number 2013 B 19.

On October 14, 2015, the Company announced the review of its production strategy and its decision to outsource all its current and future production activities, in order to focus on its high value-added activities, namely research, clinical development and strategic partnerships. As a result of this reorganization, the manufacturing site in Besançon was closed. Therefore, the secondary establishment is expected to be removed from the trade and companies register in 2016.

8. REAL ESTATE PROPERTIES, PLANTS AND EQUIPMENTS

8.1 Description of real estate properties

- Head office in Sophia Antipolis

The Company entered into a lease agreement on July 1, 2007 with S.C.P.I. INVESTIPIERRE in respect of premises located in Valbonne – Sophia Antipolis, ZAC des Bouillides, locality Les Cardoulines, consisting of the entire HT1 building (constructed on enclosed private land), for use as the Company's head office. The building has a total surface area of approximately 1,304 m^2, and has 30 outside parking spaces. The premises are rented for mixed use as offices and for company operations. This lease was entered into for a nine-year period (i.e. until June 30, 2016) for an annual rent of €125 thousand net of taxes (adjusted annually according to the national construction costs index).

SCI WENGEN purchased the premises on June 30, 2014. Under the lease contract, the sale of the property by S.C.P.I. INVESTIPIERRE did not lead to the novation of the lease.

On December 22, 2015, the Company entered into an addendum in order to renew the commercial lease with SCI WENGEN for a nine–year period from July 1, 2016 (i.e. until June 30, 2025) for an annual rent of €147 thousand (such amount corresponding to the initial index-linked rent, which is now indexed annually to the service business rental index, "*l'indice des loyers des activités tertiaires*"). The Company can only give an early termination notice every three years, as well as, in exceptional circumstances, at the end of each of the first two years of the renewed lease.

- Development and transfer of manufacturing processes facility in Sophia Antipolis

The Company entered into a lease agreement with SAS Genbiotech, that is an exception under the commercial lease regime (pursuant to article L. 145-5 of the French commercial code), effective February 1, 2016 for premises located at 280, rue de Goa, 06901 Sophia Antipolis. The rented premises, with a surface area of approximately 188 m^2 are for a mixed use as offices, research and development activities and warehousing.

The lease was entered into for a two-year period (i.e. from February 1, 2016 to January 31, 2018) renewable once for a one-year period. The annual rent is €209 thousand net of taxes the first year and €198 thousand net of taxes the second year. This rent is not indexed. In case of early termination of the lease, the Company will continue to be liable to SAS Genbiotech for the remaining rents due from the termination date to the end of the lease with a monthly 5% discount as of January 31, 2017.

- Manufacturing site in Besançon

The Company and the *Etablissement Français du Sang Bourgogne Franche-Comté* ("EFS") entered into a partnership agreement on May 15, 2013 under which the EFS was to provide premises and a certain number of services connected with the manufacturing of products developed by the Company.

The Company and EFS mutually agreed to terminate this partnership agreement with effect on June 30, 2016 following the Company's strategic decision to outsource its existing and future production activities and to close its GMP unit in Besançon. The Company will continue to pay the corresponding rents and service charges up to the termination date. The annual rent (excluding service charges) amounts to €59k, net of taxes.

8.2 Environmental issues

The nature of the Company's activities does not entail any significant risk to the environment.

9. REVIEW OF RESULTS AND FINANCIAL POSITION

This analysis of the results and financial position is based on the financial statements for the financial year ended December 31, 2015 prepared in accordance with IFRS, as adopted by the European Union, the notes to which appear in paragraph 20.1 "Financial information on the issuer's assets/liabilities, financial position and results" of the *Document de Référence*.

9.1 General presentation

9.1.1 Introduction

Created in 2001 through a spin-off from the National Institute of Health and Medical Research (*Institut National de la Santé et de la Recherche Médicale* - INSERM), the Company develops innovative personalized cellular immunotherapy platforms from regulatory T cells for the treatment of chronic and severe autoimmune inflammatory diseases with a high unmet medical need. Each platform may allow the Company to develop several drug candidates.

The first platform developed by the Company, ASTrIA (Antigen-Specific Tregs for Inflammation and Autoimmunity), is a proprietary technology platform for the Company's cellular immunotherapy products consisting of antigen-specific autologous type 1 regulatory T cells (Ag-Tregs).

Ovasave®, the first drug candidate to come from the ASTrIA platform, consists of ovalbumin-specific type 1 Ag-Treg cells and is developed to treat inflammatory bowel diseases. The Phase IIb clinical study, called CATS29, to evaluate the efficacy of Ovasave® in moderate-to-severe Crohn's disease, was launched in December 2014 and continued during the first half of 2015, but had to be momentarily stopped in June 2015 following the Company's decision to interrupt its production activities and to externalize the manufacturing of Ovasave® to MaSTherCell, a Contract Manufacturing Organization ("CMO"). The resumption of CATS29 is subject to approval by European regulatory authorities via the VHP procedure. The Company expects to receive the approval from the European regulatory authorities in Q2 2016. The recruitment of patients for CATS29 study may resume once the Company has received the approval from the European regulatory authorities, once the manufacturing technology transfer to MaSTherCell has been completed, and once the Company has obtained the necessary funds to finance the study.

Col-Treg, the second drug candidate to come from the ASTrIA platform, consists of type II collagen-specific type 1 Treg cells and is developed to treat corticoid-resistant non-infectious uveitis. In 2015, the Company published preclinical efficacy results of Col-Treg in a model of autoimmune uveitis in Investigative Ophthalmology and Visual Science (IOVS), a leading journal in the field of ophthalmic and vision research.

In 2015, alongsides the ASTrIA platform based on antigen-specific type 1 regulatory T lymphocytes (Ag-Tregs), the Company has diversified its technology base by addressing other populations of regulatory T lymphocytes, particularly the so-called FoxP3+ cells. The work on these other lymphocytic populations has been grouped into one platform called ENTrIA (Engineered Tregs for Inflammation and Autoimmunity). Whereas the ASTrlA platform is based on the therapeutic use of pre-existing, non-genetically modified type 1 Treg lymphocytes, the ENTrIA platform offers cellular immunotherapy products based on the use of genetically modified FoxP3+ regulatory cells (CAR-Tregs).

During the financial year 2015, the Company reviewed its production strategy to outsource all its current and future production activities in order to focus on its high value-added activities, namely research, clinical development and strategic partnerships. This reorganization led to the closing of the Besançon production site and to the transfer of the production of Ovasave® to MaSTherCell.

9.1.2 Main factors affecting business and results

In 2015, the Company's revenue was derived solely from the revenues generated by the collaboration, development, option and license agreement with Ferring/Trizell concerning Ovasave®, which the Company terminated on December 2, 2015.

Other income consisted of research tax credits and subsidies received by the Company due to the innovative nature of its business, and the remaining balance as at December 2, 2015 of the deferred income under the collaboration, development, option and license agreement with Ferring/Trizell concerning Ovasave® (see paragraph 9.2.1 below).

The results are, and will continue to be, largely influenced by the amounts allocated to R&D, which to date have been recorded in full as expenses.

9.2 Presentation and analysis of annual financial statements

The financial statements presented and commented in this chapter are the IFRS restated financial statements. The statutory financial statements prepared in accordance with French GAAP for the 2015 financial year are also appended to the *Document de Référence*.

9.2.1 Revenue and other income

In €k	12/31/2015	12/31/2014
Business revenue	920	1,327
Revenue	**920**	**1,327**
Grants	89	58
Research tax credit	3,023	2,035
Other income	605	1
Other income	**3,718**	**2,094**
Revenue and other income	**4,637**	**3,421**

In 2015, the Company's revenue corresponded exclusively to the revenue generated by the collaboration, development, option and license agreement on Ovasave® entered into with Ferring/Trizell between January 1, 2015 and December 2, 2015, the date on which the Company terminated the agreement and took over all the rights to the product.

The revenue breaks down as follows, up to December 2, 2015:

- €719 thousand in revenue related to the financing by Trizell of the initial phases of the process and manufacturing development of Ovasave® for the Company's future Phase III clinical study and commercialization;
- €201 thousand in revenue relating to the payment of €1,000 thousand received upon signature of the collaboration, development, option and license agreement on Ovasave® entered into with Ferring/Trizell, and amortized over the estimated duration of the involvement of the Company in future developments of the object of the agreement.

The balance remaining as at December 2, 2015 of the deferred income under the collaboration, development, option and license agreement was recognized as other income in the amount of €605 thousand.

Other income mainly comprises:

- grants in the amount of €89 thousand;
- a 2015 research tax credit receivable of €3,023 thousand, compared to €2,035 thousand as at December 31, 2014;
- other income, corresponding to the balance of deferred income as at December 2, 2015 under the collaboration, development, option and license agreement on Ovasave® entered into with Trizell, in the amount of €605 thousand.

The Company considers it operates in a single aggregate segment: the conduct of research and development for pharmaceutical products with a view to future commercialization.

Furthermore, the totality of the Company's research and development activity is located in France. All the Company's tangible assets are located in France. For these reasons the Company's management does not believe it appropriate to break its activity into separate business geographies.

9.2.2 Operating expense by function and operational result

9.2.2.1 Cost of sales

As the Company is still in the research and development phase, the purchases necessary to the manufacture of its products are considered as research and development costs, therefore they do not figure in the cost of sales.

Raw materials costs are mainly denominated in euros. The risks applicable to purchases associated with foreign exchange rates applicable to purchases are therefore considered as insignificant (see Note 25.2 in paragraph 20.1 of the *Document de Référence*).

9.2.2.2 Research and development costs

The Company carries out research and development activities in order to develop treatments for chronic and severe inflammatory and autoimmune diseases.

Research costs are recorded as expenses. In accordance with IAS 38, development costs are recorded as intangible assets if all of the following criteria are met:

a) the technical feasibility study required to complete the development project is done;

b) the Company intends to complete the project and launch it;

c) ability to put the intangible asset into service;

d) demonstration of the probability of future economic benefits associated with the asset;

e) availability of adequate technical, financial and other resources to complete the project; and

f) reliable assessment of development expenditure.

Pursuant to this standard, to date the Company has not capitalized research and development costs. All development costs have therefore been recorded as expenses.

Spending on research and development over the past two financial years is as follows:

In thousands of euros	12/31/2015	12/31/2014
Purchase of raw materials	1,942	2,199
Scientific fees, studies and other expenses	5,097	2,163
Salaries and social security expenses	3,666	3,068
Depreciation, amortization and provisions	153	398
Retirement benefits	(19)	9
Total research and development expenses	**10,839**	**7,836**

The 11.7% decrease in raw material purchases in 2015 versus 2014 is due to the shutdown of the production activities at the Besançon site as at June 2015, despite the increase in raw materials purchases during the first half of 2015 as part of the Ovasave® Phase IIb clinical study launched in December 2014.

The 135.6% increase in studies, scientific fees and other expenses in 2015 versus 2014 was mainly due to:

- the recognition of the advancement of subcontracting contracts with the CROs (Contract Research Organizations) for the Phase IIb clinical study of Ovasave® launched in December 2014;

- the costs related to the development and industrialization program for the manufacturing process of the products from the ASTrIA platform. Furthermore, most of these costs were re-invoiced under the collaboration, development, option and license agreement entered into with Trizell concerning Ovasave® and recognized as revenue (see Note 2.13 of paragraph 20.1 of the *Document de Référence)*;
- the costs related to the technology transfer to MaSTherCell, the CMO (Contract Manufacturing Organization) for producing Ovasave® in Europe, launched in September 2015;
- the costs related to the ENTrIA research program, the second platform of products of the Company based on modified regulatory T cells.

The 19.5% increase in salaries and social security expenses in 2015 versus 2014 was mainly due to the reinforcement of the management team and by an increase in the annual average headcount following the launch of the Phase IIb clinical study of Ovasave®.

The 61.6% decrease in amortization, depreciation and provision expenses in 2015 versus 2014 was mainly due to the reversal in 2015 of the provisions for risks related to subsidies, which amounted to €313 thousand as at December 31, 2014.

The decrease in retirement benefits in 2015 versus 2014 was mainly due to the adjustments as at December 31, 2015 for the change in headcount as part of the closing of the Besançon site.

9.2.2.3 Sales, distribution and marketing expenses

As its products are at the research and development stage, the Company has not incurred any sales, distribution and marketing expenses over the last two financial years.

9.2.2.4 General and administrative expenses

General and administrative expenses over the past two financial years are as follows:

In thousands of euros	12/31/2015	12/31/2014
Rent, fees and other expenses	2,158	1,232
Salaries and social security expenses	1,249	959
Depreciation, amortization and provisions	55	52
Retirement benefits	(2)	1
Total general and administrative expenses	**3,460**	**2,243**

The 75.2% increase in rents, fees and other expenses in 2015 versus 2014 is mainly due to:

- the increase in investor relations and communication expenses after the Company's stock-market listing in April 2014;
- recruitment fees related to the changes made to the executive team and the reinforcement of the management team; and
- the increase in legal fees for contract matters.

The increase in salaries and social security expenses is mainly due to the changes made to the executive team.

9.2.2.1 Other operating income and expense

Other operating income and expenses correspond to the cost of restructuring the Company's activities as part of the closing of the Besançon site. They total -€1,167 thousand and break down as follows:

- -€820 thousand for the costs related to the Employment Protection Plan (redundancy costs and accompanying measures, outplacement costs, fees);
- -€151 thousand for the costs related to closing the site (termination indemnities and expenses remaining due after the closure of the site);

- -€196 thousand for the depreciation expenses of the fixtures and fittings at Besançon specifically related to the prospective adjustment of the depreciation plans for the closure of the site, for the impairment of the site's laboratory equipment and furniture recognized at their liquidation value, and for the capital gains and losses made in 2015 on the sale of capital assets of the Besançon site.

9.2.3 Composition of net earnings

9.2.3.1 Financial income and expense

Financial income and expense (in thousands of euros)	12/31/2015	12/31/2014
Foreign exchange gains	10	1
Other financial income	(0)	0
Sub-total other financial income	**10**	**1**
Gains on cash and cash equivalents	1	10
Interest on cash and cash equivalents	41	58
Sub-total income from cash and cash equivalents	**42**	**68**
Total financial income	**52**	**69**
Contractual interest on bonds	0	(60)
Sub-total cost of gross financial debt	**0**	**(60)**
Foreign exchange losses	(20)	(5)
Other financial expense	(17)	0
Sub-total other financial expense	**(37)**	**(5)**
Total financial expense	**(37)**	**(65)**
Total financial income and expense	**15**	**4**

Income from cash and cash equivalents corresponds to accrued interest and short-term gains on investment securities.

Other financial expenses comprise the accretion of the financial flows for the zero-interest innovation loan (*Prêt à Taux Zéro innovation*) and for the payables on non-current assets (see Notes 11 and 14.2 of paragraph 20.1 of the *Document de Référence*).

The Company only uses financial instruments recorded as cash and cash equivalents. These instruments are used to finance the Company's activities. It is the Company's policy not to use financial instruments for speculative purposes. The Company does not use derivative financial instruments.

The Company's exposure to interest rate risk relates primarily to cash equivalents and securities. These consist of open-ended money market funds (*SICAV monétaires*) and negotiable medium-term notes (*Bons à Moyen Terme Négociables*).

As at December 31, 2015, the Company had not taken out any loans with credit institutions, exception for the zero-interest innovation loan from Bpifrance Financement, and is therefore only marginally exposed to interest rate risk (see Note 25.4 of paragraph 20.1 of the *Document de Référence*).

9.2.3.2 Corporation tax

The Company has not recorded any corporation tax expense since its formation.

As at 31 December 2015, the Company had tax losses which can be carried forward indefinitely in France for a total amount of €67.6 million.

The booking of this loss is capped at €1 million plus 50% of the amount of taxable profit for the year in excess of €1 million. The unused balance of losses may be carried forward to the following financial years, and can be booked under the same conditions with no time limit.

9.2.3.3 Basic earnings per share

The basic earnings per share is calculated by dividing the net profit attributable to the shareholders of the Company by the weighted average number of shares outstanding during the financial year.

The shareholders' meeting held on March 7, 2014 decided the reverse stock split at a ratio of five old shares for one new share. In accordance with IAS 33 "Earnings per share", the net earnings and the diluted earnings per share are presented with a retrospective adjustment of the reverse stock split over the periods reported so as to allow comparability.

Net earnings par share	12/31/2015	12/31/2014
Net income / (loss) (in thousands of euros)	(11,297)	(8,269)
Weighted average number of shares in circulation	12,289,456	10,560,913
Basic earnings par share (in euros)	**-0.92**	**-0.78**

Diluted earnings per share are calculated by dividing the net profit (loss) attributable to the Company's shareholders by the following sum:

- the weighted average number of shares outstanding during the financial year;
- plus the number of shares that may result from the conversion of instruments giving deferred access to the share capital, as soon as such instruments have been issued.

The instruments giving deferred access to the share capital (warrants and stock options) are considered to be anti-dilutive as they result in higher earnings per share. As a result, diluted and basic earnings per share are identical.

Diluted earnings per share	12/31/2015	12/31/2014
Net income / (loss) (in thousands of euros)	(11,297)	(8,269)
Weighted average number of potential shares*	13,760,045	11,757,317

** This weighted average number of potential shares takes into account the shares which could result from exercising the warrants and stock options, as soon as such instruments are issued.*

9.3 Presentation and analysis of the statement of financial position

9.3.1 Non-current assets

In €k	12/31/2015	12/31/2014
Intangible assets	5,907	8
Property, plant and equipment	876	1,404
Financial assets	155	131
Total non-current assets	**6,939**	**1,543**

The costs of research and development and of patent registration have so far been entirely recorded as expenses (see Note 2.3 of paragraph 20.1 of the *Document de Référence*).

On December 2, 2015, the Company and Trizell concluded an agreement terminating their collaboration, development, option and license agreement on Ovasave®. Under this agreement the Company recovered all of Trizell's rights over Ovasave® in return for paying amounts which could reach €15 million, €6 million of which is fixed and €9 million of which is conditional upon the future revenues generated by Ovasave®. In 2015, the acquisition costs, i.e. €6 million, for these rights, the amount and maturity of which can be fixed definitely, were recognized as an asset. These acquisition costs were discounted in accordance with IAS 38. The 10-year French Government bond rate (*taux OAT*) as at December 31, 2015 of 0.995% was used as the discount rate. The repurchase of these rights after discounting therefore

totaled €5.9 million. This intangible asset is recognized as in progress insofar as it has not satisfied the conditions for being put into service.

Property, plant and equipment consist mainly of fixtures and fittings, technical plant, machinery and equipment, furniture, and office and IT equipment. The net value was €876 thousand as at December 31, 2015 versus €1,404 thousand at December 31, 2014. The 37.6% decrease in net property, plant and equipment resulted primarily from the disposals of laboratory equipment in 2015 as part of the closing of the Besançon site, as well as impairments of Besançon laboratory equipment and furniture recognized at their liquidation value.

Non-current financial assets consist mainly of:

- €45 thousand of security deposits (including €37 thousand relating to the commercial lease of the Valbonne premises). Because the Valbonne security deposit is indexed to the rent, any rent increase automatically leads to an increase in this item;
- a €5 thousand tax free construction loan in 2011;
- the cash balance of the liquidity contract taken out with ODDO Corporate Finance for €105 thousand. Under this liquidity contract, 16,280 treasury shares were recognized as a reduction in shareholders' equity at December 31, 2015 compared to 16,637 shares at December 31, 2014.

9.3.2 Current assets

In €k	12/31/2015	12/31/2014
Trade receivables	4	1,000
Other current assets	4,570	3,583
Cash and cash equivalents	9,208	13,917
Total current assets	**13,781**	**18,501**

Since the Company's operations exclusively involve research and development programs, the purchases relating to its operation are charged as expenses and have no impact on inventories or work in progress.

Trade receivables at December 31, 2014 were collected in January 2015. These receivables of €1 million reflected the invoice of the second installment of the Ferring/Trizell partnership agreement.

Other current assets include:

- a receivable for the immediate payment of the 2015 research tax credit (*CIR*) in the amount of €3,023 thousand, compared to €2,035 thousand in 2014. It should be noted that during the financial year 2015 the tax authorities audited the Company with respect to the 2011 to 2014 research tax credits, and this did not lead to any adjustment;
- VAT credits pending reimbursement of €139 thousand for October, November, and December 2015;
- prepaid expenses regarding operating expenses and more specifically the staggering of the advance for subcontracting with the CRO (Contract Research Organization), including €606 thousand for SGS, the main CRO for the clinical trial of Phase IIb of Ovasave®.

Cash and cash equivalents consist of immediately available cash and short-term available-for-sale securities. The increase in this item is detailed in paragraph 10.1 of the *Document de Référence*.

9.3.3 Equity

In €k	12/31/2015	12/31/2014
Share capital	2,577	2,333
Issue premiums	29,885	21,993
Reserves	(9,576)	(1,344)
Net profit / (loss) for the year	(11,297)	(8,269)
Total shareholders' equity	**11,589**	**14,712**

As at December 31, 2015, the share capital was €2,577,465.20. It is divided into 12,887,326 shares, subscribed and fully paid up, with a par value of €0.20.

This amount excludes share warrants and stock options granted to executives and employees, which have not yet been exercised.

9.3.4 Non-current liabilities

In €k	12/31/2015	12/31/2014
Portion of long and medium-term financial payables maturing over one year	1,641	1,627
Other non-current liabilities	23	363
Total non-current liabilities	**1,664**	**1,990**

In 2014, the Company obtained a zero-interest innovation loan (*Prêt à Taux Zéro innovation*) from Bpifrance Financement in the gross amount of €1.7 million, received in December 2014. This sum was paid within the scope of the Phase IIb clinical trial for Ovasave® which started in December 2014. The repayments of the zero-interest innovation loan were discounted to the reporting date (see Note 11.1 of paragraph 20.1 of the *Document de Référence*).

Other non-current liabilities total €23 thousand, and correspond to the over-one-year portion of the staggering of the zero-interest innovation loan grant.

9.3.5 Current liabilities

In €k	12/31/2015	12/31/2014
Trade and other payables	1,608	1,395
Other current liabilities	5,087	1,554
Current provisions	772	392
Total current liabilities	**7,467**	**3,341**

As at December 31, 2015 provisions recognized for risks related to subsidies of €313 thousand were completely reversed based on estimates made by the Company.

The provisions for expenses as at December 31, 2015 correspond to:

- a retirement benefits provision of €21 thousand, compared to €80 thousand at December 31, 2014;
- a restructuring provision of €750 thousand, corresponding to the expected costs of closing the Besançon site in 2016.

Other current liabilities primarily comprise the balance in supplier payables on non-current assets of €3.9 million for the purchase of Trizell's rights to Ovasave®. When the termination agreement was signed on December 2, 2015, €2 million of the original debt of €6 million had been repaid. Of the

balance, €2 million is due on December 2, 2017 and €2 million on December 2, 2018, for a total of €3.9 million when present discounted (see Note 3 of paragraph 20.1 of the *Document de Référence*).

10. LIQUIDITY AND CAPITAL RESOURCES

See also Notes 9 and 10 to the financial statements prepared in accordance with IFRS, in paragraph 20.1 of the *Document de Référence*.

10.1 Information on equity, liquidity and sources of funding

As at December 31, 2015, cash and cash equivalents held by the Company were €9.2 million versus €13.9 million as at December 31, 2014. Cash and cash equivalents include cash and short-term financial instruments held by the Company, which consist of open-ended money market funds (*SICAV monétaire*) and negotiable medium-term notes (*Bons à Moyen Terme Négociables*). This cash and these marketable securities are used to finance the Company's activities.

Since its creation, the Company has financed its growth by strengthening its equity capital through successive capital increases, and by obtaining public grants for innovation and research tax credit payments.

The breakdown of net financial debt is as follows:

In thousands of euros	12/31/2015	12/31/2014
Short-term bank deposits	3,201	263
Open-ended money market funds (SICAV)	6,007	13,654
Total cash and cash equivalents	**9,208**	**13,917**
Current financial liabilities	0	0
Non-current financial liabilities	(1,641)	(1,627)
Total financial debt	**(1,641)**	**(1,627)**
Net financial cash / (debt)	**7,567**	**12,290**

10.1.1 Equity financing

The table below summarizes the capital increases by value until December 31, 2015.

Period	Gross amount raised (in millions of euros)	Operations
2001-2004	0.3	Incorporation of the Company and fundraising from the founders, minority shareholders and INSERM
2004-2007	10.6	Successive share issues marking equity investments by financial investors in 2004 (Auriga Partners, Seventure, CDC Entreprises, CDC Innovation and AXA Private Equity) for €10.5 million and the raising of €0.1 million from minority shareholders and INSERM
2008-2009	10.0	Successive share issues (Auriga Partners, Seventure, CDC Entreprises, CDC Innovation and AXA Private Equity) whose second tranche was only 87% subscribed, that is, €9.8 million, and the raising of €0.2 million from minority shareholders
2010	3.5	Funds raised from existing financial investors (Auriga Partners, Seventure andt CDC Entreprises)
2012-2013	12.4	Conversion of the bonds issued in 2011 and 2012 (see Note 5.11.2 of paragraph 20.1) for a total of €2.9 million, share issue for a total amount of €6.5 million (Auriga Partners, Seventure et CDC Entreprises) in 2012 and exercise of BSA Tranche 2 warrants for a total amount of €3 million in 2013
2014	21.2	Issue and conversion of €3.5 million bond; Initial public offering for €16.2 million gross; Additional equity round of €1.5 million gross.
2015	7.9	Funds raised by private placement of €7.9 million gross from mostly internationaland healthcare investors.
Total	**65.9**	

10.1.2 Government grants for innovation

The Company receives or has received a variety of grants and subsidies to finance some of its projects and accelerate its development.

In 2015, France's Joint Inter-Ministerial Fund (*Fonds Unique Interministériel*, FUI) awarded a subsidy of €1.3 million to the TRUST project (TRegs in Uveitis STudy), overseen by a consortium led by the Company and dedicated to the process development and clinical development of Col-Treg, the Company's second drug candidate for the treatment of autoimmune uveitis. The portion of the subsidy granted to the Company amounts to €0.8 million. No payment was received in 2015 in connection with this subsidy.

The Company did not receive significant cash in 2015 in connection with government grants for innovation.

10.1.3 Financing from research tax credits

The Company has received research tax credits since its incorporation.

The 2014 research tax credit was received on December 31, 2015 in the amount of €2,035 thousand.

The 2015 research tax credit receivable was €3,023 thousand and is expected to be paid in 2016.

10.1.4 Debt financing

The Company did not contract any bank loans for its financing. During the financial year 2014 the Company obtained a zero-interest innovation loan (*Prêt à Taux Zéro Innovation*) of €1.7 million gross as part of the clinical development of the product Ovasave®. This loan is repayable over eight years, with a repayment deferral of three years.

The repayments on the zero-interest innovation loan (*Prêt à Taux Zéro Innovation*) were discounted to the reporting date. The discounted value is treated as a subsidy within the meaning of IAS 20 and amortized on a straight line basis over the duration of the project to which the advance is attached (see Note 11 of paragraph 20.1 of the *Document de Référence*).

The following table shows the simplified schedule of repayments as at December 31, 2015 after discounting the liability.

In thousands of euros	Gross amount	One year at most	Over one year and 5 years at most	Over 5 years
Zero-interest innovation loan	1,641	0	1,156	485
Total loans and financial payables	**1,641**	**0**	**1,156**	**485**

10.1.5 Off-balance sheet commitments

Off-balance sheet commitments are described in Note 21 of paragraph 20.1 of the *Document de Référence*.

10.2 Cash flows

The cash flow statement for the past two financial years is as follows:

In €k	12/31/2015	12/31/2014
Net income / (loss)	**(11,297)**	**(8,269)**
Elimination of items with no impact on cash and cash equivalents		
Elimination of depreciation, amortization and provisions	1,135	460
Share-based payment	483	1,615
Financial expenses arising from bonds		60
Other eliminations with no impact on cash and cash equivalents	(7)	(13)
OPERATING CASH FLOW	(9,687)	(6,148)
Change - non-current	**(313)**	**(362)**
Other eliminations of non-current items with no impact on cash and cash equivaler	27	(70)
Change in other non-current liabilities	(340)	(292)
Change - current	**(66)**	**(423)**
Change in trade receivables	997	
Change in other current assets	(987)	(1,367)
Change in trade payables	213	577
Change in other current liabilities (excluding fixed asset suppliers)	(288)	368
CHANGE IN WORKING CAPITAL REQUIREMENTS	(379)	(785)
Net cash from operating activities	(10,066)	(6,933)
Acquisition of intangible assets	(5,902)	(8)
Sale of intangible assets		
Change in intangible assets supplier account	3,905	
Other eliminations of intangible items with no impact on cash and cash equivalents	(3)	
Acquisition of property, plant and equipment	(214)	(582)
Sale of property, plant and equipment	23	17
Change in property, plant and equipment supplier account	(83)	
Acquisition of non-current financial assets	(3)	(84)
Sale of non-current financial assets	3	2
Net cash from investing activities	(2,274)	(656)
Capital increases or contributions	7,631	15,691
Receipts from loans		5,200
Interest on bonds		(60)
Loan repayments		(1)
Net cash from financing activities	7,631	20,830
NET CASH FLOWS	(4,710)	13,242
OPENING CASH	13,917	676
CLOSING CASH	9,208	13,917

10.2.1 Cash flows from operating activities

Cash used in operating activities for the financial years ended December 31, 2015 and December 31, 2014 amounted to respectively €10,066 thousand and €6,933 thousand.

The net cash flows from operating activities relate primarily to:

- the net loss of €11,297 thousand in 2015, which increased mainly due to:

- the recognition of the advancement of subcontracting contracts with the CROs (Contract Research Organizations) for the Phase IIb clinical study of Ovasave® launched in December 2014;
- the costs related to the development and industrialization program for the manufacturing process for products for the ASTrIA platform. Most of these costs were re-invoiced under the collaboration, development, option and license agreement and recognized in revenue (see Note 2.13 of paragraph 20.1 of the *Document de Référence;*
- the costs related to the technology transfer to MaSTherCell, the CMO (*Contract Manufacturing Organization*) for producing Ovasave®, launched in September 2015;
- the costs related to the ENTrIA research program, the second platform of products of the Company based on modified regulatory T cells.

- Other non-cash items restated in net income:
  - depreciation, amortization and provision expenses for 2015 in the amount of €1,135 thousand, including provisions for reorganization of €750 thousand in connection with the closing of the Besançon site;
  - the expense for share-based payments as per IFRS 2 of €483 thousand in 2015.
- The change in working capital requirements, which resulted primarily from:
  - the increase in other current assets, notably the 2015 research tax credit receivable of €3,023 thousand versus a 2014 research tax credit receivable of €2,035 thousand;
  - the decrease in other non-current liabilities, due to the remaining deferred income at December 31, 2014 recognized as profit or loss for 2015 (see Note 15 of paragraph 20.1 of the *Document de Référence*);
  - the decrease in trade receivables, for which the balance as at December 31, 2014 was received in January 2015.

10.2.2 Cash flows from investing activities

Cash flows used in investing activities amounted, for the years ended December 31, 2015 and 2014, to respectively €2,274 thousand and €656 thousand.

The period ended December 31, 2015 included €2 million of net cash flow from investment in intangible assets. This amount corresponds to the first payment made to Trizell on signing the agreement terminating the collaboration, development, option and license agreement dated December 2, 2015.

For the financial year 2015 capital expenditures mainly involved purchasing of laboratory equipment as part of the program to develop and industrialize the Ovasave® production process. In 2014 capital spending was mainly for the purchase of laboratory equipment necessary to conduct the Phase IIb clinical study.

10.2.3 Cash flows from financing activities

Cash flows for financing activities were €7.6 million as at December 31, 2015 after allocating the costs of the capital increase and reflect the exercise in 2015 of 58,011 stock options for a gross total amount of €0.3 million and the proceeds of the private placement undertaken in July 2015 in the gross amount of €7.9 million. The costs of the capital increase amounted to €0.7 million.

10.3 Information on borrowing terms and the funding structure

See Note 11 of the notes to the financial statements prepared in accordance with IFRS, in paragraph 20.1 of the *Document de Référence*.

10.4 Restriction on the use of capital

None.

10.5 Future sources of financing required

Since its creation, the Company has financed its growth by strengthening its equity capital through successive capital increases, and by obtaining public grants for innovation and research tax credit payments.

As at March 31, 2016, the Company's cash and cash equivalents amounted to €5 million. This amount takes into account the €2 million paid to Trizell on December 11, 2015 on signing the agreement to terminate the exclusive licensing and distribution of Ovasave® and includes the €2 million received on December 31, 2015 due to the 2014 research tax credit. However, the amount does not include the 2015 research tax credit of €3 million expected by the end of the first half 2016.

Given the contemplated development plan and the operational expenses of the first quarter 2016, the Company's cash available on March 31, 2016, supplemented by the 2015 CIR to be received, will enable the Company to continue its activities until the end of July 2016. Additional financial resources will therefore be necessary.

The Company has an optional line of equity financing signed with Société Générale in December 2015 involving 1,150,000 new shares issuable over a 24-month period through the exercise of stock warrants. As at the date of the *Document de Référence*, this line of financing had not been drawn down.

The Company expects to find other sources of financing for its working capital requirement over the next 12 months, in particular through new capital increases or by signing strategic partnerships, to pursue its development plan. Otherwise, it could defer expenditure for certain programs.

In the future, the Company will continue to have substantial financing requirements for developing its technology, continuing its clinical development programs, equipping its R&D facilities and, eventually, producing and marketing its products.

11. RESEARCH AND DEVELOPMENT, PATENTS, LICENSES, TRADE NAMES AND DOMAIN NAMES

11.1 Innovation policy

The Company carries out its work in the "biotech" field (therapeutic research), where it focuses its innovation policy.

Since its creation, the vast majority of Company resources have been devoted to research and development ("R&D") permitting it to have its own products platform, called ASTrIA (Antigen-Specific Tregs for Inflammation and Autoimmunity*)*, which offers a novel approach to customized cellular immunotherapy and a program of clinical trials for the treatment of Crohn's disease and other inflammatory pathologies, such as autoimmune uveitis. The candidate products which the Company has developed with this platform are suspensions of competent regulator type 1 Treg cells (Ag-Treg), generated ex-vivo from the patient's blood.

In addition to its ASTrIA platform, the Company is developing a second platform of products called ENTrIA (Engineered Tregs for Inflammation and Autoimmunity*)* based on redirected Chimeric Antigen Receptor engineered regulatory T lymphocytes (CAR-Treg) and their use for the treatment of autoimmune and inflammatory pathologies. This new platform is in line with the Company's goal of developing a new products able to deliver their immunomodulant action independently of the antigenic presentation via the molecules of the major histocompatibility complex ("MHC") and to express, on their surface, chimeric antigenic receptors ("CAR").

The inventions developed and owned by the Company are based on its know-how in the field of type-1 regulatory T cells. They involve the use of cell isolation and culture techniques that in some cases make use of only ordinary tools and methods, such as isolation by immuno-affinity or by cell sorting, as well as the culture of T regulatory cells in the presence of growth factors and antibody activators. The Company has developed isolation protocols, culture conditions, and expansion protocols, specific to the products, which constitute proprietary know-how. It may not be desirable to file a patent application (which would be published) for some of these techniques. Procedures to protect the confidentiality of this know-how are in place. Thus, the Company ensures that all researchers and partners must enter into a confidentiality agreement with the Company. In addition, the know-how in question is fragmented among different people in order to optimize the protection of secrets.

In the years to come, the Company will continue its R&D work on the protocol of identifying, obtaining and expanding regulatory T cells, as well as on the mechanisms of action in order to broaden the scope of its industrial property portfolio.

Before marketing authorizations are granted, the Company writes off R&D costs in compliance with existing accounting rules (IAS 38). These expenses mainly comprise salaries and fees paid to partners working on R&D for the Company

11.2 Patents and patent applications

11.2.1 Policy of protection of intellectual property

The Company considers that patents, patent applications and other intellectual property rights are of crucial importance in the Company's sector of activity. The Company conducts case-by-case examinations of the necessity of submitting patent applications to protect certain technical processes, innovative candidate products and certain medical treatment methods. It can also be authorized to use rights (under the terms of the license agreement) or acquire rights over patents, patent applications or other intellectual property rights which are of interest to it and/or its sectors of activity such as the Treg cells sector or the sector for treating inflammatory diseases, which belong to third parties, partner universities or commercial companies.

The Company has had a policy of protection of intellectual property since 2007 under which any research result is examined by the innovation department from the patentability and innovation point of

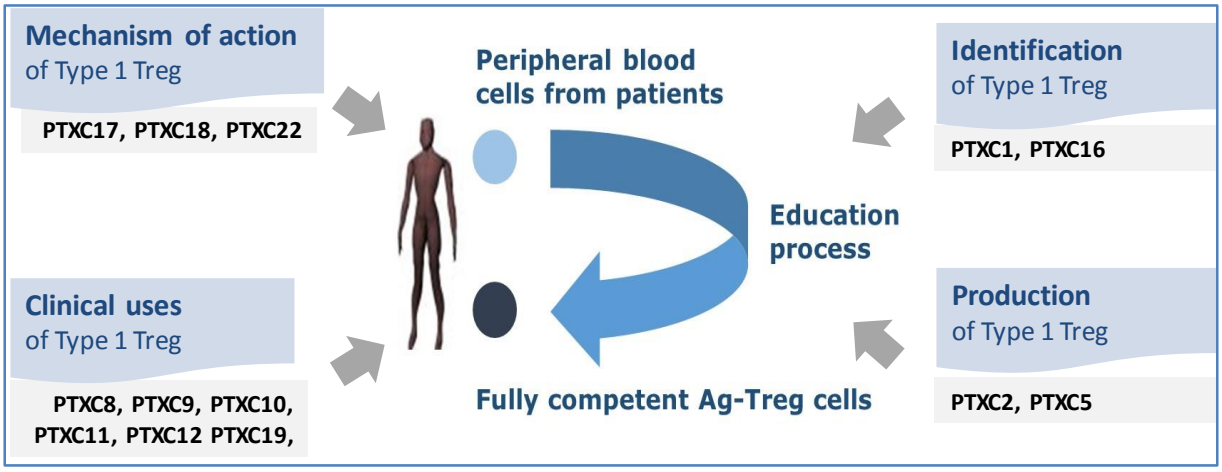
view, in partnership with a firm of industrial intellectual property lawyers, to determine the benefit or otherwise of a patent application to protect this result.

Other than the exclusive licensing rights to intellectual property resulting from its work with the INSERM, pursuant to the license agreement provisions described in paragraph 11.3, the Company has decided to protect its basic technologies and candidate products by numerous patent applications, while looking to protect some of its key products used for the production of cells and in proprietary research programs by placing them in the category of exclusive know-how. The Company has significantly improved its portfolio (see table 11.2.3) since its industrial property protection policy was set up.

The Company's portfolio of patents, patent applications, trademarks and trademark applications are managed in-house with the help of outside intellectual property lawyers.

As at the date of the *Document de Référence*, the portfolio of patents and patent applications of which the Company is the owner, co-owner or exclusive licensee comprises 13 families of patents and patent applications and more than 125 registered patents, which can be divided into four distinct fields, as stated below:

- "Production" field: PTXC2 and PTXC5 families concerning production processes of type 1 regulatory T cells;
- "Identification" field: PTXC1 and PTXC16 families concerning cell markers of type 1 regulatory T cells;
- "Clinical use" field: PTXC8, PTXC9, PTXC10, PTXC11, PTXC12 and PTXC19 families concerning the clinical use of type 1 regulatory T cells; and
- "Mechanism of action" field: PTXC17, PTXC18 and PTXC22 families concerning the mechanism of action of type 1 regulatory T cells.



11.2.2 Ownership of rights over patents and patent applications comprising the Company's portfolio

Patents and patent applications of the PTXC1 and PTXC5 families have resulted from work with the INSERM and are jointly owned with this research institute.

The family of PTXC2 patents has been filed in the INSERM's name alone. The Company is the holder of an exclusive worldwide license, dated January 30, 2006, over all the patents in this family.

Patents or patent applications of the PTXC11 family have resulted from work with the University of Montpellier and the Regional University Hospital Center of Montpellier, and are jointly owned with these bodies.

The other nine patent families of the portfolio have been deposited in the Company's name alone.

11.2.3 Nature and scope of patents

Through its development, the Company is continuing to create new technological inventions and to protect these innovations by filing new patent applications in Europe and in many countries abroad. The Company regularly assesses its portfolio of patents to ensure that the Company's projects are protected in the best possible way and to continue a policy of abandoning patents and patent applications so that no resources are allotted to patent applications and patents which no longer protect the Company's products or processes.

11.2.3.1 "Production" field:

This field comprises two families of patents dealing with production processes of type 1 regulatory T cells.

The PTXC2 family (WO2002/092793*)* entitled *"Method for obtaining antigen-specific Tr1 regulatory lymphocytes",* describes a method for preparing antigen-specific Tr1 regulatory lymphocytes. The inventive method involves the use of artificial antigen-presenting cells, expressing a molecule from the HLA class II system and a human LFA-3 molecule and expressing none of the B7-1, B7-2, B7-H1, CD40, CD23 or ICAM-1 co-stimulation molecules.

The PTXC5 family (WO2007/010406) entitled "*Obtention of food or auto-antigen specific Tr1 cells from a leukocyte or PBMC population"* deals with a method for obtaining type 1 regulatory T cells *in vitro* that are specific to one dietary allergen or an auto-antigen. This method enables the production of type 1 Treg cells specific to an antigen selected for the pathology to treat. This is the method currently used for the ASTrIA platform.

Family	Applicant	Priority date* [1]	Expiry date* [2]	Status* [3]
Production method				
PTXC2	INSERM	05/11/2001	2022	**Granted** in Europe (and validated in the following countries: Belgium, Switzerland, Germany, Denmark, Spain, Finland, France, England, Ireland, Italy, the Netherlands, Sweden), the United States, Japan and Canada
PTXC5	TXCELL INSERM	07/01/2005	2026	**Granted** in Europe (and validated in the following countries: Austria, Belgium, Bulgaria, Switzerland, Cyprus, Czechoslovakia, Germany, Denmark, Estonia, Spain, Finland, France, Greece, Hungary, England, Ireland, Iceland, Italy, Lithuania, Luxembourg, Latvia, Monaco, the Netherlands, Poland, Portugal, Romania, Sweden, Slovenia, Slovakia, Turkey), the United States, Japan and Australia

* Terms defined below are used in this table and subsequent tables in this section

[1] The patent's priority date is the date on which the first filing was made. Subject to being granted, patents are granted for a period of 20 years from their respective filing dates (i.e. the date of filing of the corresponding national, European or international application, it being noted that European patent applications and international patent applications must be made within a period of 12 months following the filing date of the priority patent application), it being noted that when products are registered (i.e. marketing authorizations have been obtained) the patent protection period can be prolonged by 6 months to 5 years, at most, depending on the case.

[2] The expiration date corresponds to the 20 years running from the date the granted patent was filed. This expiry date can be prolonged by obtaining an extension to the patent's term in the United States, for example, or by obtaining an additional patent certificate.

[3] Being examined: the patent application is currently being examined by the Patents Offices.
Notification of grant: the Patents Offices have given notice that they intend to grant a patent.
Granted: patent granted after examination of the company's application in a country/region by the competent authority in that country/region

				Notification of grant in Europe (Austria, Belgium, Bulgaria, Switzerland, Cyprus, Czechoslovakia, Germany, Denmark, Estonia, Spain, Finland, France, England, Greece, Hungary, Ireland, Iceland, Italy, Lichtenstein, Lithuania, Luxembourg, Latvia, Monaco, the Netherlands, Poland, Portugal, Romania, Sweden, Slovenia, Slovakia, Turkey) and Canada

11.2.3.2 "Identification" field:

This field comprises two patent families concerning specific surface markers of type 1 regulatory T cells, and the use of these markers for the identification and isolation of type 1 regulatory T cells.

The PTXC1 family (WO2005/000344*)* entitled *"Method for identification of Tr1 lymphocytes regulators by the presence and over expression of specific molecules and application thereof"* concerns processes for the identification, quantification and enrichment of type 1 regulatory T cells by the presence of surface markers CD4, CD18 and/or CD11a, and CD49b, and possibly by the over-expression of genes coding for CD4, PSGL-1, PECAM-1 and alphaV/beta3 molecules.

The PTXC16 family (WO2011/128779) entitled "*New methods for isolating Tr1 cells"* describes methods to identify, enrich or eliminate activated or quiescent type 1 regulatory T cells from a preparation by the detection of a defined group of surface markers (in particular CD62L and CD127).

Family	Applicants	Priority Date	Expiry date	Status
Cell markers				
PTXC1	TXCELL INSERM	06/24/2003	2024	**Granted** in France, the United States, Europe (and validated in the following countries: Austria, Belgium, Switzerland, Germany, Denmark, Spain, Finland, France, England, Ireland, Italy, the Netherlands, Sweden) Australia, Canada and Japan
PTXC16	TXCELL	04/15/2010	2031	**Granted** in Australia, South Africa, China and New Zealand **Being examined** in Brazil, Canada, Korea, Europe, India, Indonesia, Japan, Russia and the United States **Notification of grant** in Mexico

11.2.3.3 "Clinical use" field

This field comprises six families of patents and concerns the clinical use of type 1 regulatory T cells.

The PTXC8 family (WO2009/050283*),* entitled *"Compositions for treating multiple sclerosis*", describes type 1 regulatory T cells specific for an antigen involved in multiple sclerosis, e.g. MBP or MOG, as well as their use to treat this pathology.

The PTXC9 family (WO2009/068575*),* entitled *"Compositions for treating an intestinal inflammatory condition*", involves a composition including at least one population of type 1 regulatory T cells specific for a dietary antigen in many foods consumed by humans to treat inflammatory intestinal diseases such as Crohn's disease, ulcerative colitis, food allergies or food intolerances, for example to milk proteins or coeliac disease.

The PTXC10 family (WO2009/050282*)* entitled *"Tr1 cells, mesenchymal stem cells and uses thereof*", describes a composition of type 1 regulatory T cells and mesenchymal stem cells and the use of this

composition to induce immunological tolerance (specific for an antigen), in particular to treat diseases involving an immune response with excessive, dysfunctional or uncontrolled T cell mediation.

The PTXC11 family (WO2009/132941), entitled *"Compositions for treating an arthritic condition*", describes a composition containing at least one population of type 1 regulatory T cells specific for a joint-related antigen, e.g. collagen II, and the use of this composition to treat arthritic disorders.

The PTXC12 family (WO2009/132939), entitled *"Compositions for treating an inflammatory autoimmune condition*", describes a composition containing at least one population of type 1 regulatory T cells specific for human heat shock protein (HSP), and the use of this composition to treat autoimmune inflammatory diseases such as intestinal inflammatory diseases, arthritic disorders, multiple sclerosis, vasculitis, etc.

The PTXC19 family (WO2012/131419), entitled *"Method for using regulatory T cells in therapy*", describes the dose of cells to administer to a patient with an inflammatory or autoimmune disease receiving cell therapy using regulatory T cells.

Family	Applicants	Priority Date	Expiry date	Status
Clinical Use				
PTXC8	TXCELL	10/17/2007	2028	**Granted** in Australia, China and Russia **Notification of grant** in Europe (Austria, Belgium, Bulgaria, Switzerland, Cyprus, Czechoslovakia, Germany, Denmark, Estonia, Spain, Finland, France, England, Greece, Croatia, Hungary, Ireland, Iceland, Italy, Lichtenstein, Lithuania, Luxembourg, Latvia, Monaco, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Sweden, Slovenia, Slovakia, Turkey) **Being examined** in the United States, Canada and Japan
PTXC9	TXCELL	11/26/2007	2028	**Granted** in Australia, the United States, Russia and Japan **Being examined** in Europe (Austria, Belgium, Bulgaria, Switzerland, Cyprus, Czechoslovakia, Germany, Denmark, Estonia, Spain, Finland, France, England, Greece, Croatia, Hungary, Ireland, Iceland, Italy, Lichtenstein, Lithuania, Luxembourg, Latvia, Monaco, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Sweden, Slovenia, Slovakia, Turkey), the United States, Brazil, Canada, China and Korea
PTXC10	TXCELL	10/17/2007	2028	**Granted** in Australia, Japan, Russia and China **Notification of grant** in Europe (Austria, Belgium, Bulgaria, Switzerland, Cyprus, Czechoslovakia, Germany, Denmark, Estonia, Spain, Finland, France, England, Greece, Croatia, Hungary, Ireland, Iceland, Italy, Lichtenstein, Lithuania, Luxembourg, Latvia, Monaco, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Sweden, Slovenia, Slovakia, Turkey)

				Being examined in the United States, Canada and Korea
PTXC11	TXCELL University of Montpellier Regional University Hospital Center of Montpellier	04/28/2008	2029	**Granted** in Australia and Russia **Notification of grant** in Europe (Austria, Belgium, Bulgaria, Switzerland, Cyprus, Czechoslovakia, Germany, Denmark, Estonia, Spain, Finland, France, England, Greece, Croatia, Hungary, Ireland, Iceland, Italy, Lichtenstein, Lithuania, Luxembourg, Latvia, Monaco, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Sweden, Slovenia, Slovakia, Turkey) **Being examined** in the United States, Canada, China, Japan, and Korea
PTXC12	TXCELL	04/28/2008	2029	**Granted** in Australia, Europe (Austria, Belgium, Bulgaria, Switzerland, Cyprus, Czechoslovakia, Germany, Denmark, Estonia, Spain, Finland, France, England, Greece, Croatia, Hungary, Ireland, Iceland, Italy, Lichtenstein, Lithuania, Luxembourg, Latvia, Monaco, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Sweden, Slovenia, Slovakia, Turkey) and Japan **Being examined** in the United States and Canada
PTXC19	TXCELL	03/25/2011	2032	**Being examined** in Europe (Albania, Austria, Belgium, Bulgaria, Switzerland, Cyprus, Czechoslovakia, Germany, Denmark, Estonia, Spain, Finland, France, England, Greece, Croatia, Former Yugoslav Republic of Macedonia, Hungary, Ireland, Iceland, Italy, Lichtenstein, Lithuania, Luxembourg, Latvia, Monaco, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Serbia, San Marino, Sweden, Slovenia, Slovakia, Turkey), the United States, Australia, Brazil, Canada, China, Japan and Russia

11.2.3.4 "Mechanism of action" field

This field comprises three patent families and concerns the particular mechanisms of action of type 1 regulatory T cells.

The PTXC17 family (WO2012/001533), entitled *"IL-13 producing Tr1-like cells and uses thereof*", involves the isolation, identification and enrichment of a sub-population of type 1 regulatory T cells capable of producing interleukin 13 and having immunosuppressive actions. This new population can be used to diagnose or treat inflammatory and autoimmune diseases, allergies and disorders from organ transplants.

The PTXC18 family (WO2012/046139), entitled *"Method for determining the efficacy of a therapy using type 1 regulatory T cells in a subject*", describes a method to determine if a patient receiving therapy using type 1 regulatory T cells responds to the treatment. This involves the determination of proliferation of T cells specific for an antigen *in vitro*, the T cells being obtained from a sample of patient blood that is compared to a reference, for example antigen-specific proliferation determined before the patient was treated.

The PTXC2 family (EP2982746), entitled *"Regulatory T cells with a therapeutic potential"*, concerns populations of and processes for obtaining regulatory T cells expressing several cytotoxic molecules at

specific levels of expression. These new populations can be used to treat inflammatory and autoimmune diseases, allergies and disorders from organ transplants.

Family	Applicants	Priority Date	Expiry date	Status
Mechanism of action				
PTXC17	TXCELL	07/29/2010	2028	**Granted** in Australia**,** South Africa and New Zealand **Being examined** in Europe (Albania, Austria, Belgium, Bulgaria, Switzerland, Cyprus, Czechoslovakia, Germany, Denmark, Estonia, Spain, Finland, France, England, Greece, Croatia, Former Yugoslav Republic of Macedonia, Hungary, Ireland, Iceland, Italy, Lichtenstein, Lithuania, Luxembourg, Latvia, Monaco, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Serbia, San Marino, Sweden, Slovenia, Slovakia, Turkey), the United States, Brazil, Canada, Chile, China, Japan, Korea, Mexico and Russia
PTXC18	TXCELL	10/08/2010	2031	**Granted** in the United States and Australia **Being examined** in Europe (Albania, Austria, Belgium, Bulgaria, Switzerland, Cyprus, Czechoslovakia, Germany, Denmark, Estonia, Spain, Finland, France, England, Greece, Croatia, Former Yugoslav Republic of Macedonia, Hungary, Ireland, Iceland, Italy, Lichtenstein, Lithuania, Luxembourg, Latvia, Monaco, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Serbia, San Marino, Sweden, Slovenia, Slovakia, Turkey) Canada and Japan
PTXC22	TXCELL	08/07/2014	2035	**Being examined** in Europe (Albania, Austria, Belgium, Bulgaria, Switzerland, Cyprus, Czechoslovakia, Germany, Denmark, Estonia, Spain, Finland, France, England, Greece, Croatia, Former Yugoslav Republic of Macedonia, Hungary, Ireland, Iceland, Italy, Lichtenstein, Lithuania, Luxembourg, Latvia, Monaco, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Serbia, San Marino, Sweden, Slovenia, Slovakia, Turkey) **At the international phase**[4]

11.2.3.5 New patent applications

During the period covered by the *Document de Référence*, the Company continued to create new technological inventions, which could result in the filing of new patent applications.

[4] At the international phase: international patent application for which the decision of entry into the national phase expires in February 2017.

11.2.3.6 Abandoned patents and patent applications

During the period covered by the *Document de Référence*, certain patents and patent applications were abandoned by the Company because they were no longer of interest to the Company or covered technologies which at the time were no longer used by the Company.

11.2.4 Disputes

As at the date of the *Document de Référence* and to the best knowledge of the Company, its intellectual property was not contested, except for the normal examination of its applications by patent offices, nor had any infringement been reported.

11.2.5 Patents currently used

As at the date of the *Document de Référence*, no patent in the Company's patent portfolio is being used.

11.2.6 Scope of patent protection

Before 2005, priority filing (i.e. the first filing starting a 12 month priority period and confirmed by a subsequent application, generally an international patent application, within this 12 month period) was performed in the form of a French patent application. Since 2005, all priority applications are European and/or American.

The Company's patent applications are then extended internationally (international "PCT" application--Patent Cooperation Treaty) within a maximum period of 12 months.

The geographic coverage adopted for national or regional phases depends on corporate strategy. In general, patents systematically include Europe and the United States, and generally Australia, Canada and Japan. Entries into national or regional phases in China, Korea, Russia, Brazil, Chile, India, Indonesia, Mexico, New Zealand and South Africa are also considered, on a case-by-case basis, depending on the strategic importance of the patent family in question.

11.3 Contracts covering joint work, research, external services and licenses granted or conceded to the Company

11.3.1 License contract conceded by the INSERM to the Company

Following joint work between the INSERM and the Company between July 1999 and November 2004, patent applications were submitted for the PTXC1, PTXC2 and PTXC5 families. The PTXC1 and PTXC5 patent families are jointly owned by the Company and the INSERM; the PTXC2 patent family belongs exclusively to the INSERM.

In the license contract of January 30, 2006 (as amended on December 9, 2013), the INSERM granted the Company an exclusive worldwide license to use its share of property of these PTXC1 and PTXC5 patent families.

Information on the contract is provided in paragraph 22.1 of the *Document de Référence*.

11.3.2 Exclusive joint ownership and license agreement for the PTXC11 family

The Company is currently negotiating with the Regional University Hospital Center of Montpellier to sign the joint ownership and exclusive license agreement for the family of PTXC11 patent applications.

11.3.3 Exclusive option agreement granted by Yeda Research and Development Co. Ltd.

On June 30, 2015 the Company entered into an exclusive option agreement with *Yeda Research and Development Co. Ltd.*, the technology transfer arm of the Weizmann Institute of Sciences, based in Rehovot, Israel.

This agreement grants the Company an exclusive 12 month period for exercising the option. This will enable it to negotiate the terms of an exclusive worldwide license over the family of patent applications (Europe, the US, Israel) for redirected, genetically engineered regulatory T cells (CAR-Treg) and their

use for the treatment of autoimmune and inflammatory pathologies. If this option is exercised it will enable the Company to gain exclusive access to this family of patent applications.

The terms of the agreement give the Company the right to exercise this option up until June 30, 2016. A Letter of Intention was signed on October 28, 2015 to define the main terms of the license agreement, should it be concluded, following the possible exercise of the option by the Company.

Information on the agreement is provided in paragraph 22.3 of the *Document de Référence*.

11.3.4 Agreement to terminate the collaboration, option, development and license agreement signed with Ferring International Center and transferred to Trizell Holding SA

On December 2, 2015, the Company and Trizell entered into an agreement terminating the *"Collaboration, option, development and license agreement"* and the "*Development agreement*" signed by them. In this agreement Trizell waived its option to obtain an exclusive worldwide license for the development, manufacture and marketing of Ovasave® to treat inflammatory bowel diseases (IBD), among which Crohn's disease. Trizell also transferred to the Company intellectual property rights which it and Ferring could hold over Ovasave®. In return, the Company undertook to pay Trizell, over several years, certain sums either as fixed payments or as part of the revenues generated by the products initially covered by the collaboration, option, development and license agreement.

Information on the contract is provided in paragraph 22.2 of the *Document de Référence*.

11.4 Other intellectual property aspects

The Company has protected its "Ovasave®" and "CellArthrix®" brand names by registering trademarks in France.

The Company also owns three domain names: www.txcell.fr; www.txcell.com; www.txcell-finance.com. It uses these domain names to provide public access to its two websites: the Company's "corporate" site and the Company's "finance" site.

12. TRENDS

12.1 Recent changes since closing of financial year 2015

On February 25, 2016, the Company announced the achievement of the most important milestone in the transfer of its manufacturing technology to MaSTherCell, according to the framework agreement of December 3, 2015 (see paragraph 22.6 of the *Document de Référence* for more detail).

In addition, the Company announced on February 29, 2016, the launch on the premises of Genbiotech located in Sophia Antipolis, of its new manufacturing process development laboratories (see paragraph 8.1 of the *Document de Référence* for more detail).

Under the agreement dated March 9, 2016, between the Company and PCT LLC, the latter will operate a preliminary strategic evaluation of the existing TxCell manufacturing processes of its ASTrIA platform (see paragraph 22.7 of the *Document de Référence* for more detail).

On March 31, 2016, the Company announced the appointment of its new Scientific Advisory Board ("SAB") chaired by Professor Zelig Eshhar (see paragraph 6.1 of the *Document de Référence* for more detail) in order to strengthen scientific expertise and strategic directions of the Company in the development of its new ENTrIA platform.

As of March 31, 2016, the cash and cash equivalents of the Company amounted to €5 million, excluding proceeds from the 2015 research tax credit of €3 million. Furthermore, no revenue was generated in the first quarter of 2016.

On April 25, 2016, the Company announced the signing of a strategic collaboration agreement with Ospedale San Raffaele (OSR). The collaboration includes development arm on CAR-Tregs focused on lupus nephritis, as well as a research program dedicated to CAR-Treg biology.

12.2 Perspectives

The prime objectives of the Company in the current financial year are:

- Resumption of Phase IIb trial on Ovasave®;
- Generation of pre-clinical proof of concept data on the ENTrIA platform;
- Improvements to TxCell's production process for the ASTrIA platform and initiation of the development of a production process for the ENTrIA platform;
- Signature of strategic partnerships with major pharmaceuticals and biotech players to further speed up development of ASTrIA and ENTrIA platforms;
- Completion of pre-clinical development and regulatory dossier for Col-Treg, with the aim of starting a first clinical trial in non-infectious uveitis.

12.3 Know trends, uncertainties, demand or commitments or events that could reasonably have a notable effect on Company perspectives

On the basis of TxCell's development plan described in paragraph 12.2 above, and notably the resumption of clinical trial on Ovasave®, the Company's cash burn is likely to be around €15 million in 2016.

13. PROFIT FORECASTS AND ESTIMATES

The Company does not intend to make any profit forecasts or estimates.

14. ADMINISTRATIVE, MANAGEMENT, SUPERVISORY AND EXECUTIVE BODIES

The Company is a French limited liability company (*société anonyme)* with a board of directors (*conseil d'administration*). During the meeting held on September 6, 2013, the board of directors chose to separate the functions of chairman of the board and Chief Executive Officer (*directeur général)*.

A brief description of the main provisions of the Company's bylaws and its special committees' internal regulations can be found in paragraph 21.2 and in the board of directors' report on corporate governance, internal control and risk management set out in paragraph 16.3 of the *Document de Référence*, respectively.

14.1 Executive officers and members of the board of directors

14.1.1 Executive officers

The Company is a French limited liability company (*société anonyme*) with a board of directors, the roles and responsibilities of which are described in the bylaws and summarized in paragraphs 21.2.2 and 16.3 of the *Document de Référence*.

The Company is managed by Mr. Stéphane Boissel as Chief Executive Officer. Following the definitive closure of the pharmaceutical establishment in Besancon, notified to the French National Health Products Safety Agency (*Agence Nationale de Sécurité du Médicament et des produits de santé*, "ANSM") on January 25, 2016, Mr. Eric Pottier resigned from his position as head pharmacist (*pharmacien responsable*) and from his position as Deputy Chief Executive Officer effective February 2, 2016. At its meeting held on February 3, 2016, the board acknowledged this resignation. Mr. Eric Pottier was then dismissed for economic reasons dated March 17, 2016 in connection with the closing of the Besancon site.

As of the date of the *Document de Référence*, the list of executive officers is as follows:

Name	Office	Date of first appointment or most recent renewal, term of office	Main functions within the Company	Main functions outside the Company
Stéphane Boissel	Chief Executive Officer (not a member of the board of directors)	First appointment as Chief Executive Officer: April 27, 2015* Term of office: following the general meeting convened to vote on the financial statements for the financial year ending on December 31, 2017	Chief Executive Officer	• Chairman of the board of directors, Elsalys Biotech SAS

* Mr. Stéphane Boissel succeeded Mr. Damian Marron, who resigned from his position as Chief Executive Officer of the Company effective April 27, 2015.

The business address of the Chief Executive Officer is the head office of the Company.

The Chief Executive Officer's expertise and experience in management results from his previous positions as employee and/or executive officer (please refer to paragraph 14.1.4 of the *Document de Référence*).

14.1.2 Members of the board of directors

At the date of the *Document de Référence*, the Company's board of directors is composed of the following members:

Name	Office	Date of first appointment or most recent renewal, term of office	Main functions within the Company	Main functions outside the Company
François Meyer	Chairman of the board of directors	First appointment to the board: September 28, 2012 Term of office as a member of the board of directors: following the general meeting convened to vote on the financial statements for the financial year ending on December 31, 2017 First appointment as chairman of the board of directors: September 28, 2012	None	None
Auriga Partners represented by Bernard Daugeras	Director	First appointment: September 28, 2012 Term of office: following the general meeting convened to vote on the financial statements for the financial year ending on December 31, 2017	None	● Member of the executive board, Auriga Partners ● Member of the board of directors, Domain Therapeutics, Isocell and Population Genetics
Bpifrance Investissement represented by Marie-Laure Garrigues	Director	First appointment: September 28, 2012 Term of office: following the general meeting convened to vote on the financial statements for the financial year ending on December 31, 2017	None	● Member of the board of directors, EOS Imaging and Medtech
Bpifrance Participations represented by Thibaut Roulon	Director	First appointment: May 26, 2015 Term of office: following the general meeting convened to vote on the financial statements for the financial year ending on December 31, 2020	None	● Investment Director at Bpifrance Investissement
Marie-Yvonne Landel-Meunier *	Independent director	First appointment: March 7, 2014 Term of office: following the general meeting convened to vote on the financial statements for the financial year ending on December 31, 2019	None	● Chairman, Marie Landel & Associates ● Member of the board of directors, Hepatochem, Cellnovo and Safe
David Horn Solomon *	Independent director	First appointment: March 30, 2015 Term of office: following the general meeting convened to vote on the financial statements for the financial year ending on December 31, 2017	None	● Member of the board of directors, Onxeo and Promosome

* Temporary appointment decided by the board of directors and definitely ratified by the combined Ordinary and Extraordinary Shareholders' Meeting held on May 26, 2015, in accordance with Article L.225-24 of the French commercial code.

The expertise and experience in management of the people listed above result from their previous positions as employees and/or executive officers (please refer to paragraph 14.1.3. of the *Document de Référence*).

The board of directors appointed Mr. Laurent Arthaud and Mr. Laurent Higueret as observers (*censeurs*) on March 7, 2014 and May 22, 2014, respectively, for six-year terms, which expire following the general meeting convened to vote on the financial statements of the financial year ending December 31, 2019. In accordance with the Company's bylaws, these appointments were ratified by the combined ordinary and extraordinary shareholders' meeting held on May 26, 2015.

14.1.3 Other corporate offices

Other corporate offices currently held by the Chief Executive Officer

	Other corporate offices currently held outside the Company	
	Type of office	**Company**
Stéphane Boissel	Chairman of the board of directors	Elsalys Biotech SAS
	Chairman	SAS Cottages Participations

Other corporate offices currently held by the members of the board of directors

	Type of office	**Company**
François Meyer	None	None
Auriga Partners represented by Bernard Daugeras	*Bernard Daugeras as representative of Auriga Partners*	
	Member of the board of directors	Domain Therapeutics
	Member of the board of directors	Isocell
	Member of the board of directors	Population Genetics
	Member of the supervisory board	Firalis
	Member of the supervisory board	Theranexus
	Offices held by Bernard Daugeras in his own name	
	Member of the board of directors	CNRS Fondation
	Member of the board of directors	IHU Strasbourg
	Member of the management board	Auriga Partners
Bpifrance Investissement represented by Marie-Laure Garrigues	*Marie-Laure Garrigues as representative of Bpifrance Investissement*	
	Member of the board of directors	EOS Imaging
	Member of the board of directors	Medtech
	Offices held by Marie-Laure Garrigues in her own name	
		None
Bpifrance Participations represented by Thibaut Roulon	*Thibaut Roulon as representative of Bpifrance Participations*	
		None
	Thibaut Roulon as representative of Bpifrance Investissement	
	Member of the board of directors	Biom'Up
	Member of the supervisory board	Step Pharma
	Observer	Gensight Biologics
	Offices held by Thibaut Roulon in his own name	
	Member of the board of directors	Advicenne Pharma
	Observer	Poxel
Marie-Yvonne Landel Meunier	Member of the board of directors and treasurer	Hepatochem
	Member of the board of directors and chairman of the audit committee	Cellnovo
	Member of the board of directors and chairman of the audit committee	Safe orthopedics
David Horn Solomon	Member of the board of directors	Onxeo
	Member of the board of directors	Promosome
	Member of the board and executive committee	American chamber of commerce in Denmark

Corporate offices held by the Chief Executive Officer over the five previous financial years, now expired:

	Corporate offices held over the five previous financial years, now expired	
	Type of office	Company
Stéphane Boissel	Chief Executive Officer	Genclis
	Member of the board of directors	Genclis
	Member of the management board	Innate Pharma
	Member of the board of directors	Innate Pharma
	Member of the board of directors	Erytech Pharma
	Member of the board of directors	Transgene
	Member of the board of directors	Transgene
		BioPharmaceutical Technology
	Member of the board of directors	Platine Pharma Services
	Member of the board of directors	Pharmaxon
	Chairman	BP Food

Corporate offices held by the members the board of directors over the five previous financial years, now expired:

	Corporate offices held over the five previous financial years, now expired	
	Type of office	Company
François Meyer	Member of the supervisory board	UniQure NV
	Chairman of the scientific board	FNR Luxembourg
Auriga Partners represented by Bernard Daugeras	*Bernard Daugeras as representative of Auriga Partners*	
	Member of the management board	Bioalliance
	Member of the board of directors	Median Technologies
	Member of the management board	Nemoptic
	Member of the management board	Novagali
	Member of the supervisory board	Supersonic Imagine
	Offices held by Bernard Daugeras in his own name	
	Member of the supervisory board	Inserm Transfert
Bpifrance Investissement represented by Marie-Laure Garrigues	*Marie-Laure Garrigues as representative of Bpifrance Investissement*	
	Member of the board of directors	Cytheris
	Offices held by Marie-Laure Garrigues in her own name	
	Member of the board of directors	Ingen Biosciences
	Manager	Bio Thema Consulting
Bpifrance Participations represented by Thibaut Roulon	*Thibaut Roulon as representative of Bpifrance Participations*	
		None
	Thibaut Roulon as representative of Bpifrance Investissement	
	Member of the supervisory board	TxCell
	Offices held by Thibaut Roulon in his own name	
	Member of the board of directors	Gamamabs Pharma
	Member of the board of directors	Sensorion
Marie-Yvonne Landel-Meunier	None	None
David Horn Solomon	President and Chief Executive Officer	Bionor
	President and Chief Executive Officer	Zealand Pharma

14.1.4 Representations relating to the executive officers, the members of the board of directors and the observers

None of the mentioned persons have any family ties among each other.

During the last five years, none of these persons:

- have been convicted for fraud;
- have been associated to a bankruptcy, receivership or liquidation, as executive officer or member of a governing body;
- have been prohibited from managing a company; or
- have been the subject of any allegations or official public sanctions by statutory or regulatory authorities.

14.1.5 Biographies of the chairman of the board of directors, the Chief Executive Officer, the members of the board of directors and the Observers.

François Meyer, chairman of the board of directors, was previously chairman and Chief Executive Officer of the Company from 2011 to 2013. From 2010 to 2014, he was also a member of the supervisory board of uniQure NV, a Dutch gene therapy company (AMX and NASDAQ). From 2006 to 2010, he was a member of the board of the Luxembourg National Research Fund, and was president of its scientific board from 2010 to 2014. From 1996 to 2006, François was successively senior vice president of research world-wide at Rhône Poulenc Rorer, senior vice president R&D at d'Aventis Pharma France and Chief Executive Officer of Gencell, a wholly-owned subsidiary of Aventis. From 1993 to 1996, he held various management positions at Sandoz within R&D, in particular, he was global head of the gene and cell therapy business. François started his career in Industry in 1980 by creating and integrating the first molecular biology department of Ciba-Geigy, which led to the first biotechnology products coming from the pharmaceutical industry.

From 1993 to 1996, he has been a member of boards of directors and scientific boards for a number of biotechnology companies specialized in gene and cell therapy, including Introgen Therapeutics, Inc., Gene Therapy Inc., Systemix, Inc., and Biotransplant Inc.

François holds a Ph.D. in Molecular Biology from the University of Zurich in 1978 and a diploma in chemistry from the Swiss Federal Institute of Technology in Zurich in 1972. In 2014, he got awarded *Grand Officier de l'ordre du Mérite du Grand-Duché de Luxembourg* for his contributions to the development of Research in Luxembourg.

Stéphane Boissel, Chief Executive Officer, holds a degree in management and finance from the universities of Lyon and Paris-Dauphine. He also holds an MBA from the University of Chicago, United States of America. Stéphane has solid experience in the fields of both investment banking and immunotherapy. At the beginning of his career, from 1990 to 2002, Stéphane worked for PwC and then for the Lazard investment bank, primarily as an investor in France, Singapore, and Hong Kong. He then became a member of the Innate Pharma SA team from 2002 to 2010, first as a Chief Financial Officer, and then as a Deputy Chief Executive Officer. From 2010 to 2014, he served as Deputy Chief Executive Officer of Transgene. He oversaw several public offerings and private placements and negotiated several international agreements while he was at Transgene and Innate Pharma. He was also a member of the board of directors of Erytech Pharma SA between 2005 and 2010. In 2014, Stéphane served as Chief Executive Officer of Genclis, a molecular diagnostic company, prior to becoming the Chief Executive Officer of TxCell in April 2015. Stéphane is also the non-executive chairman of the board of directors of Elsalys Biotech SAS.

Bernard Daugeras, permanent representative of Auriga Partners, member of the board of directors, is co-founder and member of the management board of Auriga Partners. He is a specialist of life sciences. Bernard has engineered a number of investments such as Onxeo (formerly BioAlliance Pharma) (Euronext Paris: ONXEO), NicOx (Euronext Paris: COX) and SuperSonic Imagine (Euronext Paris: SSI), and is a member of the French Academy of Technologies.

Researcher in particle physics at the University of Orsay, the University of California at Berkeley and the CNRS (the French national scientific research center), Bernard held a number of senior posts in the French Ministry of Industry and Research, including being responsible for relations between research and businesses and for promoting technology transfer. As such, he participated in establishing the industrial research agreement system (*conventions industrielles de formation par la recherche – CIFRE*). In 1986 he was part of the creation of Innolion, the Crédit Lyonnais's venture capital structure, before joining Finovelec in 1990.

Bernard is a graduate of the Ecole Polytechnique and holds a PhD from the University of Orsay.

Marie-Laure Garrigues, permanent representative of Bpifrance Investissement, member of the board of directors, is the director of investments for Bpifrance Investissement (formerly CDC Enterprises) since 2008. Previously, she founded Bio-Thema Consulting in 2002, and carried out consulting missions in the biotechnologies sector. She has been member of the boards of directors of Faust Pharmaceuticals, BioAlliance Pharma, GeneSystems, Palumed, Fournitures Hospitalières, Proteus and Ingen Biosciences, and was appointed chairman of the management board of Pherecydes Pharma in 2007. Between 1986 and 2002, she directed the R&D and marketing teams at Sanofi Diagnostics Pasteur before working as director of the microbiology division of Bio-Rad laboratories, a Californian company that manufactures diagnostic products. Between 2012 and 2014, she was observer of TxCell.

Marie-Laure Garrigues is a pharmacist and a former hospital intern in medical biology. She holds a postgraduate diploma (DEA) in microbiology from the University of Paris V.

Thibaut Roulon, permanent representative of Bpifrance Participations, member of the board of directors, graduated in engineering from the Ecole Centrale de Paris and holds a doctorate from the University Pierre and Marie Curie. He began his career as a researcher in a U.S. biotechnology company developing anticancer immunotherapies.

In 2005, he joined Bioam Gestion, a venture capital firm investing in the field of life sciences. In 2010, Bioam was acquired by Bpifrance Investments (formerly CDC Entreprises), a subsidiary of Caisse des Dépôts in charge of investments in small and medium-sized enterprises (*petites et moyennes entreprises - PMEs*) and mid-tier enterprises (*entreprises de taille intermédiaire – ETIs*). He is responsible for investments in companies specialized in life sciences (seed or venture capital, listed companies).

Marie-Yvonne Landel-Meunier, independent member of the board of directors, moved to Boston in 1990 and founded Marie Landel & Associates, a company whose focus is worksharing financial management and whose clients - French and European companies essentially working in the high-tech and biotech sectors – are based throughout the U.S.. The firm is a member of the Constantin network.

Marie-Yvonne graduated from the European Business School in 1975 and then qualified as an independent accountant (*expert-comptable*) in 1989.

David Horn Solomon, independent member of the board of directors, obtained his doctorate in medical science from the Cornell University Graduate School of Medical Science of New York in 1991. He was a member of the faculty of the College of Physicians and Surgeons at the University of Columbia (New York, NY, USA).

From 2003 to 2006, David headed healthcare investments for Carrot Capital Healthcare Ventures in New York. He has also held various management positions in biotechnology and pharmaceutical companies and medical systems, including Remedy Pharmaceuticals, Critical Diagnostics, and Vital Sensors. He thus acquired broad experience in listed companies in the fields of biotechnology, healthcare investment and pharmacological research. David then served as Chairman and Chief Executive Officer of Zealand Pharma A/S (NASDAQ CO: ZEAL) from 2008 to 2015, and as President and Chief Executive Officer of Bionor Pharma ASA (OSE: BIONOR and NASDAQ: BNRPF) from 2015 to 2016. He is currently a member of the boards of directors of Onxeo in Paris (Euronext Paris and NASDAQ OMX: ONXEO) and of Promosome in La Jolla, California (USA).

Laurent Arthaud, observer, is a graduate of the Ecole Polytechnique and of the French National School of Statistics and Economic Administration. Laurent Arthaud was Vice-chairman of Aventis Capital, the capital investment subsidiary of the pharmaceutical group Aventis, and chairman of Pharmavent Partners, before joining Bpifrance Investissement (formerly CDC Entreprises) in 2006 as Deputy Chief

Executive Officer in charge of new developments. In 2009, he took the head of all the life sciences activities of CDC Enterprises and became manager of the InnoBio investment fund. Since 2013, he has been managing the investment activities in Lifesciences, Cleantech and French Tech Acceleration of Bpifrance Investissement.

Laurent Higueret, observer, is an investment director in the Large Venture Fund team at Bpifrance, specializing in healthcare and life sciences investments. He is currently member of the board of directors of Biom'Up and formely at Poxel. Laurent is responsible for Bpifrance's investments in Cerenis, DBV Technologies and MedDay. Before Joining Bpifrance in 2014, he spent six years as an investment banker with BNP Paribas' Healthcare M&A Group. Laurent Higueret holds a PhD in Pharmacy from the University of Bordeaux and holds a Master Degree in Financial Engineering from the EM Lyon Business School.

The biographies of the members of senior management who are not executive officers are set out in paragraph 6.1.5.3 of the *Document de Référence*.

14.2 Conflicts of interest between members of the administrative and executive management bodies

The members of the board of directors are all direct or indirect shareholders of the Company and/or hold securities that give access to the Company's capital (please refer to paragraph 17.2 of the *Document de Référence*). The observers are not shareholders and do not hold any instruments that give access to the capital of the Company.

The Chief Executive Officer, Mr. Stéphane Boissel, declared on July 28, 2015 that he had subscribed to 20,000 new shares issued as part of a private placement that took place in July 2015. The Chief Executive Officer also holds financial instruments that give access to the Company's share capital (please refer to paragraph 21.1.4 of the *Document de Référence*).

The regulated agreements entered into by the Company are described in paragraph 19.3. "Reports by the statutory auditors on the regulated agreements entered into with respect to the financial year ended on December 31, 2015."

The Company is not aware of any current or potential conflict of interest between the private interests and/or other duties of the members of the Company's administrative, management and executive management bodies, as listed in paragraph 14.1 above, and their duties to the Company.

As part of the investment by Bpifrance Participations, a Shareholders' Agreement was entered into on March 27, 2014 by and among Auriga Partners, Seventure Partners, Bpifrance Participations, Innobio, and Mr. François Meyer, Mr. Miguel Forte, Mr. Arnaud Foussat, Mr. Raphaël Flipo, Mr. Damian Marron and Mr. Eric Pottier (the "Shareholders' Agreement").

Following the resignation of Mr. Damian Marron from his positions as Chief Executive Officer and member of the board of directors of the Company on April 27, 2015, the parties to the Shareholders' Agreement entered into an addendum to the Shareholders' Agreement on May 6, 2015, under which they decided that Mr. Damian Marron is no longer subject to the rights and obligations of the Shareholders' Agreement.

Following the resignation of Mr. Eric Pottier from his position as Deputy Chief Executive Officer on February 2, 2016, the parties to the Shareholders' Agreement entered into an addendum to the Shareholders' Agreement on February 3, 2016, having the same purpose as the aforementioned addendum.

The key commitments of this Shareholders' Agreement include:

- A commitment to hold shares:

Innobio and the investment funds managed by Auriga Partners and Seventure Partners (the "Funds") have committed towards the other parties to the Shareholders' Agreement to hold the Shares (as that term is defined by the Shareholders' Agreement) that they hold or will come to hold directly or indirectly as follows: (i) 100% of their Shares during the six months from the date of the first listing of the

Company's shares, (ii) 75% of their Shares during the six months that follow the preceding period, (iii) 50% of their Shares during the six months that follow the preceding period, and (iv) 25% of their Shares for the six months following the preceding period.

Messrs. François Meyer, Miguel Forte, Arnaud Foussat and Raphaël Flipo (the "Managers") have committed towards the other parties to the Shareholders' Agreement to hold the Shares that they hold or will come to hold directly or indirectly, as follows: (i) 100% of their Shares for two years from the date of the first listing of the Company's shares, (ii) 75% of their Shares during the one year period that follows the preceding period, and (iii) 50% of their Shares during the one year period that follows the preceding period.

Bpifrance Participations has committed towards the other parties to the Shareholders' Agreement to hold 100% of the Shares to which it subscribed to during the Offering for two years from the date of first listing of the Company's Shares.

Notwithstanding the above, Bpifrance Participations and the Funds may freely transfer all or a part of their Shares to a third party in the event of: (i) transfer to any entity that it controls, that controls it, or is under joint control within the meaning of Article L.233-3 of the French commercial code; (ii) violation of any of the commitments under the Shareholders' Agreement, other than a simple omission that is not likely to challenge the commitments provided for in the Shareholders' Agreement, and; (iii) a public offer of the Company's Shares.

In addition, Bpifrance Participations may also freely transfer its ownership: (i) in the event of a modification of the list of important decisions mentioned in article 2.1.3 of the Shareholders' Agreement, that has not been approved by Bpifrance Participations, and (ii) in the event of a change in Company strategy that is not approved by Bpifrance Participations.

- Orderly disposal procedure:

The parties related to the Shareholders' Agreement (the "Related Parties") may, if they wish, institute an orderly disposal procedure without disturbing the market. Any Related Party wishing to dispose of Shares that are not subject to a lock-up pursuant to the Shareholders' Agreement may provide notice to the other Related Parties of the number of Shares it wishes to dispose of.

Each of the other Related Parties thus informed will have a period of five days to notify the other Related Parties of its intention to dispose of its Shares by indicating the number of Shares that it wishes to transfer. The Related Parties having indicated their desire to transfer Shares will mutually agree on a recognized investment services provider to transfer the Shares under the best terms, and will mutually define in good faith the procedure and the terms of the sale, in particular the sale price or the terms for setting the price. All Related Parties having communicated their intention to transfer may participate in the sale on the same terms (including price).

In the event that one of the Related Parties decides to no longer participate in the sale, it may withdraw from the process and the other Related Parties, in the absence of another agreement, will reallocate among themselves, proportionally to the number of Shares sold, the number of Shares that would have been sold by the withdrawing party. The withdrawing party will then be free to sell all or part of the number of Shares (such as that number was communicated to the other Related Parties) at any time after the expiration of the time frame provided for in the following paragraph.

In the event that one or several Related Parties provides notice of their intention to proceed with a disposal in accordance with the foregoing terms, no Related Party may transfer Shares prior to the expiration of a 30-day period following the date of completion (or withdrawal) of the sale in accordance with the orderly disposal procedure, with the exception of transfers implemented in accordance with that procedure by the party or Related Parties that provided notice of the intention to sell.

In the event that no party has provided notice of their intention to proceed with a disposal in accordance with the foregoing terms, each Related Party will be free to transfer at any time any Shares that are not subject to a lock-up. This orderly disposal procedure will remain in effect for a period of two years from the date of first listing of the Company's Shares.

- The appointment of a member to the board of directors upon proposal by Bpifrance Participations and that this member serves on at least one of the special committees of the board of directors.
- Bpifrance Participations may request the appointment of an observer to the board of directors.

The Shareholders' Agreement has been entered into for a ten-year period, given that it can be terminated in the event that Bpifrance Participations sells more than half of its investment in the Company.

The Shareholders' Agreement is not intended by the parties, and the parties do not intend to act in concert.

To the best of the Company's knowledge, no other agreements or contracts whatsoever have been entered into with shareholders, clients, suppliers, or any other party under which any of the Company's executive officers or members of the board have been appointed.

To the best of the Company's knowledge, as at the date of the *Document de Référence*, no restrictions accepted by the persons listed in paragraph 14.1. "Executive officers and members of the board of directors" concerning the transfer of their interest in the Company's capital, other than the aforementioned Shareholders' Agreement, exist.

15. COMPENSATION AND BENEFITS

15.1 Compensation of the corporate officers

The information in this chapter has been prepared with reference to the Corporate Governance Code for Midcap and Smallcap Companies published in December 2009 by MiddleNext and approved as a reference document by the AMF (the "MiddleNext Code"). The tables included in the AMF recommendation no. 2009-16 are set out below.

The Company is a French limited liability company *(société anonyme*) with a board of directors (*conseil d'administration*). At the meeting held on September 6, 2013, the board of directors opted to separate the functions of Chairman of the board and Chief Executive Officer. Readers are advised to refer to the additional information provided below each table.

- **Table 1:** Summary of compensation, stock options and shares allocated to each executive corporate officer

In thousands of euros Name	2015 financial year	2014 financial year
François Meyer – Chairman of the board of directors		
Compensation for the financial year (1)	82	60
Value of multiannual variable compensation allocated during the financial year	0	0
Value of options and warrants allocated during the financial year as per method used in the financial statements prepared in accordance with IFRS (2) (3)	84	470
Value of free shares allocated during the financial year	0	0
Total	**166**	**530**
Stéphane Boissel – Chief Executive Officer (4)		
Compensation for the financial year (1)	210	0
Value of multiannual variable compensation allocated during the financial year	0	0
Value of options and warrants allocated during the financial year as per method used in the financial statements prepared in accordance with IFRS (2) (3)	451	0
Value of free shares allocated during the financial year	0	0
Total	**661**	**0**
Damian Marron – Chief Executive Officer (5)		
Compensation for the financial year (1)	271	244
Value of multiannual variable compensation allocated during the financial year	0	0
Value of options and warrants allocated during the financial year as per method used in the financial statements prepared in accordance with IFRS (2) (3)	0	809
Value of free shares allocated during the financial year	0	0
Total	**271**	**1,053**
Eric Pottier – Deputy Chief Executive Officer (6)		
Compensation for the financial year (1)	98	111
Value of multiannual variable compensation allocated during the financial year	0	0
Value of options and warrants allocated during the financial year as per method used in the financial statements prepared in accordance with IFRS (2) (3)	19	111
Value of free shares allocated during the financial year	0	0
Total	**118**	**223**
Total	**1,215**	**1,806**

(1) See Table 2.

(2) See Table 4.

(3) The valuation of the warrants and stock options awarded during the financial year, according to the method used in IFRS accounting, corresponds to the probability-weighted value of the awarded plans after a non-transferability discount. In the financial statements presented in paragraph 20.1 of the *Document de Référence*, these charges are spread over the vesting periods of the warrants and the stock options.

(4) Mr. Stéphane Boissel was appointed CEO of the Company by the board of directors on April 27, 2015.

(5) Mr. Damian Marron was appointed CEO of the Company by the board of directors on September 6, 2013, a position which he resigned from on April 27, 2015. As part of his departure, Mr. Damian Marron received during the financial year 2015 a severance package in an amount that complies with the MiddleNext Code recommendations.

(6) Mr. Eric Pottier was hired as Vice President for the Supply Chain on January 14, 2013 and was appointed Deputy Chief Executive Officer of the Company by the board of directors on January 22, 2013, a position which he resigned from on February 2, 2016. Eric Pottier was dismissed on economic grounds on March 17, 2016 in connection with the shutdown of the Besançon site.

- **Table 2** Summary of compensation allocated to each executive corporate officer

The following tables presents the compensation allocated to the executive corporate officers for the past two financial years, and the actual compensation received during the same periods:

In thousands of euros Name	2015 financial year		2014 financial year	
	Amount due (1)	Amount paid (2)	Amount due (1)	Amount paid (2)
François Meyer – Chairman of the board of directors (3)				
Fixed compensation (7)	82	82	60	60
Variable compensation (8)	0	0	0	28
Exceptional compensation	0	0	0	0
Director's attendance fees	0	0	0	0
Benefits in kind	0	0	0	0
Total	**82**	**82**	**60**	**88**
Stéphane Boissel – Chief Executive Officer (4)				
Fixed compensation (9)	186	186	0	0
Variable compensation (10)	17	0	0	0
Exceptional compensation	0	0	0	0
Director's attendance fees	0	0	0	0
Benefits in kind (11)	7	7	0	0
Total	**210**	**194**	**0**	**0**
Damian Marron – Chief Executive Officer (5)				
Fixed compensation (12)	60	60	184	184
Variable compensation (13)	0	46	46	22
Exceptional compensation (14)	211	211	15	15
Director's attendance fees	0	0	0	0
Benefits in kind	0	0	0	0
Total	**271**	**316**	**244**	**220**
Eric Pottier – Deputy Chief Executive Officer (6)				
Fixed compensation (15)	96	96	86	86
Variable compensation (16)	0	18	18	9
Exceptional compensation (17)	0	0	3	3
Director's attendance fees	0	0	0	0
Benefits in kind (18)	2	2	4	4
Total	**98**	**116**	**111**	**102**
Total	**661**	**708**	**415**	**410**

(1) For the financial year. The variable compensation owed for one financial year is paid in the next financial year.

(2) During the financial year.

(3) Mr. François Meyer held the office of Chairman and CEO of the Company until the meeting of the board of directors held on September 6, 2013, during which he resigned from his office as CEO. Mr. François Meyer still holds the office of Chairman of the board of directors.

(4) Mr. Stéphane Boissel was appointed CEO of the Company by the board of directors on April 27, 2015.

(5) Mr. Damian Marron was appointed CEO of the Company by the board of directors on September 6, 2013, a position from which he resigned on April 27, 2015.

(6) Mr. Eric Pottier was hired as Vice President for the Supply Chain on January 14, 2013 and was appointed Deputy Chief Executive Officer of the Company by the board of directors on January 22, 2013, a position from which he resigned on February 2, 2016. Mr. Eric Pottier was dismissed on economic grounds on March 17, 2016 in connection with the shutdown of the Besançon site.

(7) The board of directors' meeting held on September 6, 2013 set Mr. François Meyer's gross annual compensation at €60 thousand, covering his functions as Chairman, as well as his general management support function. The board of directors' meeting held on February 10, 2015 revalued and revised the apportionment of François Meyer's compensation to make a distinction between his compensation as Chairman of the board of directors (€60 thousand gross per year) and the compensation for his specific mission (€24 thousand gross per year) effective February 1, 2015.

(8) There is no plan to pay François Meyer any variable compensation for his duty as Chairman of the board of directors. The variable compensation he was paid in 2014 was related to his work as Chairman and CEO from 2013 up to the board of directors meeting held on September 6, 2013, during which he resigned as CEO. It was approved by the board of directors of January 22, 2014 on a proposal from the nomination and compensation committee after the Company achieved 55% of its objectives in 2013.

(9) The Company entered into a management agreement with Stéphane Boissel following his appointment as the Company's CEO by the board of directors on April 27, 2015, with a view to determining the main terms and conditions of his duties as CEO. The signature of the management contract was authorized by the board at its meeting held on April 27, 2015. As consideration for his duties, Stéphane Boissel will receive (i) a yearly fixed compensation of €275 thousand euros, (ii) a variable compensation that may not exceed 30% of the said fixed compensation, based on the achievement of objectives set annually by the Company's board of directors, and (iii) in-kind benefits consisting of the payment of business travel, expense, an unemployment insurance policy for executives, and supplementary social security, healthcare and retirement protection (see paragraph 16.2 of the *Document de Référence*).

(10) On February 3, 2016 the board of directors, upon the proposal of the nomination and compensation committee, set at 20% the percentage of completion at that date of the objectives set in Stéphane Boissel's management contract, representing €16,500 of variable compensation, it being understood that a substantial part of this variable compensation will be evaluated as of June 30, 2016.

(11) Mr. Stéphane Boissel's benefits in kind are, pursuant to the management agreement entered into with the Company on April 27, 2015, the provision of a vehicle and unemployment insurance.

(12) On September 6, 2013, the board of directors set the fixed annual compensation allocated to Damian Marron at €180 thousand, to be paid pro rata according to his presence in the Company until December 2013 to take into account a transition period. Damian Marron's compensation was increased to €184 thousand by the board of directors on January 22, 2014, as part of its general increase policy for 2014. Damian Marron resigned as Chief Executive Officer effective April 27, 2015.

(13) The variable compensation allocated to Damian Marron was capped at €70 thousand and is conditional upon the achievement of corporate objectives defined and reviewed annually on the basis of proposals made by the nomination and compensation committee. The achievement of the 2013 and 2014 objectives was confirmed respectively by the board of directors on January 22, 2014, and on February 10, 2015. No variable compensation was paid to Damian Marron for the 2015 financial year.

(14) In respect of the 2014 financial year, Damian Marron received an exceptional bonus granted by the board of directors' meeting held on May 22, 2014, upon the recommendation of the nomination and compensation committee, in order to reflect of his involvement in the Company’s initial public offering process. Damian Marron received a severance package in the financial year 2015, in view of his departure and pursuant to the MiddleNext Code's recommendations.

(15) Mr. Eric Pottier did not receive any compensation as Deputy Chief Executive Officer. He was remunerated only for his position as Vice President for the Supply Chain and Qualified Pharmacist (*pharmacien responsable*).

(16) The board of director's meeting held on January 22, 2014 set Eric Pottier's variable compensation for 2014 at a maximum of €25 thousand, for 50% conditional upon attaining the corporate targets and for 50% conditional upon attaining his personnel targets, as defined and reviewed annually on a proposal by the nomination and compensation committee. The achievement of the 2014 targets was confirmed by the

board of directors on February 10, 2015. No variable compensation was paid to Eric Pottier for the 2015 financial year.

(17) In respect of the 2014 financial year, Eric Pottier received an exceptional bonus granted by the board of directors' meeting held on May 22, 2014, upon the recommendation of the nomination and compensation committee, in order to reflect his involvement in the Company's initial public offering process.

(18) Mr. Eric Pottier's benefits in kind relates to the provision of a vehicle.

- **Table 3:** Directors' attendance fees and other compensation received by non-executive corporate officers

In thousands of euros Name	2015 financial year		2014 financial year	
	Amount due	Amount paid	Amount due	Amount paid
Bernard Daugeras – Director				
Director's attendance fees	0	0	0	0
Other compensation	0	0	0	0
Total	0	0	0	0
Emmanuel Fiessinger – Director (1)				
Director's attendance fees	0	0	0	0
Other compensation	0	0	0	0
Total	0	0	0	0
Marie-Laure Garrigues – Director				
Director's attendance fees	0	0	0	0
Other compensation	0	0	0	0
Total	0	0	0	0
Thibaut Roulon – Director (2)				
Director's attendance fees	0	0	0	0
Other compensation	0	0	0	0
Total	0	0	0	0
Marie Yvonne Landel Meunier – Independent Director				
Director's attendance fees (4) (5)	35	30	30	0
Other compensation (6)	0	0	42	0
Total	35	30	72	0
David Horn Solomon – Independent Director (3)				
Director's attendance fees (5)	35	0	0	0
Other compensation (6)	34	0	0	0
Total	69	0	0	0
Laurent Arthaud – Observer				
Director's attendance fees	0	0	0	0
Other compensation	0	0	0	0
Total	0	0	0	0
Laurent Higueret – Observer				
Director's attendance fees	0	0	0	0
Other compensation	0	0	0	0
Total	0	0	0	0
Total	**104**	**30**	**72**	**0**

(1) Seventure Partners, represented by Emmanuel Fiessinger, resigned its seat on the board effective March 9, 2015.

(2) Bpifrance Participations, represented by Thibaut Roulon, was appointed a director by the Shareholders' Meeting of May 26, 2015.

(3) David Solomon was named an independent member of the board of directors by the board of directors on March 30, 2015.

(4) The 2014 directors' attendance fees allocated to Marie-Yvonne Landel-Meunier, authorized by the Ordinary and Extraordinary Shareholders' Meeting held on March 7, 2014 was set by the board of directors on May 22, 2014 at a maximum of €30 thousand depending on her attendance and the time actually spent on her duties. After reviewing these two criteria for 2014, the board of directors on November 19, 2014 voted to allocate to Marie-Yvonne Landel-Meunier the maximum director's attendance fee.

(5) On March 30, 2015 the board of directors set the directors' attendance fees to be paid to Marie-Yvonne Landel-Meunier and David Horn Solomon at a maximum of €35 thousand depending on their attendance and the time actually spent on their duties. After reviewing these two criteria for 2015, the board of directors on February 3, 2016 voted to award these two directors the maximum director's fee.

(6) Other compensation refer to the valuation of the warrants awarded during the year, according to the method used in IFRS accounting, corresponds to the probability-weighted value of the awarded plan after a non-transferability discount. In the financial statements given in paragraph 20.1 of the *Document de Référence*, these charges are spread over the vesting periods of the warrants.

- **Table 4:** Warrants and stock options (subscription or purchase) allocated to each executive corporate officer during the financial year

Name	Date of grant	Value of warrants and stock options as per method used in the financial statements published in accordance with IFRS (in thousands of euros)	Number of warrants and stock options allocated	Subscription price per share (€)	Expiry date
François Meyer – Chairman of the board of directors					
BSA 03-15	03/30/2015	84	50,000	5.97	03/30/2025
Stéphane Boissel – Chief Executive Officer					
SB 2015 Options	04/27/2015	451	300,000	5.56	04/27/2025
Eric Pottier – Deputy Chief Executive Officer					
2015 Options	04/27/2015	19	10,000	5.56	04/27/2025
TOTAL		**555**	**360,000**		

- **Table 5:** Warrants and stock options (subscription or purchase) exercised by each executive corporate officer during the financial year

None.

- **Table 6:** Free shares granted during the year to each corporate officer

No free shares were allocated during the financial year 2015. However, the board of directors of May 2, 2016 allocated 150,000 free shares to Stéphane Boissel, fully subject to performance conditions (see paragraph 21.1.4.3 of the *Document de Référence*).

- **Table 7:** Free shares that became available during the year

None.

- **Table 8:** Past awards of warrants and stock options (purchase or subscription)

Please refer to the tables in paragraphs 21.1.4.1 and 21.1.4.2 of the *Document de Référence*.

- **Table 9:** Stock options (subscription or purchase) allocated to the top ten beneficiary employees who are not corporate officers, and options exercised by them

Stock options granted to the first ten eligible employees who are not corporate officers and options exercised by them	Total number of options allcoated / of shares subscribed or purchased	Weighted average price (in €)	2014 T1 Options	2014 T2 Options	2015 Options
Stock options granted during the financial year by the Company or any company within the scope of option allocations, to the ten employees of the issuer or any other company within this scope, who received the highest number of such options (aggregate information)	137,968	5.56	0	0	92,968
Stock options held on the Company and the aforesaid companies, exercised during the financial year, by the ten employees of the issuer and these companies who purchased or subscribed to the highest number of such options (aggregate information)	58,011	5.58	45,543	11,093	0

- **Table 10:** Past awards of free shares

Please refer to the tables in paragraph 21.1.4.3 of the *Document de Référence*.

- **Table 11:** Details of compensation and other benefits granted to executive corporate officers

Executive corporate officers	Contract of employment		Supplementary pension plan		Compensation or benefits that will or may be paid if the officer leaves office or changes office		Payments under non-competition clause	
	Yes	No	Yes	No	Yes	No	Yes	No
François Meyer **Chaiman of the board of directors**		X		X		X		X
Start of office:	By decision of the shareholders' metting hel on September 28, 2012, member for a six-year term of office to expire following the general meeting convened to vote on the financial statements for the financial year ending on December 31, 2017 By decision of the board of directors on September 6, 2013, Chairman of the board of directors (separation of the functions of Chairman and Chief Executive							
Term of office:	Following the general meeting convened to vote on the financial statements for the financial year ending on December 31, 2017							
Stéphane Boissel **Chief Executive Officer**		X	(1)			X	(2)	
Start of office:	By decision of the board of directors on April 27, 2015							
Term of office:	Following the general meeting convened to vote on the financial statements for the financial year ending on December 31, 2017							
Eric Pottier **Deputy Chief Executive Officer**	X			X		X	(3)	
Start of office:	By decision of the board of directors on January 22, 2013							
Term of office:	Resignation with effect on February 2, 2016							

(1) In accordance with the management contract signed on April 27, 2015 (see paragraph 16.2 of the *Document de Référence*), the Company has implemented an Article 83-type supplemental pension policy effective April 1, 2016, for Mr. Stephane Boissel, as for all employees of the Company.

(2) Stéphane Boissel is obliged to comply with a non-competition clause until 12 months have passed after the expiration of his term of office as Chief Executive Officer. In consideration for this clause he will receive, for as long as it is in effect, a monthly compensation equal to 40% of his last monthly gross fixed compensation.

(3) Eric Pottier was subject to a non-competition clause, which was lifted by the board of directors on February 3, 2016.

15.2 Provisions for the payment of pensions, retirement benefits and other benefits to corporate officers

The Company has not recorded any provision for the payment of pensions, retirement benefits and other benefits to members of the board of directors and executive officers.

The Company has subscribed to directors and officers insurance from AIG. This policy covers all the de facto and de jure executive officers of the Company and its subsidiaries within a limit of €5 million, worldwide, with the exception of claims relating to professional misconduct committed in subsidiaries located in common law countries (please refer to paragraph 4.8 of the *Document de Référence*).

The Company has subscribed to an unemployment insurance policy for executives (*Garantie Sociale des Chefs dirigeants d'entreprise - GSC*) for Stéphane Boissel, effective August 1, 2015.

15.3 Free shares, warrants and stock options allocated to corporate officers

A detailed description of each of the above-mentioned plans can be found in paragraph 21.1.4 of the *Document de Référence*. The figures correspond to the total number of shares that can be subscribed following the exercise, or as appropriate the acquisition, of all the rights or securities giving access to the Company's share capital.

16. FUNCTIONING OF ADMINISTRATIVE AND MANAGEMENT BODIES

16.1 Management of the Company

The Company is a French limited liability company (*société anonyme*) with a board of directors, whose operation is described in the bylaws, which are available on the Company's website: www.txcell.com.

The Company's board of directors is chaired by Mr. François Meyer as Chairman of the board of directors. The Company is managed by Mr. Stéphane Boissel as Chief Executive Officer, appointed by the board of directors on April 27, 2015, succeeding to Mr. Damian Marron, who resigned from his position as Chief Executive Officer of the Company effective April 27, 2015.

Mr. Eric Pottier resigned from his position as Qualified Pharmacist (*pharmacien responsable*) and from his office as Deputy Chief Executive effective February 2, 2016. On February 3, 2016 the board of directors acknowledge this resignation and waived Eric Pottier's non-competition clause. Mr. Eric Pottier was then dismissed on economic grounds on March 17, 2016 in connection with the closing of the Besançon site.

Powers of the Chief Executive Officer

The powers of the Chief Executive Officer are described in Article 14 of the Company's bylaws. The Chief Executive Officer is vested with the broadest powers to act in the Company's name in all circumstances. He exercises his authority within the limits of the Company's purpose and subject to the authority expressly granted by law to the general shareholders' meetings and to the board of directors.

In addition, the shareholders agreement dated on March 27, 2014 provides that the following major decisions require prior consent by the board of directors:

- actions likely to affect the Company's strategy, its capital, its financial structure or the scope of its activity;
- approval or alteration of the Company's business plan and adoption of the annual budget;
- merger, spin-off, partial asset transfer or any similar or equivalent operation, dissolution, liquidation, management lease or sale of business assets, or the transfer of critical assets, with respect to both the Company and its subsidiaries;
- acquisitions or disposals, equity investments or sale of equity in other entities, or joint-ventures, for an amount greater than €1 million each or a combined amount greater than €5 million; any exchanges of property or securities as part of an acquisition or disposal;
- investments or disinvestments (in the form of capital expenditures or operating expenditures), commitments or de-commitments, acquisitions or disposals of assets not in the annual budget and for an amount greater than €5 million each including credit facilities and leasing agreements; any decision by the Company or one of its subsidiaries that might put the Company or its subsidiary in default under the financing subscribed by the Company or its subsidiaries;
- offering sureties, endorsements or guarantees on the property of the Company or its subsidiaries, granting any off-balance sheet commitment outside the normal course of business;
- agreements establishing or altering the main terms and conditions of any agreement related to strategic partnerships;
- sale or transfer of intellectual property rights and R&D results, as well as any license associated therewith, outside the normal course of business or not anticipated in the annual budget;
- implementing and conducting significant disputes and transactions related to such disputes;
- amending the rules concerning the composition of the board of directors or the voting on issues brought before the board of directors;
- changing the important decisions made as to the above;

- recruiting facility managers or department managers employed by the Company or one of its subsidiaries categorized in group XI as defined in rider no. 1 to the national collective agreement of the pharmaceutical industry of April 6, 1956 entitled "*Accord du 11 mars 1997 relatif aux classifications et aux salaires*";
- any signing, amending and/or terminating by the Company or one of its subsidiaries of an agreement directly or directly concluded with an affiliate, shareholder, member of the board of directors, a director and/or any other officer of the Company or one of its subsidiaries, (including any regulated agreement as defined by the French commercial code (*code de commerce*));
- convening the general shareholders' meeting or proposing any resolution to that body.

16.2 Agreements entered into between managers and the Company, and other tasks assigned to the managers by the Company

Mr. Eric Pottier resigned from his office as Deputy Chief Executive Officer effective February 2, 2016 and from his position as Qualified Pharmacist (*pharmacien responsable)*; under which position he had the powers and attributions referred to in Article R. 5124-36 of the French public health code (*code de la santé publique*). Mr. Eric Pottier was then dismissed on economic grounds on March 17, 2016 in connection with the closing of the Besançon site.

The Company entered into a management agreement with Stéphane Boissel following his appointment as the Company's Chief Executive Officer by the board of directors on April 27, 2015, with a view to determining the main terms and conditions of his duties as Chief Executive Officer. The board of directors, at a meeting held on April 27, 2015 authorized the signature of said management agreement. This agreement was approved by the general combined shareholders' meeting held on April 21, 2016. As consideration for his duties, Mr. Stéphane Boissel receives (i) a yearly fixed compensation, (ii) a variable compensation based on the achievement of objectives set annually by the Company's board of directors, and (iii) in-kind benefits consisting of the payment of business travels, an unemployment insurance policy for managers (*Garantie Sociale des Chefs et dirigeants d'entreprise* - GSC), and an "Article 83" type supplementary social security, healthcare and retirement protection. This supplemental pension was implemented as of April 1, 2016 for Stéphane Boissel, as it was for all employees of the Company;

On September 6, 2013, the Company's board of directors entrusted Mr. François Meyer to assist the executive management team in connection with a certain number of specific topics (assisting the Chief Executive Officer with the Company's development, giving access to his professional network, regular visits to the Company's facilities, and pursuing negotiations related to a pharmaceutical partnership). The board decided that from October 1, 2013 François Meyer would receive an annual compensation for this special assignment and his normal duties. The meeting held by the board of directors on February 10, 2015 re-evaluated and reviewed the allocation of the compensation to be received by Mr. François Meyer as of February 1, 2015 in order to make a clear distinction between the sums received for his duties as Chairman of the board of directors and the sums received as part of his specific mission. This modification was approved by the general combined shareholders' meeting held on April 21, 2016. On February 3, 2016, the board of directors modified the terms of this mission in order to exclude the pursuit of negotiations related to the pharmaceutical partnership, the latter having been terminated. Subject to this modification, the board approved the continuation of this specific mission for 2016.

None of the other officers have entered into any contracts with the Company.

16.3 Operation of the board of directors and of the special committees

16.3.1 The board of directors

The composition and information relating to the members of the management bodies are developed in chapter 14 and paragraph 21.2 of the *Document de Référence*.

The members of the board of directors may be remunerated through the allocation of attendance fees allocated on the basis of their assiduousness the board of directors' meetings and their involvement in special committees.

The board of directors meeting held on March 30, 2015 set the maximum amount of attendance fees to be allocated to Marie-Yvonne Landel-Meunier and to David Horn Solomon at €35,000 depending on their attendance and on the time actually dedicated to their duties. On February 3, 2016, after reviewing these two criteria, the board of directors decided to allocate to both members of the board, for the financial year 2015, the maximum amount of attendance fees.

The Company's bylaws and the board of directors' internal regulations are also available on the Company's website: www.txcell.com.

The internal regulations include, in particular, the rules of conduct and obligations of the members of the Company's board of directors. Each member of the board of directors undertakes to maintain his independence of analysis, judgment and action and to actively participate in the work of the board. He informs the board of directors of conflict of interest situations that he may encounter. Furthermore, these regulations recall the rules relating to the dissemination and use of privileged information in force and specify that its members must abstain from engaging in transactions on securities of the Company when they hold privileged information. Each member of the board of directors is bound to report to the Company and to the AMF all transactions that he carries out, directly or indirectly, on the Company's securities.

The board of directors believes that it has two independent members as defined by the MiddleNext Code, Ms. Marie-Yvonne Landel-Meunier and Mr. David Horn Solomon, inasmuch as each of these individuals:

- are not employees or officers of the Company or a company in its group, nor have they been for the past three years;
- are not a major customer, supplier or bank of the Company or one for which the Company or its group represents a significant proportion of its business;
- are not major shareholders of the Company;
- have no close family ties with any officer or major shareholder; and
- have not been an auditor of the Company during the past three years.

The number of meetings of the board of directors takes into account the different events concerning the Company's life. Hence, the members of the board are convened as regularly as the interest of the Company dictates.

The board of directors met eleven times during the financial year 2015, with an attendance rate of 84%.

It is reminded that at the date of the *Document de Référence*, the board of directors comprises of two observers (*censeurs*). The observers are convened to the meetings of the board of directors under the same conditions as the board members and benefit, to this end, of a right to information prior to the meetings of the board under the same conditions as the board members. They attend the board of directors' meetings and take part in the deliberations without having any voting rights (see paragraph 21.2.2.2 of the *Document de Référence* related to the statutory provisions regarding the observers).

16.3.2 Special committees

On March 7, 2014, the board of directors approved the internal regulations with regard to its audit committee and its nomination and compensation committee.

16.3.2.1Audit committee

The audit committee's internal regulations have been modified by the board of directors on February 10, 2015. The main terms of the audit committee's internal regulations are described below.

16.3.2.1.1 Composition

The audit committee is composed, if possible, of two members appointed by the board of directors on the basis of recommendations by the nomination and compensation committee. Members of the audit committee are chosen from amongst the board of directors, with the exception of those who hold an

executive management position. At least one member of the committee must be an independent member with specific financial or accounting expertise, and all the members must have a minimum understanding of financial and accounting matters.

It is emphasized that none of the members of the board of directors who also holds a management position within the Company can sit on the audit committee.

The composition of the audit committee was modified by the board of directors on March 30, 2015, subject to the appointment of Bpifrance Participations at the general shareholders' meeting held on May 26, 2015. Bpifrance Participations, represented by Thibaut Roulon, was appointed as a member of the board of directors by the general shareholders' meeting held on May 26, 2015.

Thus, from January 1, 2015 to May 26, 2015, the audit committee was composed of:

- Marie-Yvonne Landel-Meunier, as chairman of the committee; and
- Bpifrance Investissement, represented by Marie-Laure Garrigues.

Since May 26, 2015, the audit committee has been composed of:

- Marie-Yvonne Landel-Meunier, as chairman of the committee; and
- Bpifrance Participations, represented by Thibaut Roulon.

It is stated that Marie-Yvonne Landel-Meunier, an independent member, has specific financial and accounting expertise.

16.3.2.1.2 Assignments

The audit committee's assignments include, in particular:

- monitoring the process for preparing the financial information;
- monitoring the effectiveness of the internal control and risk management systems;
- monitoring the legally required audit of the annual financial statements by the statutory auditors;
- issuing a recommendation concerning the statutory auditors to be proposed for appointment at the general shareholders' meeting, and reviewing the terms of their compensation;
- monitoring the independence of the statutory auditors;
- examining the conditions under which derivatives are used;
- regularly reviewing major disputes; and
- generally, providing advice and issuing appropriate recommendations in connection with any of the above matters.

16.3.2.1.3 Operation

The audit committee meets at least four times a year, with the statutory auditors if the committee chairman considers it necessary, in accordance with a schedule determined by the committee chairman, in order to examine, inter alia, the annual financial statements, half yearly financial statements and, if applicable, quarterly financial statements, on the basis of an agenda drawn up by the committee chairman and sent to the members of the audit committee at least seven days before the date of the meeting. It will, in any event, meet to examine the annual financial statements before the board of directors is convened to approve them. It will also meet whenever requested by its chairman, by two of its members or by the Chairman of the Company's board of directors.

The audit committee may interview any of the members of the Company's board of directors, and may organize any internal or external audit covering any topic that it considers being within the scope of its assignment. In that case, the chairman of the audit committee will inform the board of directors in advance. The audit committee is in particular entitled to interview any person involved in the preparation of the financial statements or their verification (Chief Executive Officer, senior financial managers).

The audit committee interviews the statutory auditors. It may interview them without any Company representatives being present.

16.3.2.1.4 Reports

The chairman of the audit committee will ensure that reports presented to the board of directors on the committee's work are sufficiently detailed to ensure the board is fully informed, thus facilitating its deliberations.

The annual report will contain a presentation of the committee's work over the past financial year.

If, in the course of its work, the audit committee detects any material risk which, in its opinion, is not being dealt with adequately, the committee chairman will immediately inform the Chairman of the board of directors.

16.3.2.2Nomination and compensation committee

16.3.2.2.1 Composition

By means of a decision of the board of directors dated March 7, 2014 the Company has set up a nomination and compensation committee. The members of this committee have defined how the committee operates in internal regulations that were approved by the board of directors on the same day. The main terms of the nomination and compensation committee's internal regulations are described below.

If possible, the nomination and compensation committee is composed of at least two members of the board of directors, designated by the board. As far as possible, independent board members will make up the majority of its members.

It is stated that none of the members of the board of directors who also hold an executive management position within the Company can sit on the nomination and compensation committee.

The composition of the nomination and compensation committee was modified by the board of directors on March 30, 2015, following the resignation on March 9, 2015 of Seventure Partners, represented by Emmanuel Fiessinger.

Thus, from January 1, 2015 to March 30, 2015, the nomination and compensation committee was composed of:

- Seventure Partners, represented by Emmanuel Fiessinger, as chairman of the committee;
- Bpifrance Investissement, represented by Marie-Laure Garrigues; and
- Marie-Yvonne Landel-Meunier.

Since March 30, 2015, the nomination and compensation committee has been composed of:

- David Horn Solomon, as chairman of the committee;
- Bpifrance Investissement, represented by Marie-Laure Garrigues; and
- Auriga Partners, represented by Bernard Daugeras.

16.3.2.2.2 Assignments

The nomination and compensation committee's assignments include, in particular:

- with regard to appointments:
    - presenting recommendations to the board of directors concerning the composition of the board of directors and its committees;
    - proposing to the board of directors once a year a list of its members who qualify as "independent members" in accordance with the criteria defined by the MiddleNext; Code
    - setting up a succession plan for the Company's officers and assisting the board of directors in the selection and assessment of the members of the board of directors;

- preparing a list of individuals whose appointment to the board of directors can be recommended; and
- preparing a list of individuals whose appointment to one of the board's committees can be recommended.

- with regard to compensation:
  - examining the main objectives proposed by the executive management in connection with the compensation of Company managers who are not officers, including free share and stock option plans;
  - examining the compensation of Company managers who are not officers, including free share and stock option plans, retirement and benefits schemes and other benefits in kind;
  - presenting recommendations and proposals to the board of directors concerning:
    - officers' compensation, retirement and benefits schemes, benefits in kind and other pecuniary rights, including when they leave office. The committee proposes amounts and compensation structures, including in particular the rules for calculating variable compensation taking into consideration the Company's strategy, objectives and results, as well as market practices, and
    - free share plans, stock option plans and any other similar incentive scheme including, in particular, specific allocations by name to the officers eligible for this type of scheme,
  - examining the total amount of attendance fees and their system of allocation amongst board members, as well as the terms of reimbursement of any expenses incurred by members of the board of directors;
  - preparing and presenting any reports required, when appropriate, by the board of directors' internal regulations; and
  - preparing any recommendations concerning compensation that the board of directors may ask it to present.

Generally, the nomination and compensation committee provides advice and issues appropriate recommendations in connection with any of the above matters.

16.3.2.2.3 Operating modalities

The nomination and compensation committee meets at least four times a year, in accordance with a schedule determined by the committee chairman and on the basis of an agenda drawn up by the committee chairman and sent to the members of the nomination and compensation committee at least seven days before the date of the meeting. It will also meet whenever requested by its chairman, by two of its members or by the Chairman of the board of directors.

Members of the board of directors who are not managers and who are not members of the nomination and compensation committee may attend any of its meetings.

If the Chairman of the Company's board of directors is not a member of the committee, he may be invited to attend committee meetings. The committee will invite him to present his proposals. He will not be entitled to vote and will neither take part, nor assist, in any discussion concerning his own situation.

The nomination and compensation committee can submit a request to the Chairman of the board of directors that it be assisted by any of the Company's senior managers whose skills and expertise might facilitate the discussion of any matters on the agenda. The chairman of the nomination and compensation committee or the chairman of the session will draw to the attention of any person attending a committee meeting the confidentiality obligations arising from their attendance.

16.3.2.2.4 Reports

The chairman of the nomination and compensation committee will ensure that reports presented to the board of directors on the committee's work are sufficiently detailed to ensure the board is fully informed, thus facilitating its deliberations.

The annual report will contain a presentation of the committee's work over the past financial year.

The nomination and compensation committee inter alia reviews the Company's draft report on the compensation of managers.

16.4 Corporate governance

For the sake of transparency and information to the public and in order to comply with the requirements of Article L. 225-37 of the French commercial code (*code de commerce*), the Company adopted the MiddleNext Code as its reference code.

The following table lists the various recommendations of the MiddleNext Code and specifies those with which the Company is or is not in compliance at the date of the *Document de Référence*.

MiddleNext Code recommendations	Compliance	Non-compliance
I. Executive authority		
R 1: Corporate officers with employment contracts	X	
R 2: Definition and transparency of the compensation of executive corporate officers	X	
R 3: Severance pay	X	
R 4: Supplemental pension plans	X	
R 5: Stock options and allocation of free shares	X (1)	
II. Supervisory authority		
R 6: Implementation of the board internal regulations	X	
R 7: Code of conduct for the members of the board of directors	X	
R 8: Composition of the board - Presence of independent members	X	
R 9: Selection of directors	X	
R 10: Terms of office of the members of the board	X	
R 11: Information provided to members of the board	X	
R 12: Implementation of committees	X	
R 13: Meetings of the board and the committees	X	
R 14: Compensation of the member of the board of directors	X	
R 15: Implementation of an assessment process of the board's work	X (2)	

(1) On April 27, 2015 the board of directors allocated stock options to Mr. Stéphane Boissel (see paragraph 21.1.4.1 of the *Document de Référence*). These stock options can only be exercised if certain performance conditions, linked to the clinical development plan of the Company, have been met, the completion of which will be ascertained by the board of directors. On May 2, 2016, the board of directors allocated free shares to Mr. Stéphane Boissel (see paragraph 21.1.4.3 of the *Document de Référence*). The vesting of these free shares is subject to

performance conditions linked to the realization of annual objectives, as determined by the board of directors.

(2) During the financial year 2015 the Company implemented a formalized method for assessing the board of directors' work. For this purpose, all the members of the board received a questionnaire to gather their evaluations, suggestions and comments on the way the board and the different committees are organized and function, in order to improve their effectiveness. On February 3, 2016, the board of directors made an assessment of the work done by the board and the committees, taking note of the observations made by the members of the board and the points needing improvement.

16.5 Internal control

As required by the provisions Article 222-9 of the AMF's general regulation (*règlement general*) and in accordance with Article L. 225-37 of the French commercial code (*code de commerce*), the Chairman of the board of directors will present in a report, the composition of the board, compliance with gender equality principles within the board, the conditions under which the board of directors prepares and organizes its work, and the internal control and risk management procedures existing within the Company. This report is presented in Appendix 1 of the 2015 annual financial report (*Rapport Financier Annuel 2015)* of the Company, available on the Company's website (www.txcell.com).

At the date of the *Document de Référence*, the Company has internal control procedures as described in the report prepared by the Chairman of the board of directors on corporate governance, internal control and risk management.

17. EMPLOYEES

17.1 Human Resources

17.1.1 Number of employees and breakdown

The Company's employed workforce has changed as follows at the end of each period presented:

Category	03/31/16	12/31/2015	12/31/2014
VP	6	6	4
Directors	7	4	5
Managers and Scientists	16	18	16
Technicians and workers	20	32	31
Total	**49**	**60**	**56**

On October 14, 2015, the Company announced a review of its production strategy, consisting of outsourcing all its current and future production activities in order to focus on its principal, high value-added activities, namely research, clinical development and strategic partnerships. As part of this reorganization, the Company initiated on the same day a procedure for informing and consulting with its employee representatives on the plan to permanently shut down operations at the Besançon site.

In this regard, the Company carried out an "employment preservation plan" (*Plan de Sauvergarde de l'Emploi*, "PSE") at the Besançon site. This plan called for elimination, though with the possibility of intra-company transfers, all 26 jobs with permanent contracts related to production at the Besançon site and the termination of those employees. The PSE was unanimously accepted by the Company's employee representatives on November 12, 2015 and was approved by the Franche-Comté DIRECCTE, a French government agency, on December 10, 2015.

The permanent workforce affected by the PSE breaks down as follows:

Category	PSE
VP	1
Directors	0
Managers and Scientists	5
Technicians and workers	20
Total	**26**

The headcount of 60 employees at December 31, 2015 reflects the first three economic terminations under the PSE, involving two "Technician and workers" and one "Manager and Scientists" position.

As of the date of the *Document de Référence*, all 26 employees from the Besançon site affected by the PSE have been given notice of termination, with the exception of three employees occupying a "Technician and workers" position, who were transferred to the Valbonne site.

17.1.2 Staff representatives

As part of the closing of the Besançon site, on February 8, 2016 the Company obtained authorization from the Labor Inspection Service (*Inspection du travail*) to give the Besançon employee representative notice of termination, which was done on February 9, 2016.

As of the date of the *Document de Référence*, the Company's employees are represented by two principal employee representatives and two alternate representatives, elected on April 7, 2015.

The Company believes that it maintains a good relationship with its employees, including with its employee representatives.

17.2 Equity interests and stock options held by corporate officers

Please refer to paragraph 21.1.4 of the *Document de Référence*.

17.3 Company shares held by employees

As of the date of the *Document de Référence*, the Company has not been informed of any stock ownership by an employee in the Company's share capital. The employees do however, hold 495,746 stock subscription options representing approximately 3.08% of the Company's share capital on a fully diluted basis (see paragraph 21.1.4.1 of the *Document de Référence*) and 450,000 free shares, representing approximately 2.79% of the Company's share capital on a fully diluted basis (see paragraph 21.1.4.3 of the *Document de Référence*).

17.4 Incentive and profit-sharing agreements

None.

18. MAIN SHAREHOLDERS

18.1 Capital ownership and voting rights

The following table presents the ownership of the Company's equity and voting rights as at the date of the *Document de Référence*, based on the information available:

	Situation as at the date of the *Document de Référence*, on an undiluted basis		Situation as at the date of the *Document de Référence*, on a fully diluted basis (1)			
	Number of shares	% of capital and voting rights (2)	Number of shares susbscribable on exercise of warrants and stock options	Number of free shares not vested	Number of shares after exercise of warrants and stock options and after vesting of free shares	% of capital and voting rights after exercise of warrants and stock options and after vesting of free shares (2)
Auriga Ventures II FCPR	3,912,619	30.36%	-	-	3,912,619	24.29%
Total Auriga Partners	3,912,619	30.36%	-	-	3,912,619	24.29%
Seventure Partners	1,093,442	8.48%	-	-	1,093,442	6.79%
Total Seventure Partners	1,093,442	8.48%	-	-	1,093,442	6.79%
BIOAM FCPR	295,688	2.29%	-	-	295,688	1.84%
BIOAM 1 B FCPR	147,810	1.15%	-	-	147,810	0.92%
Innobio FCPR	3,102,716	24.08%	-	-	3,102,716	19.26%
Total Bpifrance Investissement	3,546,214	27.52%	-	-	3,546,214	22.01%
Large Venture	1,451,612	11.26%	-	-	1,451,612	9.01%
Total Bpifrance Participations	1,451,612	11.26%	-	-	1,451,612	9.01%
Sub-total Bpifrance	4,997,826	38.78%	-	-	4,997,826	31.03%
Other shareholders holding less than 5% (3)	2,863,439	22.22%	169,999	-	3,033,438	18.83%
Marie-Yvonne Landel Meunier	-	0.00%	20,000		20,000	0.12%
David Horn Solomon		0.00%	20,000		20,000	0.12%
Meyer François	-	0.00%	425,251		425,251	2.64%
Stéphane Boissel	20,000	0.16%	300,000	150,000	470,000	2.92%
Total corporate officers	20,000	0.16%	765,251	150,000	935,251	5.81%
Total Scientific Advisory Board	-	0.00%	40,000	-	40,000	0.25%
Total employees	-	0.00%	495,746	450,000	945,746	5.87%
Optional equity line financing	-	0.00%	1,150,000	-	1,150,000	7.14%
TOTAL	12,887,326	100.00%	2,620,996	600,000	16,108,322	100.00%

(1) The figures appearing in the column "Number of shares after exercise of warrants and stock options" are given on a fully-diluted basis, i.e. assuming that every outstanding stock subscription option and every stock subscription warrant is exercised.

(2) At the date of the *Document de Référence* there are no existing shares with double voting rights and only treasury shares held as part of the liquidity contract have no voting rights. Therefore the difference between share capital and voting rights is considered not material and is not shown in this table due to the low number of treasury shares (16,280 treasury shares as at December 31, 2015 and no material change as of the date of the *Document de Référence*).

(3) "Other shareholders holding less than 5%" includes all the new shares of the Company issued pursuant to a private placement completed in July 2015, except for 20,000 shares subscribed by Stéphane Boissel and listed in the category of corporate officers.

The evolution of the share capital and voting rights over the last three years is presented in paragraph 21.1.7.2 of the *Document de Référence*.

During the 2015 financial year the Company received the following declarations that ownership thresholds had been crossed:

- on June 24, 2015 Seventure Partners, acting on behalf of funds that it manages, declared as an adjustment that on June 17, 2015 it had fallen below the 15% thresholds of capital and voting rights in the Company as a result of a sale of shares on the market and that on June 24, 2015 it held 1,595,020 shares in the Company, representing the same number of voting rights;
- on August 3, 2015 Auriga Partners, acting on behalf of the Auriga Ventures II venture capital mutual investment fund (*Fonds Communs de Placement à Risques* – FCPR) that it manages, declared as an adjustment that on July 28, 2015 it had fallen below the one-third threshold of

capital and voting rights in the Company as a result of the Company's capital increase and that on behalf of such fund it held 3,912,619 shares in the Company, representing the same number of voting rights;

- on August 31, 2015 Seventure Partners, acting on behalf of funds that it manages, declared as an adjustment that on August 3, 2015 it had fallen below the 10% threshold of capital and voting rights in the Company as a result of a sale of shares on the market and that on August 28, 2015 it held 1,093,442 shares in the Company, representing the same number of voting rights.

The Company has received no threshold declarations from December 31, 2015 to the date of the *Document de Référence*.

In addition, Stéphane Boissel, Chief Executive Officer, subscribed for 20,000 new shares in the Company that were issued as part of the private placement done in July 2015.

As part of the implementation of a PACEO® optional equity line financing signed on December 22, 2015, the Company issued 1,150,000 stock subscription warrants all of which were subscribed by Société Générale on January 27, 2016 at a unit price of €0.0001, for a share premium impact of €115. As of the date of the *Document de Référence*, no warrants have been exercised.

To the Company's knowledge there is no significant difference in the allocation of capital and voting rights as of the date of the *Document de Référence*.

18.2 Major shareholders not represented on the board of directors

As of the date of the *Document de Référence*, Seventure Partners holds over 5% of the Company's capital through its various funds and is not represented on the board of directors.

18.3 Major shareholders represented on the board of directors

As of the date of the *Document de Référence*, Auriga Partners, Bpifrance Participations and Bpifrance Investissement each own over 5% of the capital and are represented on the board of directors.

18.4 Voting rights held by main shareholders

As of the date of the *Document de Référence*, all shares in the Company are ordinary shares. There are no double voting rights.

The Company's treasury stock comprises shares held in connection with a liquidity contract. These shares confer no voting rights.

18.5 Control of the Company

As of the date of the *Document de Référence*, there is no controlling shareholder as defined by Article L. 233-3 of the French commercial code (*code de commerce*).

The Company has not implemented any measures to prevent any abusive exercise of control.

18.6 Shareholders' agreements and concerted actions

A shareholders' agreement was entered into on March 27, 2014 among Auriga Partners, Seventure Partners, Bpifrance Participations, Innobio, Mr. François Meyer, Mr. Miguel Forte, Mr. Arnaud Foussat, Mr. Raphaël Flipo, Mr. Damian Marron and Mr. Eric Pottier (the "Shareholders' Agreement").

Following the resignation of Damian Marron from his positions as Chief Executive Officer and member of the board of directors of the Company on April 27, 2015, the parties to the Shareholders' Agreement entered into an addendum to the Shareholders' Agreement on May 6, 2015, pursuant to which they decided that Mr. Damian Marron is no longer subject to the rights and obligations of the Shareholders' Agreement.

Following the resignation of Eric Pottier from his position as Deputy Chief Executive Officer of the Company on February 2, 2016, the parties to the Shareholders' Agreement entered into an addendum to the Shareholders' Agreement on February 3, 2016, having the same purpose as the aforementioned addendum.

This agreement does not provide for any concerted, or group, action. The details of the Shareholders' Agreement are spelled out in paragraph 14.2 of the *Document de Référence*.

Bpifrance Participations and Bpifrance Investissement, both controlled by Bpifrance S.A., have both declared that they are acting in concert with each other with regard to the Company in terms of (i) investments in the Company by the Innobio and Bioam funds managed by Bpifrance Investissement and (ii) the investment in the Company held by Bpifrance Participations and managed by Bpifrance Investissement. At December 31, 2015 Bpifrance Investissement and Bpifrance Participations held in total 38.78% of the Company's equity through the funds that they manage.

To the Company's best knowledge, there are no other shareholders acting in concert.

18.7 Agreements that could result in a change of control

To the Company's best knowledge, no agreements exist that could result in a change of control in the Company.

18.8 Pledges of Company shares

None.

19. RELATED PARTIES TRANSACTIONS

19.1 Intra-group agreements

None.

19.2 Related parties transactions

All the agreements with related parties are mentioned in the statutory auditors' special report reproduced below.

19.3 Statutory auditors' special report on regulated agreements

Audit Conseil Expertise
Membre de PKF International

ERNST & YOUNG Audit

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

TxCell

General meeting of shareholders to approve the financial statements for the year ended December 31, 2015

Statutory auditors' report on related party agreements and commitments

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TxCell

General meeting of shareholders to approve the financial statements for the year ended December 31, 2015

Statutory auditors' report on related party agreements and commitments

To the Shareholders,

In our capacity as statutory auditors of your company, we hereby report on certain related party agreements and commitments.

We are required to inform you, on the basis of the information provided to us, of the terms, the conditions and the reasons for the company's interest of those agreements and commitments indicated to us, or that we may have identified in the performance of our engagement. We are not required to comment as to whether they are beneficial or appropriate or to ascertain the existence of any such agreements and commitments. It is your responsibility, in accordance with article R. 225-31 of the French commercial code (*Code de commerce*), to evaluate the benefits resulting from these agreements and commitments prior to their approval.

In addition, we are required, where applicable, to inform you in accordance with article R. 225-31 of the French commercial code (*Code de commerce*) concerning the implementation, during the year, of the agreements and commitments already approved by the general meeting of shareholders.

We performed those procedures which we considered necessary to comply with professional guidance issued by the national auditing body (*Compagnie nationale des commissaires aux comptes*) relating to this type of engagement. These procedures consisted in verifying that the information provided to us is consistent with the documentation from which it has been extracted.

Agreements and commitments submitted for approval by the general meeting of shareholders

In accordance with article L. 225-40 of the French commercial code (*Code de commerce*), we have been advised of certain related party agreements and commitments which received prior authorization from your board of directors.

With Mr Stéphane Boissel, CEO of your company

Nature, purpose and conditions

Management agreement

On April 27, 2015 the board of directors, following the appointment of Mr Stéphane Boissel as CEO of the company, authorized the signing of the aforementioned management contract, including in particular the implementation of a supplementary pension as mentioned in article 83 of the French commercial code (*Code de commerce*).

This supplementary pension has not been signed yet by your company, thus no impact was noticed in 2015.

Reasons for the company's interest of this commitment

Your board of directors motivated this commitment as followed:

The chairman has informed the board of directors that a mandate conferred by shareholders will be concluded between your company and Mr Stéphane Boissel in order to determine his rights and obligations and to fix his net pay in conformity with his mandate.

Agreements and commitments already approved by the general meeting of shareholders

In accordance with article R. 225-30 of the French commercial code (*Code de commerce*), we have been advised that the implementation of the following agreements and commitments which were already approved by the general meeting of shareholders in prior years continued during the year.

With Mr François Meyer, chairman of the board of directors

Nature, purpose and conditions

Specific assistance mission to the head office

On September 6, 2013 the board of directors gave to Mr François Meyer "considering his history within the company and his knowledge of the company and the market on which it operates" a special assistance mission to the head office concerning the following specific fields:

- assistance to the CEO under the production process development and its industrialization, under the strategic development of the company, in particular concerning the choices of therapeutic indications, and also under the technological platforms development;
- providing his professional relationships network, particularly in order to formalize relationships with pharmaceutical labs or potential investors;
- regular visits of Sophia and Besançon sites and also visits of all other sites where the company could develop its activities, in order to be informed of the current achievements realized (at least six times a year);
- performing further negotiations under the development of a pharmaceutical partnership.

This related party agreement has been reviewed by the board of directors during the February 10, 2015 meeting which confirmed its execution pursuing.

The February 10, 2015 board of directors reevaluated and reviewed the allocation of Mr François Meyer's pay in order to proceed in a distinction between the sums received in conformity with his function as chairman of the board of directors and the sums received in conformity with his specific mission.

From February 1, 2015, Mr François Meyer's pay reaches € 60,000 annually as chairman of the board of directors and € 24,000 annually in conformity with his specific mission, more outlays providing evidence.

In this regard, the amount of the expenses booked as at December 31, 2015 is as follows:

- € 5,000 in January 2015 and relative to Mr François Meyer's pay as chairman of the board of directors, including his specific mission pay;

- € 22,000 from February to December 2015, relative to his specific mission.

Marseille and Paris-La Défense, March 9, 2016

The statutory auditors
French original signed by

AUDIT CONSEIL EXPERTISE *Membre de PKF International*	ERNST & YOUNG Audit
Guy Castinel	Cédric Garcia

20. FINANCIAL INFORMATION ON THE ISSUER'S ASSETS, FINANCIAL POSITION AND RESULTS

Only the annual audited accounts prepared in accordance with French GAAP have any legal value. These are included in paragraph 26.1 of the *Document de Référence*.

20.1 Historical financial information

20.1.1 Statement of financial position

20.1.1.1 Assets

Assets (in €k)	Note	12/31/2015	12/31/2014
Intangible assets	3	5,907	8
Property, plant and equipment	4	876	1,404
Financial assets	5	155	131
Total non-current assets		**6,939**	**1,543**
Trade receivables	6	4	1,000
Other current assets	7	4,570	3,583
Cash and cash equivalents	9	9,208	13,917
Total current assets		**13,781**	**18,501**
Total assets		**20,720**	**20,043**

20.1.1.2 Liabilities

Liabilities (in €k)	Note	12/31/2015	12/31/2014
Share capital	10	2,577	2,333
Issue premiums		29,885	21,993
Reserves		(9,576)	(1,344)
Net profit / (loss) for the year		(11,297)	(8,269)
Total shareholders' equity		**11,589**	**14,712**
Portion of long and medium-term financial payables maturing over one year	11	1,641	1,627
Other non-current liabilities	12	23	363
Total non-current liabilities		**1,664**	**1,990**
Trade and other payables	14	1,608	1,395
Other current liabilities	14	5,087	1,554
Current provisions	13	772	392
Total current liabilities		**7,467**	**3,341**
Total Liabilities		**20,720**	**20,043**

20.1.2 Statement of net income and comprehensive income

Statement of net income (in thousands of euros)	Note	12/31/2015	12/31/2014
Revenue	15	920	1,327
Other income	15	3,718	2,094
Revenue and other income		**4,637**	**3,421**
Research and development expenses	17	10,839	7,836
General and administrative expenses	18	3,460	2,243
Expenses related to share-based payments	18	483	1,615
Current operating profit / (loss)		**(10,145)**	**(8,273)**
Other operating expenses	19	1,189	0
Other operating income	19	22	0
Operating profit / (loss)		**(11,312)**	**(8,273)**
Income from cash and cash equivalents	20	42	68
Cost of gross financial debt	20	0	60
Cost of net financial debt		**42**	**8**
Other financial income	20	10	1
Other financial expenses	20	37	5
Net profit / (loss) before tax		**(11,297)**	**(8,269)**
Income taxes	21	0	0
Net profit / (loss)		**(11,297)**	**(8,269)**
Basic earnings per share (in €)	24	-0.92	-0.78

Items of other comprehensive income:

Net profit / (loss) (in thousands of euros)		(11,297)	(8,269)
Non-recyclable elements in income statement:			
Revaluations of net liabilities arising from defined benefit schemes		38	(21)
Items of other comprehensive income		**38**	**(21)**
Comprehensive income		**(11,260)**	**(8,290)**

20.1.3 Statement of changes in equity

In thousands of euros	NUMBER OF SHARES	CAPITAL	SHARE PREMIUMS	RESERVES AND RETAINED EARNINGS	OTHER ITEMS OF COMPREHENSIVE INCOME	INCOME	TOTAL
12/31/2014	**11,663,015**	**2,333**	**21,993**	**(1,312)**	**(33)**	**(8,269)**	**14,712**
Allocation of net profit / (loss) for the previous period				(8,269)		8,269	0
Subscription of BSA 03-15 warrants			21				21
S1 2015 - Exercise of 2014 Options	54,203	11	292				302
24/07/2015 - Private placement	1,166,300	233	7,698				7,931
Allocation of capital increase costs			(645)				(645)
S2 2015 - Exercise of 2014 Options	3,808	1	20				21
Expense arising from share-based payments			483				483
Liquidities Contract - Treasury shares			23				23
Actuarial gains and losses					38		38
Net profit / (loss) for the period						(11,297)	(11,297)
12/31/2015	**12,887,326**	**2,577**	**29,885**	**(9,581)**	**5**	**(11,297)**	**11,589**

20.1.4 Statement of cash flows

In thousands of euros	12/31/2015	12/31/2014
Net profit / (loss)	**(11,297)**	**(8,269)**
Elimination of items with no impact on cash and cash equivalents		
Elimination of depreciation, amortization and provisions	1,135	460
Share-based payment	483	1,615
Financial expenses arising from bonds		60
Other eliminations with no impact on cash and cash equivalents	(7)	(13)
OPERATING CASH FLOW	**(9,687)**	**(6,148)**
Change - non-current	**(313)**	**(362)**
Other eliminations of non-current items with no impact on cash and cash equivaler	27	(70)
Change in other non-current liabilities	(340)	(292)
Change - current	**(66)**	**(423)**
Change in trade receivables	997	
Change in other current assets	(987)	(1,367)
Change in trade payables	213	577
Change in other current liabilities (excluding fixed asset suppliers)	(288)	368
CHANGE IN WORKING CAPITAL REQUIREMENTS	**(379)**	**(785)**
Net cash from operating activities	**(10,066)**	**(6,933)**
Acquisition of intangible assets	(5,902)	(8)
Sale of intangible assets		
Change in intangible assets supplier account	3,905	
Other eliminations of intangible items with no impact on cash and cash equivalents	(3)	
Acquisition of property, plant and equipment	(214)	(582)
Sale of property, plant and equipment	23	17
Change in property, plant and equipment supplier account	(83)	
Acquisition of non-current financial assets	(3)	(84)
Sale of non-current financial assets	3	2
Net cash from investing activities	**(2,274)**	**(656)**
Capital increases or contributions	7,631	15,691
Receipts from loans		5,200
Interest on bonds		(60)
Loan repayments		(1)
Net cash from financing activities	**7,631**	**20,830**
NET CASH FLOWS	**(4,710)**	**13,242**
OPENING CASH	**13,917**	**676**
CLOSING CASH	**9,208**	**13,917**

20.1.5 Notes to the financial statements

Note 1: The Company

TxCell (the "Company") is a listed biotechnologies company which develops innovative personalized cellular immunotherapies for the treatment of severe chronic inflammatory and autoimmune diseases with high unmet medical need. TxCell is the only clinical stage cellular therapy company with focuses exclusively on regulatory T lymphocytes (Tregs). Tregs are a recently discovered T cell population for which anti-inflammatory properties have been demonstrated.

Highlights for the financial year

The main highlights for the 2015 financial year are as follows:

- changes in the Company's governance bodies:
    - appointment of Dr. David Horn Solomon as a new independent director and chairman of the nomination and compensation committee,
    - appointment of Stéphane Boissel as Chief Executive Officer,
    - promotion of Miguel Forte as director of operations,
    - reinforcement of the executive team with the appointment of five new vice-presidents;
- Capital increase through a private placement of €7.9 million (i.e. around 9.95% of the capital) in July 2015; the vast majority of the investors are international and healthcare specialists;
- Award of a €1.28 million grant by the Single Inter-Ministerial Fund (*Fonds Unique Interministériel* - FUI) to the consortium led by the Company for the TRUST project (TRegs in Uveitis STudy) dedicated to the production process and clinical development of Col-Treg for the treatment of autoimmune Uveitis. TxCell will receive €843 thousand as the head of the consortium;
- Review of the Company's production strategy: decision to outsource all its current and future production activities, in order to focus on its high value-added activities, namely research, clinical development and strategic partnerships. This reorganization led to the closing of the Besançon manufacturing facility;
- Signature of a subcontracting contract with MaSTherCell, a cell therapy production company based in Belgium, to produce the clinical batches of Ovasave® for the CATS29 study and an exclusivity contract to manufacture in Europe the cell therapy products arising from the Company's ASTrIA platform;
- Obtaining exclusive rights over a key patent application for CAR-Treg by signing an option agreement in November 2015 with Yeda, the famous Weizmann Institute of Sciences' recycling company;
- Signature of an agreement in December 2015 terminating the collaboration, option, development and license agreement on Ovasave® with Trizell. Under this agreement the Company regains all Trizell's rights over Ovasave® in return for paying amounts which could reach €15 million, €2 million of which at the time of signing the agreement;
- Signature of a Standby Equity Facility (PACEO®) with Société Générale, to issue up to 1,150,000 new shares (i.e. 8.92% of the capital) for 24 months from the warrant subscription date;

Note 2: Accounting principles and methods

Note 2.1: Basis of preparation of the financial statements

These financial statements were approved on March 8, 2016 by the board of directors and are not submitted to the shareholders' meeting for approval.

The principles used to compile this financial information stem from the application of:

- all the IFRS standards and interpretations adopted by the European Union and the application of which were obligatory as at December 31, 2015. They are available on the European Commission's website (http://ec.europa.eu/internal_market/accounting/ias/index_fr.htm). These principles do not differ from the IFRS standards published by the IASB;
- the accounting positions used in the absence of normative provisions.

These options and positions are as follows:

- the Company applied the following standards, amendments and interpretations adopted by the European Union and which apply from January 1, 2015:
- IFRIC 21 "Taxes";
- the annual improvements of the IFRS: 2011-2013 cycle.

The application of IFRIC 21 and other amendments and standards had no significant impact on the financial statements.

Furthermore the Company decided not to proceed with the early application of new standards, amendments of standards and interpretations, if their application was compulsory after December 31, 2015, whether they have been adopted by the European Union or not. The impact of these standards and amendments is currently being analyzed.

The financial statements have been prepared on an historical-cost basis, with the exception of financial assets, which are measured at fair value. Preparing the financial statements in accordance with IFRS requires the formulation of estimates and assumptions that affect the amounts and disclosures contained therein. Actual results may turn out to be significantly different from these estimates, depending on the different conditions and assumptions used, and where such differences are material, sensitivity analysis may be carried out as applicable. The main decisions and estimates are described in Note 2.18.

The financial statements are presented in thousands of euros.

Figures have been rounded up or down when calculating certain financial items and other information contained in the financial statements. Consequently, the totals given in certain tables may not be the exact sum of the figures that precede them.

Note 2.2: Going-concern principle

The going-concern principle was adopted in light of the following factors:

- the Company's historical loss-making position is the result of the innovative nature of its products, which require several years of research and development;
- at December 31, 2015, the Company's cash position stood at €9.2 million, and it should receive a refund from the 2015 Research Tax Credit of around €3 million between now and the end of the first semester of 2016. For its working capital requirement over the next 12 months, the Company expects to find other sources of financing, in particular through new capital increases or by signing strategic partnerships, to pursue its development plan. Otherwise, it could defer expenditure for certain programs.

Note 2.3: Intangible assets

In accordance with IAS 38, acquired intangible assets are recognized at acquisition cost on the statement of financial position.

Note 2.3.1: Research and development costs

Research costs are systematically recognized as an expense.
In accordance with IAS 38, development costs are recognized in intangible assets only if the Company can demonstrate all of the following:

- the technical feasibility of completing the intangible asset so that it will be available for use or sale;
- its intention to complete the intangible asset and use or sell it;
- its ability use or sell the intangible asset;
- how the intangible asset will generate probable future economic benefits;
- the availability of adequate technical, financial and other resources to complete the development and to use or sell the intangible asset; and
- its ability to measure reliably the expenditure during its development.

Pursuant to this standard, the Company recognizes all its research and development costs as expenses. The Company considers that the technical feasibility of its development projects is not demonstrated until the required marketing authorizations are issued, which also corresponds to the time at which virtually all of the development costs have been incurred.

Note 2.3.2: Patents

Costs associated with filing currently valid patents, and incurred by the Company before those patents are secured, are recognized in expenses, consistent with the approach used for research and development costs.

Note 2.3.3: Software

The costs of acquiring software licenses are recorded in assets, based on the costs incurred to acquire and use the software concerned.

Software is amortized on a straight-line basis over its estimated useful life. The following useful lives are applicable:

Nature of intangible asset	Duration
Software	3 years

Note 2.3.4: Other intangible assets

The acquisition costs of other intangible assets are recorded in assets when they can be measured reliably.

Other intangible assets are recognized as in progress up until the date when they satisfy the conditions to be commissioned.

Note 2.4: Property, plant and equipment

Property, plant and equipment are recognized at acquisition cost. Costs arising from major renovation and improvement work are capitalized; repair and maintenance expenses and costs associated with other renovation work are expensed as incurred.

Property, plant and equipment are depreciated on a straight-line basis over their estimated useful lives.

The following useful lives are applicable:

Nature of property, plant and equipment	Duration
Fixtures and fittings on third-party land	10 years
Component : Major construction work	20 years
Component : Miscellaneous fixtures and fittings	5 to 8 years
Component : Plumbing	8 to 10 years
Component : Air conditioning	8 to 10 years
Component : Electricity	15 years
Laboratory fittings	4 to 5 years
Laboratory equipment	5 to 6 years
IT equipment	3 to 5 years
Office furniture	3 to 10 years

Note 2.5: Non-current financial assets

Non-current financial assets include security deposits and a construction loan (see Note 5).

Financial assets and liabilities are measured and recognized in accordance with IAS 39 - Financial Instruments: Recognition and Measurement.

Loans and receivables:

This category includes loans as well as deposits and guarantees recognized under non-current financial assets.

These are recognized initially at fair value and subsequently at amortized cost, calculated using the effective interest method. Short-term receivables with no stated interest rate are measured at the original invoice amount except where the application of an implied interest rate has a material effect. The effective interest rate matches the expected future cash inflows to the current net book value of the asset in order to determine its amortized cost.

Loans and receivables are monitored for objective indications of impairment. A financial asset is impaired when an impairment test establishes that its carrying amount is higher than its estimated recoverable amount. The resulting impairment loss is recognized in the income statement.

In accordance with the IAS 32 "Financial instruments", treasury shares held under a liquidity contract are deducted from equity and the losses and profits realized on the sale of a part of the shares are neutralized in the income statement.

Note 2.6: Recoverable value of non-current assets

Tangible and intangible assets with a finite useful life are subjected to an impairment test if doubt is cast on the recoverability of their book value. Impairment is recognized up to the excess of the book value over the asset's recoverable value. The asset's recoverable value is the higher of the fair value less costs to sell and the value in use.

Note 2.7: Cash, cash equivalents and other financial assets

Cash and cash equivalents consist of immediately available cash and short-term available-for-sale securities. Cash equivalents are held for the purpose of covering short-term liquidity requirements rather than for investment or other purposes. They can be readily converted to known amounts of cash and are not exposed to any material risk of impairment.

They are measured at fair value, and any changes in value are recorded in financial income and expense.

Note 2.8: Capital

Shares are classified in equity. Capital transaction costs directly attributable to issues of new shares or options are recognized in equity as deductions against the proceeds of those issues.

Note 2.9: Share-based payments

The Company applies IFRS 2 to the equity instruments granted to employees.

In accordance with IFRS 2, the cost of equity-settled transactions is expensed against an increase in equity over the vesting period of the equity instruments in question.

The fair value of share warrants granted to employees is determined using Monte Carlo or Black & Scholes simulation techniques, as described in Note 18.

Note 2.10: Measurement and recognition of financial liabilities

Note 2.10.1: Financial liabilities at amortized cost

Borrowings and other financial liabilities are measured initially at fair value and subsequently at amortized cost, calculated using the effective interest method.

Transaction costs directly attributable to the acquisition or issue of a financial liability are deducted from the value of said liability. These costs are then amortized on an actuarial basis over the life of the liability, using the effective interest method. The effective interest rate matches the expected future cash payments to the current net book value of the liability in order to determine its amortized cost.

Note 2.10.2: Liabilities at fair value through profit and loss are measured at fair value

Liabilities at fair value through profit and loss are measured at fair value.

Note 2.10.3: Fair value

The fair value of financial instruments traded on an active market, such as available-for-sale securities, is based on their market price at the reporting date. The market prices used for financial assets held by the Company are the market bid prices at the valuation date.

The nominal amount of current receivables and payables, less any impairment losses, is presumed to be close to the fair value of those items.

Note 2.11: Grants

The Company has received a certain number of grants, which are recognized in other income (Note 15).

Grants are recognized where there is a reasonable assurance that:

- the Company will meet the conditions of the grant, and
- the conditions of their receipt have been met.

Grants receivable either as compensation for expense or losses already incurred, or as immediate financial aid with no related future costs, are recognized in income in the year in which they become receivable.

Note 2.12: Provisions

Note 2.12.1: Provisions for risks and charges

Provisions for risks and charges correspond to financial commitments arising from various risks and legal proceedings, of an uncertain maturity and amount, which the Company may face in the course of its business.

A provision is recognized where the Company has a legal or constructive obligation to a third party resulting from a past event where it is probable or certain that payment to said third party will arise from the obligation (with no equal or greater payment expected to be received from said third party), and where future payments can be reliably estimated.

The amount recognized as a provision is management's best estimate of the amount of the expense needed to settle the liability, discounted at the reporting date as applicable.

Note 2.12.2: Retirement benefit obligations

The Company's employees are entitled to statutory French retirement benefits:

a) a lump sum paid by the Company upon their retirement (defined benefit scheme);

b) a pension paid by the social security authorities and funded by employer and employee contributions (national defined contribution scheme).

The cost of retirement benefits in a defined benefit scheme is estimated using the projected unit credit method pursuant to revised IAS 19.

Under this method, the cost is recorded in the income statement in such a way as to spread it evenly over the employee's career at the Company. Past-service costs, however, are recognized immediately in expenses (increase in benefits allocated) or in income (decrease in benefits allocated) as soon as a new scheme is implemented or an existing one is modified. Actuarial gains or losses are recognized immediately and in full under equity in items of other comprehensive income.

Retirement obligations are measured at the present value of estimated future payments, using the market rate based on long-term investment grade corporate bonds with a duration equal to the estimated length of the scheme.

The Company's payments under defined contribution schemes are recorded as expenses in the income statement for the period to which they relate.

More details on retirement obligations can be found in Note 13.

Note 2.13: Income from ordinary activities

Note 2.13.1: Revenue

In 2015, the Company's revenue corresponded exclusively to the revenue generated by a research and development project within the scope of the collaboration, development, option and license agreement on Ovasave® entered into with Ferring/Trizell and which ended on December 2, 2015.

The agreement had various financial components, such as: amounts payable upon entering into the agreement; amounts payable upon reaching certain predefined development, sales and production targets, as well as one-off payments to fund research and development costs; and royalties on future product sales.

The amounts "which were payable and not reimbursable on signature" were spread over the estimated period of the Company's involvement in the future developments under the agreement and were recognized in revenue until the agreement was terminated on December 2, 2015. The amounts which were not recognized in revenue on this date were recorded under other income.

The amounts which are payable upon reaching certain predefined development, sales and production targets, are the amounts received by partners when certain scientific, regulatory or sales milestones are reached. The Company recognized this revenue when the milestone was passed and there was no risk of repaying these amounts.

License revenues are gradually recorded over the whole period of the agreement.

Note 2.13.2: Other income

Other income is recognized in accordance with IAS 20:

- **Grants:** Since its creation, and on account of its innovative nature, the Company has received grants and aid from national and local government aimed at funding its operations or specific recruitment drives. Grants are recognized in other income as and when the associated expenses are incurred, irrespective of when payment of the grants is received.
- **Research tax credit:** The French government awards research tax credits to companies to encourage them to conduct technical and scientific research. Companies that can demonstrate expenditure meeting the required criteria are eligible for a tax credit that can be offset against corporate income tax in respect of the year in which the expenditure is incurred and the following three years, or refunded where applicable (i.e. where it exceeds the amount of corporate income tax payable). Since the Company has not paid any corporate income tax since its formation, every year it receives payment of the research tax credit relating to the previous year from the French Treasury.

- **Other income:** The amounts which were payable on signing the collaboration, development, option and license agreement on Ovasave®, and not recognized in revenue on December 2, 2015, were recognized in other income.

These amounts are recognized in "other income" for the year in which the corresponding expenses are incurred.

Note 2.14: Lease agreements

The Company does not hold any finance leases pursuant to IAS 17.

Lease agreements where a significant portion of the risks and benefits is retained by the lessor are classed as operating leases. Net of any incentive, payments under an operating lease are recognized in expenses in the income statement on a straight-line basis over the duration of the lease.

Note 2.15: Income tax

The Company is subject to corporate income tax in France in connection with its activities.

Deferred taxes are recognized using the comprehensive allocation and liability methods, for all timing differences arising from the difference between the tax base and accounting base of assets and liabilities shown in the financial statements. The main timing differences relate to tax loss carryforwards. Deferred taxes are calculated based on the tax rates enshrined in law at the reporting date.

Deferred tax assets mainly corresponding to tax loss carryforwards are recognized only to the extent that it is probable that future taxable profits will be available. The Company must use its judgment to determine the probability that future taxable profits will be available.

Note 2.16: Segment information

The Company considers it operates in a single segment: research and development for pharmaceutical products to be brought to the market in the future.

The whole of the Company's research and development activity is located in France. All the Company's tangible assets are located in France. The main operational decision-makers measure the Company's performance in terms of the cash burn rate of its activities. This is why the Company's management believes it is not appropriate to break its internal reports down into separate business segments.

Note 2.17: Items of other comprehensive income

Any components of income and expense for the period that are recognized directly in equity are posted under items of other comprehensive income. This item, for the period presented, includes the impacts of changes in actuarial assumptions for provisions for retirement indemnities.

Note 2.18: Critical accounting estimates and judgments

The estimates and judgments made by management when implementing the accounting methods described above are based on historical information and on other factors, particularly the anticipation of future events that are deemed to be likely given the current circumstances. The main estimates and judgments are as follows:

Note 2.18.1: Valuation of stock options

The fair value of stock options allocated to employees is calculated on the basis of actuarial models. These models require the Company to make certain calculation assumptions, such as expected share price volatility.

Note 2.18.2: Recognizing deferred taxes for tax loss carryforwards

The Company is subject to corporate income tax in France in connection with its activities.

Deferred tax assets mainly corresponding to tax loss carryforwards are recognized only to the extent that it is probable that future taxable profits will be available. Given its stage of development, the Company does not recognize net deferred tax assets.

Note 2.18.3: Recognizing revenue generated within the scope of the collaboration agreement

Where the Company commits to future research and development, income is deferred and recognized over the estimated duration of said commitment. The use of estimates is required to determine this duration. These estimates are regularly updated to take into account development progress and outstanding future services.

Note 2.18.4: Evaluation of provisions for risks and charges

As part of its business, the Company may be exposed to certain risks, particularly those associated with its contractual obligations. As such, the Company's management must use its judgment to estimate the probability and, where applicable, the amount of a contingent liability, as well as the relevant information it will need to provide.

Note 3: Intangible assets

Changes to intangible assets break down as follows:

In thousands of euros	01/01/2015	Increases	Decreases	12/31/2015
Acquisition cost				
Software	8	0	0	8
Intangible assets in progress	0	5,902	0	5,902
Gross intangible assets	**8**	**5,902**	**0**	**5,910**
Amortization				
Software	0	3	0	3
Intangible assets in progress	0	0	0	0
Amortization of intangible assets	**0**	**3**	**0**	**3**
Net total intangible assets	**8**	**5,899**	**0**	**5,907**

On December 2, 2015, the Company and Trizell concluded an agreement terminating their collaboration, development, option and license agreement on Ovasave®. Under this agreement the Company recovered all Trizell's rights over Ovasave® in return for paying amounts which could reach €15 million, €6 million of which is fixed and €9 million of which is conditional on the future revenues generated by Ovasave®.

In 2015, the acquisition costs, for these rights, for which the amount and maturity can be fixed definitely, were recognized as an asset, i.e. €6 million. These acquisition costs were discounted in accordance with IAS 38. The 10-year French Government bond rate (*taux OAT*) at December 31, 2015 of 0.995% was used as the discount rate. The repurchase of these rights after discounting therefore totals €5.9 million

This intangible asset is recognized as in progress insofar as it has not satisfied the conditions for being put into service as at the date of this document.

Note 4: Property, plant and equipment

Changes to property, plant and equipment break down as follows:

In thousands of euros	01/01/2015	Increases	Decreases	12/31/2015
Acquisition cost				
Fixtures and fittings	1,046	15	(30)	1,031
Laboratory equipment	2,326	151	(159)	2,318
Office and IT equipment	293	44	(41)	296
Gross property, plant and equipment	**3,664**	**211**	**(230)**	**3,645**
Amortization				
Fixtures and fittings	693	204	(7)	890
Laboratory equipment	1,355	440	(149)	1,646
Office and IT equipment	213	36	(17)	232
Amortization of property, plant and equipment	**2,261**	**681**	**(173)**	**2,768**
Net total plant, property and equipment	**1,404**	**(470)**	**(57)**	**876**

The main investments in 2015 related to the purchase of laboratory equipment for the development and industrialization program for the Ovasave® production process.

The decrease in net plant, property and equipment notably results from:

- sales of laboratory equipment in 2015 related to the closure of the Besançon site;
- the depreciation of the Besançon site's laboratory equipment and furniture, recognized at their liquidation value;
- depreciation expenses for the fixtures and fittings at Besançon specifically related to the forward-looking adjustment of the depreciation plans for the closure of the site.

Note 5: Non-current financial assets

In thousands of euros	01/01/2015	Increases	Decreases	12/31/2015
Loans	5	0	0	5
Deposits and guarantees	45	4	3	45
Liquidity contract	81	23	0	105
Total non-current financial assets	**131**	**27**	**3**	**155**

Non-current financial assets include the following items:

- €45 thousand of security deposits (including €37 thousand relating to the commercial lease of the Valbonne premises);
- a €5 thousand tax free construction loan in 2011;
- the cash balance of the liquidity contract taken out with ODDO Corporate Finance for €105 thousand under this liquidity contract, 16,280 treasury shares were recognized as a reduction in shareholders' equity at December 31, 2015 compared to 16,637 shares at December 31, 2014.

Note 6: Trade receivables

Trade receivables are as follows:

In thousands of euros	12/31/2015	12/31/2014
Trade receivables	4	1,000
Total Trade receivables	**4**	**1,000**

The receivable of €1,000 thousand at December 31, 2014 corresponds to the second milestone of the collaboration, development, option and license agreement on Ovasave® with Trizell, and was collected in January 2015.

Note 7: Other current assets

Other current assets break down as follows:

In thousands of euros	12/31/2015	12/31/2014
Receivables from suppliers, advances and downpayments	17	4
Staff costs and related accounts	10	12
Grants receivable	84	61
Competitiveness and employment tax credit	86	61
Research tax credit	3,023	2,035
VAT	238	234
Other receivables	33	110
Prepaid expenses	1,078	1,065
Total other current assets	**4,570**	**3,583**

Other current assets mainly correspond to:

- a receivable for the immediate payment of the 2015 research tax credit ("*CIR*") in the amount of €3,023 thousand, compared to €2,035 thousand in 2014. It should be noted that during 2015 the tax authorities audited the Company with respect to the 2011 to 2014 research tax credits, and this did not lead to any adjustment;
- VAT credits pending reimbursement of €139 thousand for October, November, and December 2015;
- a receivable of €86 thousand for the competitiveness and employment tax credit ("*CICE*"):
  - the CICE is calculated at the rate of 6% in accordance with Article 244 quater C of the French General Tax Code,
  - the CICE is credited to a subaccount dedicated to account 64 "Staff costs",
  - on December 31, 2014 the Company received a CICE of 6% in accordance with Article 244 quater C of the French General Tax Code. After consulting staff representatives, the 2014 CICE of €61 thousand, received on November 27, 2015, was used for employee expenses;
- prepaid expenses regarding operating expenses and more specifically the staggering of the advance for subcontracting with the CRO (Contract Research Organization), including €606 thousand for SGS, the main CRO for the clinical trial of Phase IIb of Ovasave®.

Note 8: Financial instruments recorded on the statement of financial position and net profit/(loss) impact

Accounting standards relating to financial instruments have been applied to the following items:

In thousands of euros	Carrying amount	Fair value by result	Loans and receivables	Liabilities at amortized cost
Financial assets	155		155	
Trade receivables	4		4	
Other current assets	4,570		4,570	
Cash and cash equivalents	9,208	9,208		
Total financial instrument assets	**13,936**	**9,208**	**4,729**	**0**
Portion of long- and medium-term financial payables m	1,641			1,641
Trade and other payables	1,608			1,608
Other current liabilities	5,087			5,087
Total financial instrument liabilities	**8,336**	**0**	**0**	**8,336**

Note 9: Cash and cash equivalents

"Cash and cash equivalents" consist of immediately available cash and short-term available-for-sale securities.

These deposits satisfy the cash and cash equivalents classification criteria described in Note 2.7.

Cash and cash equivalents break down as follows:

In thousands of euros	12/31/2015	12/31/2014
Cash	3,201	263
Cash equivalents	6,007	13,654
Total cash and cash equivalents	**9,208**	**13,917**

Note 10: Capital

Note 10.1: Issued capital

As at December 31, 2015, the share capital was €2,577,465.20. It is divided into 12,887,326 shares, subscribed and fully paid up, with a par value of €0.20.

This excludes share warrants and stock options granted to executives and employees, which have not yet been exercised.

The change in share capital over the period breaks down as follows:

Changes over the year (in €)	Number of shares	Capital	Par value (in €)	Issue premium per share (in €)
12/31/2014	**11,663,015**	**2,332,603**		
S1 2015 - Exercise of 2014 Options	54,203	10,841	0.20	5.38
07/24/2015 - Private placement	1,166,300	233,260	0.20	6.60
S2 2015 - Exercise of 2014 Options	3,808	762	0.20	5.38
12/31/2015	**12,887,326**	**2,577,465**		

The board of directors' meeting of July 15, 2015 noted that 43,543 2014 T1 Options and 10,660 2014 T2 Options were exercised during the first six months of 2015, resulting in the issue, at a price of €5.58 premium including, of 54,203 shares with a par value of €0.20 each i.e. a capital increase of €10,840.60 in nominal value.

In a decision by the Chief Executive Officer on July 24, 2015, following the delegation granted to him by the board of directors' meeting of July 21, 2015, the Company recorded a capital increase by private placement at an issue price of €6.80, premium included, by issuing 1,166,300 shares with a par value of €0.20 each, i.e. a capital increase of €233,260.00 in nominal value.

The board of directors' meeting of November 19, 2015 noted that 3,375 2014 T1 Options and 433 2014 T2 Options 2014 were exercised during the second six months of 2015, resulting in the issue, at an issuance price of €5.58 including premium, of 3,808 shares with a par value of €0.20 each, i.e. a capital increase in par value of €761.60.

Note 10.2: Treasury shares

Under the liquidity contract with ODDO Corporate Finance, the Company, at December 31, 2015, held 16,280 treasury shares compared to 16,637 shares at December 31, 2014. These treasury shares were recognized as a reduction in shareholders' equity in the financial statements established pursuant to IFRS standards, for a total amount of €95 thousand at December 31, 2015, compared to €119 thousand at December 31, 2014.

Note 10.3: Securities giving access to the share capital

At December 31, 2015, the following stock options ("SO") and warrants ("BSA") plans were in force in the Company:

Note 10.3.1: Stock-option ("SO") plans

Description of the plan	2014 T1 Options	2014 T2 Options	SB 2015 Options	2015 Options	TOTAL
Date of meeting	07/03/2014	07/03/2014	07/03/2014	07/03/2014	-
Date of the board of directors' decision	07/03/2014	07/03/2014	27/04/2015	27/04/2015	-
Total number of stock options authorized	2,400,000	2,400,000	2,400,000	2,400,000	-
Total number of stock options attributed	203,211	720,000	300,000	137,968	**1,361,179**
including number of stock options for corporate officers	*0*	*455,000*	*300,000*	*10,000*	***765,000***
Corporate officers concerned:					
Stéphane Boissel (3)	-	-	300,000	-	**300,000**
Damian Marron (4)	-	400,000	-	-	**400,000**
Eric Pottier	-	55,000	-	10,000	**65,000**
Number of non-corporate-officer beneficiaries	20	30	0	64	
Option exercise start date	(1)	(2)	(3)	(2)	-
Option expiry date	07/03/2024	07/03/2024	27/04/2025	27/04/2025	-
Subscription price	5.58 €	5.58 €	5.56 €	5.56 €	-
Exercise methods	(1)	(2)	(3)	(2)	-
Total number of options subscribed	203,211	716,400	300,000	137,968	**1,357,579**
Cumulative number of shares subscribed at December 31, 2014	3,250	0	0	0	**3,250**
Cumulative number of canceled or voided stock options at December 31, 2014	0	1,300	0	0	**1,300**
Stock options outstanding at December 31, 2014	**199,961**	**715,100**	**0**	**0**	**915,061**
Number of canceled or voided stock options in 2015	0	277,736	0	15,000	**292,736**
Number of shares subscribed in 2015	46,918	11,093	0	0	**58,011**
Stock options outstanding at December 31, 2015	**153,043**	**426,271 (5)**	**300,000**	**122,968**	**1,002,282**
Total number of shares that can be subscribed by exercising the stock options outstanding at December 31, 2015	153,043	426,271 (5)	300,000	122,968	**1,002,282**

(1) All 2014 T1 Options are exercisable for a period of 10 years, starting from their allocation by the board of directors.

(2) One third of the 2014 T2 Options and of the 2015 Options may be exercised at the end of each year following their allocation by the board of directors.

(3) Mr. Stéphane Boissel was appointed Chief Executive Officer of the Company by the board of directors on April 27, 2015. One third of the SB 2015 Options can be exercised at the end of each year following their allocation by the board of directors and are subject to conditions of performance, which will be verified by the board of directors.

(4) Mr. Damian Marron resigned as Chief Executive Officer effective April 27, 2015.

(5) The 2014 T2 Options in circulation include 133,333 exercisable options held by beneficiaries who have left the Company.

a) 2014 T1 Options

On March 7, 2014 the Company issued a plan for 203,211 2014 T1 Options to employees within the meaning of IFRS 2. All the 2014 T1 Options were subscribed free of charge. Each 2014 T1 Option gives the right to subscribe to an ordinary share with a par value of €0.20 at a price of €5.58. The 2014 T1 Options are nontransferable and can be exercised until March 7, 2024.

During the 2015 financial year 46,918 2014 T1 Options were exercised at a price of €5.58 (issue premium included), i.e. a capital increase with a nominal value of €9,383.60.

At December 31, 2015, there were 153,043 2014 T1 Options in circulation, representing a potential capital increase of a maximum nominal amount of €30,608.60.

b) 2014 T2 Options

On March 7, 2014 the Company issued a plan for 720,000 2014 T2 Options for employees within the meaning of IFRS 2. 716,400 2014 T2 Options were subscribed free of charge. Each 2014 T2 Option gives the right to subscribe to an ordinary share with a par value of €0.20 at a price of €5.58. The 2014 T2 Options are nontransferable and can be exercised until March 7, 2024.

During the 2015 financial year 11,093 2014 T2 Options were exercised at a price of €5.58 (issue premium included), i.e. a capital increase in nominal value of €2,218.60 and 277,736 2014 T2 Options were canceled.

At December 31, 2015, there were 426,271 2014 T2 Options in circulation representing a potential capital increase of a maximum nominal amount of €85,254.20.

c) SB 2015 Options

At April 27, 2015 the Company issued a plan for 300,000 SB 2015 Options to employees within the meaning of IFRS 2. All the SB 2015 Options were subscribed free of charge. Each SB 2015 Option gives the right to subscribe to an ordinary share with a par value of €0.20 at a price of €5.56. The SB 2015 Options are nontransferable and can be exercised until April 27, 2025.

At December 31, 2015, there were 300,000 SB 2015 Options in circulation, representing a potential capital increase with a maximum nominal value of €60,000.00.

d) 2015 Options

On April 27, 2015 the Company issued a plan for 137,968 2015 Options to employees within the meaning of IFRS 2. All the 2015 Options were subscribed free of charge. Each 2015 Option gives the right to subscribe to an ordinary share with a par value of €0.20 at a price of €5.56. The 2015 Options are nontransferable and can be exercised until April 27, 2025.

15,000 2015 Options were canceled during FY 2015.

At December 31, 2015, there were therefore 122,968 2015 Options in circulation, representing a potential capital increase of a maximum nominal amount of €24,593.60.

Note 10.3.1: Share warrants ("BSA") plans

Description of the plan	BSA 04-11	BSA 03-14	BSA 05-14	BSA 03-15	TOTAL
Date of meeting	04/18/2011	03/07/2014	03/07/2014	03/07/2014	-
Date of the board of directors' decision	-	03/07/2014	05/22/2014	03/30/2015	-
Number of warrants authorized	698,289	2,400,000	2,400,000	2,400,000	-
Number of warrants issued	698,289	260,000	20,000	70,000	**1,048,289**
Number of warrants subscribed	698,289	260,000	20,000	70,000	**1,048,289**
Total number of shares that can be subscribed:	139,657 (1)	260,000	20,000	70,000	**489,657** (1)
including those which can be subscribed by corporate officers	*139,657*	*260,000*	*20,000*	*70,000*	***489,657***
Corporate officers concerned:					
François Meyer	139,657	260,000	-	50,000	**449,657**
Marie-Yvonne Landel Meunier	-	-	20,000	-	**20,000**
David Horn Solomon	-	-	-	20,000	**20,000**
Number of non-corporate-officer beneficiaries	-	-	-	-	-
Warrant exercise start date	10/18/2011	(2)	(3)	(5) (6)	-
Warrant expiry date	06/30/2016	03/07/2024	05/22/2024	03/30/2025	-
Warrant issue price	0.03 €	0.28 €	0.30 €	0.30 €	-
Warrant strike price	0.55 €	5.58 €	5.94 €	5.97 €	-
Exercise methods	(4)	(2)	(3)	(5) (6)	-
Cumulative number of canceled or voided warrants at December 31, 2014	122,032		-	-	**122,032**
Cumultive number of shares subscribed at December 31, 2014	-	-	-	-	-
Number of warrants outstanding at December 31, 2014	**576,257**	**260,000**	**20,000**	**0**	**856,257**
Number of shares subscribed in 2015	-	-	-	-	-
Number of warrants voided or canceled in 2015	-	-	-	-	-
Number of warrants outstanding at December 31, 2015	**576,257**	**260,000**	**20,000**	**70,000**	**926,257**
Total number of shares that can be subscribed by exercising the warrants outstanding at December 31, 2015	115,251 (1)	260,000	20,000	70,000	**465,251** (1)

(1) This number takes account of the reverse stock split of the Company's shares at a ratio of five existing shares for one new share decided by the shareholders' meeting held on March 7, 2014. Therefore, five BSA 04-11 warrants will be required to obtain one share, i.e. a strike price of €2.75 per share.

(2) The BSA 03-14 warrants attributed to François Meyer can be exercised as follows (i) 200,000 BSA 03-14 warrants are exercisable on subscription and (ii) an additional 20,000 BSA 03-14 warrants can be exercised at the end of every year following their award by the board of directors. The BSA 03-14 warrants can be exercised providing the beneficiary holds a corporate office with the Company or is bound to the Company by a consultancy contract on the exercise date.

(3) One third of the BSA 05-14 warrants attributed to Marie-Yvonne Landel-Meunier can be exercised at the end of every year following their attribution by the board of directors, subject to the beneficiary's continuous presence on the board of directors over the acquisition period, and subject to a condition of presence on the board on the date the BSA 05-14 warrants are exercised.

(4) All BSA 04-11 warrants are exercisable, provided that, as at the exercise date, the beneficiary is a corporate officer or contracted consultant of the Company.

(5) One third of the BSA 03-15 warrants attributed to David Horn Solomon can be exercised at the end of every year following their attribution by the board of directors, subject to the beneficiary's continuous presence on the board of directors over the acquisition period, and subject to a condition of presence on the board on the date the BSA 03-15 warrants are exercised.

(6) One third of the BSA 03-15 warrants attributed to François Meyer can be exercised at the end of each year following their attribution by the board of directors, and providing he is chairman of the board of directors on the exercise date.

a) BSA 04-11

At April 18, 2011, the Company issued a plan for 698,289 BSA 04-11 warrants to an employee within the meaning of IFRS 2. All the BSA 04-11 warrants were subscribed at €0.033 generating and issue premium of €23,043.54. Each BSA 04-11 warrant gives the right to subscribe to an ordinary share with a par value of €0.04 at a price of €0.55. The BSA 04-11 warrants are nontransferable and may be

exercised up to June 30, 2016, on the condition that the holder is either a corporate officer of the Company or has a consultancy contract with the Company.

576,257 BSA 04-11 warrants were in circulation at December 31, 2015. Following the 1-for-5 reverse stock split, decided by the shareholders' meeting of March 7, 2014, five BSA 04-11 warrants are required to subscribe for one share with a par value of €0.20, i.e. a potential issue of 115,251 shares representing a capital increase with a maximum nominal value of €23,050.28.

b) BSA 03-14

On March 7, 2014, the Company issued a plan for 260,000 BSA 03-14 warrants to an employee within the meaning of IFRS 2. All the BSA 03-14 warrants were subscribed at a price of €0.28 generating an issue premium of €72,800.00. Each BSA 03-14 warrant gives the right to subscribe to an ordinary share with a par value of €0.20 at a price of €5.58. The BSA 03-14 warrants are nontransferable and can be exercised up until 03/07/2024.

At December 31, 2015, 260,000, BSA 03-14 warrants were in circulation, representing a potential capital increase with a maximum nominal amount of €52,000.00.

c) BSA 05-14

On May 22, 2014, the Company issued a plan for 20,000 BSA 05–14 warrants to an independent director. All the BSA 05-14 warrants were subscribed at €0.30 generating and issue premium of €6,000.00. Each BSA 05-14 warrant gives the right to subscribe to an ordinary share with a par value of €0.20 at a price of €5.94. The BSA 05-14 warrants are nontransferable and can be exercised up until 05/22/2024.

At December 31, 2015, 20,000 BSA 05-14 warrants were in circulation, representing a potential capital increase with a maximum nominal amount of €4,000.00.

d) BSA 03-15

On 30 March 2015, the Company issued a plan for 70,000 BSA 03-15 warrants, 50,000 to an employee within the meaning of IFRS 2, and 20,000 to an Independent Director. All the BSA 03-15 warrants were subscribed at €0.30 generating and issue premium of €21,000.00. Each BSA 03-15 warrant gives the right to subscribe to an ordinary share with a par value of €0.20 at a price of €5.97. The BSA 03-15 warrants are nontransferable and can be exercised up until 03/30/2025.

At December 31, 2015, 70,000 BSA 03-15 warrants were in circulation representing a potential capital increase with a maximum nominal amount of €14,000.00.

The impact of share-based payments on overall profit is described in Note 18.

Note 11: Borrowings and financial payables

In thousands of euros	12/31/2015	12/31/2014
Portion of long and medium-term financial payables maturing over one year	1,641	1,627
Total non current financial payables	**1,641**	**1,627**
Total current financial payables	**0**	**0**
Total financial payables	**1,641**	**1,627**

The loans and financial payables correspond to a zero-interest innovation loan (*Prêt à Taux Zéro Innovation - PTZI*) obtained by the Company from Bpifrance Financement for a gross sum of €1.7 million, received in December 2014. This sum was paid within the scope of the Phase IIb clinical trial for Ovasave®, which started in December 2014. This financing tool, which is intended to support

innovative French companies, is complimentary to the research tax credit, because it is not taken into account to calculate this tax credit. The zero-interest innovation loan is repayable over a period of eight years, with a deferred repayment of three years. The contract stipulates several causes of prepayments, which mainly involve the abandonment or suspension of the financed project, or the occurrence of an important legal or financial event with major consequences for the Company's business.

In accordance with Note 2.10, the repayment flows for the zero-interest innovation loan are discounted on the closing date. The 10-year French Government bond rate (*taux OAT*) at December 31, 2014 of 0.837% was used to discount these flows. The discounting proceeds are processed as a grant within the meaning of IAS 20 and linearized over the duration of the project to which the loan is attached. The impact of the accretion expense of the debt is recognized as a financial expense.

The table below presents the financial liabilities maturity schedule valued at amortized cost:

In thousands of euros	Gross amount	One year at most	Over one year and 5 years at most	Over 5 years
Zero-interest innovation loan	1,641	0	1,156	485
Total loans and financial payables	**1,641**	**0**	**1,156**	**485**

Note 12: Other non-current liabilities

Other non-current liabilities total €23 thousand and correspond to the over-one-year portion of the staggering of the zero-interest innovation loan grant.

Note 13: Provisions

In thousands of euros	01/01/2015	Expenses	Reversals used	Reversals not used	12/31/2015
Provisions for risks	313	0	0	(313)	0
Provisions for expenses	80	750	0	(58)	772
Total current provisions	**392**	**750**	**0**	**(371)**	**772**

At December 31, 2015, the provisions for risk associated with the grants, which totaled €313 thousand at December 31, 2014, were reversed in full, based on the Company's estimates.

The provisions for expenses at December 31, 2015 correspond to:

- a retirement benefits provision of €21 thousand, compared to €80 thousand at December 31, 2014. This fall is mainly due to the change in assumptions used to calculate these commitments. By applying the IAS 19 standard, the positive impact on income is €20 thousand for 2015. The actuarial differences relating to the variation in the discount rates and other assumptions are recognized as items of other comprehensive income (see Note 2.12.2), constituting income of €38 thousand at December 31, 2015. The assumptions used to calculate retirement indemnities for the Company's employees, defined in the collective bargaining agreement for the pharmaceutical industry, are as follows:

Valuation date	12/31/2015
Retirement method	*For all employees:* voluntary departure at 67 years
Rate of social security charges	46.00%
Discount rate	1.674% Bloomberg indice: F66710Y IND Euros Composite Zéro coupon yield AA
Life table	TGH05 - TGF05
Rate of increase in salaries (inflation included)	1.5%
Turnover rate	12%

- a restructuring provision of €750 thousand, corresponding to the expected costs of closing the Besançon site in 2016.

Note 14: Trade payables and other current liabilities

Note 14.1: Trade payables and related accounts

In thousands of euros	12/31/2015	12/31/2014
Trade payables	838	1,120
Trade payables - invoices not yet receive	770	275
Total trade payables	**1,608**	**1,395**

No discounting has been applied to this item, since none of the amounts in question were more than a year old at the end of each reporting period.

The reduction in the trade payables item is explained notably by the payment in January 2015 of the first installments of the outsourcing contract with the CROs (Contract Research Organizations) for the Phase IIb clinical trial on Ovasave® launched in December 2014.

The increase in the trade payables - invoices not yet received item is notably explained by the costs incurred but not yet invoiced at December 31, 2015 for the transfer of technology to MaSTherCell, the CMO (Contract Manufacturing Organization) for the production of Ovasave®, launched in September 2015.

Note 14.2: Other current liabilities

In thousands of euros	12/31/2015	12/31/2014
Social security payables	978	990
Tax payables	6	19
Deferred income	125	428
Other payables	70	30
Fixed asset suppliers	3,909	87
Total other current liabilities	**5,087**	**1,554**

At December 31, 2015, deferred income was exclusively connected to operating grants. The reduction in deferred income results exclusively from recognizing as "Other income" the balance of the deferred income at December 2, 2015 under the collaboration, development, option and license agreement on Ovasave® with Trizell (see Note 15).

The balance of the fixed assets suppliers' item of €3.9 million concerns the repurchase of rights over Ovasave® from Trizell. The initial debt of €6 million was partially paid by a €2 million payment upon termination agreement signature on December 2, 2015. The balance is due for €2 million on December 2, 2017 and €2 million on December 2, 2018, i.e. €3.9 million after taking discounting into account (see Note 3).

Note 15: Income from ordinary activities

In thousands of euros	12/31/2015	12/31/2014
Business revenue	920	1,327
Revenue	**920**	**1,327**
Grants	89	58
Research tax credit	3,023	2,035
Other income	605	1
Other income	**3,718**	**2,094**
Revenue and other income	**4,637**	**3,421**

In 2015, the Company's revenue corresponds exclusively to the revenue generated by the collaboration, development, option and license agreement on Ovasave® entered into with Ferring/Trizell, from January 1, 2015 to December 2, 2015, the date on which the Company terminated the agreement and took over all the rights to the product.

The revenue breaks down as follows, up to December 2, 2015:

- €719 thousand in revenue related to the financing by Trizell of the initial phases of the process and manufacturing development of Ovasave® for the Company's future Phase III clinical study and commercialization;
- €201 thousand in revenue relating to the payment of €1,000 thousand received upon signature of the collaboration, development, option and license agreement on Ovasave® entered into with Ferring/Trizell, and amortized over the estimated duration of the involvement of the Company in future developments of the object of the agreement.

The balance at December 2, 2015 of the deferred income under the collaboration, development, option and license agreement on Ovasave® with Trizell was recognized as other income in the amount of €605 thousand.

Other income mainly comprises:

- grants in the amount of €89 thousand;
- a 2015 research tax credit receivable of €3,023 thousand, compared to €2,035 thousand as at December 31, 2014;
- other income, corresponding to the balance of deferred income as at December 2, 2015, under the collaboration, development, option and license agreement on Ovasave® entered into with Trizell, in the amount of €605 thousand.

Note 16: Staff costs

In thousands of euros	12/31/2015	12/31/2014
Salaries	3,352	2,558
Social security expenses	1,563	1,469
Expense arising from share-based payments	483	1,615
Retirement benefits	(20)	10
Total staff costs	**5,378**	**5,651**

The increase in salaries and social security expenses is mainly explained by the changes made in the executive team, the reinforcement of the management team by recruiting several vice-presidents, and

the increase in the annual average headcount following the launch of the Phase IIb clinical trial for Ovasave®.

Changes in the average headcount were as follows:

Category	12/31/2015	12/31/2014
VP	4	4
Directors	5	5
Managers and Scientists	19	13
Technicians and workers	36	21
Average headcount	**64**	**43**

The expenses relating to share-based payments are described in Note 18.

Note 17: Breakdown of expenses by function

Note 17.1: Research and development

Research and development costs break down as follows:

In thousands of euros	12/31/2015	12/31/2014
Purchase of raw materials	1,942	2,199
Scientific fees, studies and other expenses	5,097	2,163
Salaries and social security expenses	3,666	3,068
Depreciation, amortization and provisions	153	398
Retirement benefits	(19)	9
Total research and development expenses	**10,839**	**7,836**

The studies, scientific fees and other expenses item breaks down as follows:

In thousands of euros	12/31/2015	12/31/2014
Cost of acquiring patents	354	322
Fees and studies	3,649	1,144
Other	1,095	698
Total studies, scientific fees and other expenses	**5,097**	**2,163**

The reduction in the purchase of raw materials item is explained by the closure of production activities on the Besançon site since June 2015, despite an increase in raw material purchases in the first six months of 2015 for the clinical study of Phase IIb of Ovasave® launched in December 2014.

The increase in the studies, scientific fees and other expenses item is mainly explained by:

- the recognition of the advancement of subcontracting contracts with the CROs (Contract Research Organizations) for the clinical study for Phase IIb of Ovasave® launched in December 2014;
- the costs related to the development and industrialization program for the manufacturing process of ASTrIA platform products. Moreover the majority of these costs have been crossed charged within the scope of the collaboration, development, option and license agreement on Ovasave® with Trizell and recognized in revenue (see Note 2.13);
- the costs related to the technology transfer to MaSTherCell, the CMO (Contract Manufacturing Organization) for producing Ovasave®, launched in September 2015;
- the costs related to the ENTrIA research program, the second platform of products of the Company based on modified regulatory T cells.

The increase in the salaries and social security expenses item is mainly due to the reinforcement of the management team and the increase in the average annual headcount following the launch of the clinical study of Phase IIb for Ovasave®.

Note 17.2: General and administrative expenses

General and administrative expenses are presented as follows:

In thousands of euros	12/31/2015	12/31/2014
Rent, fees and other expenses	2,158	1,232
Salaries and social security expenses	1,249	959
Depreciation, amortization and provisions	55	52
Retirement benefits	(2)	1
Total general and administrative expenses	**3,460**	**2,243**

The leases, fees and other expenses item breaks down as follows:

In thousands of euros	12/31/2015	12/31/2014
Property leases	179	174
Fees	884	345
Other	1,094	712
Total rent, fees and other costs	**2,158**	**1,232**

The change in the leases, fees and other expenses item is mainly due to:

- the increase in investor relations and communication expenses after the Company's stock-market listing in April 2014;
- recruitment fees related to the changes made in the executive team and the reinforcement of the management team; and
- the increase in legal fees for contract matters.

The increase in salaries and social security expenses is mainly due to the changes made in the executive team.

Note 18: Share-based payments

Options to subscribe to the Company's capital were attributed to the employees, the executives and the independent directors of the Company in the form of warrants ("*BSA*") or stock options ("*SO*").

Note 18.1 Conditions of allotment and exercise

The following table shows the number of options acquired and exercisable, whilst the characteristics of the plans are detailed in Note 10.2:

No. of rights acquired and exercisable on	12/31/2015	06/30/2016	12/31/2016	06/30/2017	12/31/2017	06/30/2018	12/31/2018
Sub-total BSA	802,923	852,922	852,922	902,923	902,923	926,257	926,257
BSA 03-14	220,000	240,000	240,000	260,000	260,000	260,000	260,000
BSA 03-15	0	23,332	23,332	46,666	46,666	70,000	70,000
BSA 04-11	576,257	576,257	576,257	576,257	576,257	576,257	576,257
BSA 05-14	6,666	13,333	13,333	20,000	20,000	20,000	20,000
Sub-total SO	380,307	620,777	620,777	861,274	861,274	1,002,282	1,002,282
2014 T1 Options	153,043	153,043	153,043	153,043	153,043	153,043	153,043
2014 T2 Options	227,264	326,764	326,764	426,271	426,271	426,271	426,271
2015 Options	0	40,970	40,970	81,960	81,960	122,968	122,968
SB 2015 Options	0	100,000	100,000	200,000	200,000	300,000	300,000
Total	**1,183,230**	**1,473,699**	**1,473,699**	**1,764,197**	**1,764,197**	**1,928,539**	**1,928,539**

Note 18.2 Assessment of the fair value of allotted equity instruments

The following evaluation methods were used to estimate the fair value of the SOs and BSAs allocated in 2014 and 2015:

- the share price on the allocation date is equal to the strike price;
- the risk free rate is determined from the average lifespan of the instruments, based on the borrowing rates of the GRFN index;
- volatility was determined on the basis of a sample of listed companies in the biotechnology sector, both at the date on which the instruments are subscribed and over a period equivalent to the life of the options;
- the discount, which reflects the fact that, unlike equivalent options, they cannot be transferred, was calculated using the estimated "forward price" loan rate model resulting from adding the 0.75% repo rate and the risk free rate together.

As an exception, the fair value of the BSA 04-11 warrants was determined using a Monte Carlo simulation, contrary to the options allocated in 2014 whose fair value was determined using the Black & Scholes assessment model. In the absence of dividends and with comparable assumptions, there is no difference in the results with the Monte Carlo simulations.

The Company's main managers made a commitment to hold securities, which is digressive over four years. According to IFRS 2, the fair value of the allotted equity instruments must be determined taking these conditions into account. This resulted in a non-transferability discount on the valuation of these plans.

The parameters used for the plan estimates and the valuation of new plans and plans in the process of acquisition are as follows:

Description of the plan (in thousand of euros)	BSA 04-11	Options 2014 T1	Options 2014 T2	BSA 03-14	BSA 05-14	BSA 03-15	Options 2015	Options SB 2015	TOTAL
Date of award	04/18/2011	03/07/2014	03/07/2014	03/07/2014	05/22/2014	03/30/2015	04/27/2015	04/27/2015	
Price on the allocation date (in €)	0.55	5.58	5.58	5.58	5.94	5.7	5.56	5.56	
Strike price (in €)	0.55	5.58	5.58	5.58	5.94	5.97	5.56	5.56	
Average maturity used	2.50	5.79	5.79	5.34	5.79	6.00	6.00	6.00	
Average risk free rate used	2.49%	1.28%	1.28%	1.13%	0.84%	0.14%	0.18%	0.18%	
Number of valued options	576,257	199,611	720,000	260,000	20,000	70,000	137,968	300,000	2,283,836
Volatility	45%	45%	45%	45%	45%	45%	45%	45%	
Subscription price of plan	23,044	0	0	72,800	6,000	21,000			122,844
Probabilized value of the plan before discount	**39**	**457**	**1,507**	**510**	**42**	**118**	**268**	**451**	**3,393**
Non-transferability discount		18	59	40		1	1		118
Probabilized value of the plan	**39**	**439**	**1,449**	**470**	**42**	**118**	**267**	**451**	**3,275**

It should be recalled that BSA 04-11 warrants must be grouped into sets of five in order to get one Company share, and that the strike price of a share then stands at €2.75.

The annual charges recognized are shown below:

Periods (in thousands of euros)	BSA 04-11	2014 T1 Options	2014 T2 Options	BSA 03-14	BSA 05-14	BSA 03-15	2015 Options	SB 2015 Options	TOTAL
12/31/2015			67	35	16	55	101	209	483
12/31/2014		439	737	420	19				1,615

Pursuant to IFRS 2, the expenses recognized at December 31, 2015 take into account the adjustment of expenses on options which were not acquired on the beneficiaries' departure date.

Note 19: Other operating income and expenses

Other operating income and expenses correspond to the cost of restructuring the Company's activities after the closure of the Besançon site. They total -€1,167 thousand and break down as follows:

- -€820 thousand for the Employment Protection Plan (cost of redundancies and accompanying measures, outplacement costs, fees);

- -€151 thousand for the costs of closing the site (termination indemnities and expenses still due after the closure of the site);
- -€196 thousand for the depreciation expenses of the fixtures and fittings at Besançon specifically related to the forward-looking adjustment of the depreciation plans for the closure of the site, for the impairment of the site's laboratory equipment and furniture recognized at their liquidation value, and for the capital gains and losses made in 2015 on the sale of capital assets of the Besançon site.

Note 20: Financial income and expense

Financial income and expense (in thousands of euros)	12/31/2015	12/31/2014
Foreign exchange gains	10	1
Other financial income	(0)	0
Sub-total other financial income	**10**	**1**
Gains on cash and cash equivalents	1	10
Interest on cash and cash equivalents	41	58
Sub-total income from cash and cash equivalents	**42**	**68**
Total financial income	**52**	**69**
Contractual interest on bonds	0	(60)
Sub-total cost of gross financial debt	**0**	**(60)**
Foreign exchange losses	(20)	(5)
Other financial expense	(17)	0
Sub-total other financial expense	**(37)**	**(5)**
Total financial expense	**(37)**	**(65)**
Total financial income and expense	**15**	**4**

Income from cash and cash equivalents corresponds to accrued interest and short-term gains on investment securities.

Other financial expenses correspond to the accretion expense for financial flows related to the zero-interest innovation loan (see Note 11) and the accretion expense for financial flows related to trade payables on fixed assets (see Note 14.2).

Note 21: Tax expense

Based on current legislation, as at December 31, 2015 the Company has tax losses amounting to €67,598 thousand which can be carried forward indefinitely.

Taxes break down as follows:

Deferred taxes (in thousands of euros)	12/31/2015	12/31/2014
Net profit / (loss)	(11,297)	(8,269)
Actual tax charge	-	-
Net income / (loss) before tax	**(11,297)**	**(8,269)**
Theoretical tax rate	33.33%	33.33%
Theoretical tax expense / (income)	**(3,766)**	**(2,756)**
Tax differences		
- Other permanent differences	(200)	(668)
- Unrecognized deferred taxes on temporary differenc	0	0
- Recoverable deferred taxes	(19)	10
- Other non-taxable income (research tax credit and competitiveness and employment tax credit)	(1,037)	(699)
- Share-based payments	161	538
- Unrecognized tax losses	4,861	3,574
Actual tax charge	**0**	**0**
Effective tax rate	0%	0%

In France, losses can be carried forward against future profits with no time limit, but the amount that can be offset against profit in the financial year is capped at €1 million plus 50% of the taxable income exceeding €1 million in that financial year.

Net deferred tax assets from timing differences have not been recognized on the grounds of prudence, in accordance with the principles described in Note 2.15.

Note 22: Commitments

Note 22.1: Obligations arising from operating leases

On December 22, 2015, the Company signed a rider to renew the commercial lease expiring on June 30, 2016, for an annual rent of €147 thousand (the initial index-linked rent, which is now indexed annually to the quarterly service businesses index). This commercial lease is granted for a term of nine consecutive years, with the possibility of giving notice to quit every three years as well as, exceptionally, at the end of each of the first two years of the renewed lease.

Future rent and charges as at December 31, 2015 break down as follows:

- due in less than one year: €147 thousand;
- due in between one and five years: €74 thousand.

The amount of rent recognized in expenses during the year ended December 31, 2015 totaled €147 thousand.

Note 22.2: Obligations under the license agreement with INSERM

On January 30, 2006, the Company signed a license agreement with INSERM concerning patent families owned by INSERM (PTXC2) or jointly owned by INSERM and the Company (PTXC1, PTXC4, PTXC5), which was amended on December 9, 2013 and December 31, 2014 (see paragraph 11.2.1 of the *Document de Référence*).

Under the agreement, INSERM granted the Company exclusive worldwide rights to develop, manufacture and market products and processes using the relevant patents in the field of cell therapy for chronic autoimmune and/or inflammatory diseases.

This agreement is valid until the latter of the following two events takes place: the expiry or invalidation of the last patent in question or the expiry of a period of 10 years from the initial marketing of a product implementing the aforementioned patent groups in the field covered by the agreement.

It provides that in the event the Company develops and markets products, it will pay INSERM a series of conditional lump sums on the achievement of milestones reached in terms of the development, the regulatory process and the first anniversary of the market launch. As at the date hereof, total future payments for all indications could amount to €889 thousand. Note that €76 thousand excluding tax has already been paid in view of the success of the first trial. In the event the Company or its subsidiaries market(s) the products, the Company will also be required to pay tiered royalties to INSERM based on a percentage of the sales (net of sundry charges, tax and discounts) for the products using the relevant patents in the field covered by the agreement.

However, in the event the Company grants a sublicense to a third party allowing it to develop and market products using the relevant patents in the field covered by the agreement, the amounts to be paid to INSERM by the Company will be calculated as a percentage of the amounts received from the third party in connection with the development and marketing of the products.

Note 22.3: Obligations under the termination agreement with Trizell

On December 2, 2015, the Company and Trizell entered into an agreement terminating their collaboration, development, option and license agreement on Ovasave®, signed on December 12, 2013 and modified by a rider dated March 30, 2015. Under this agreement, the Company recovers all of Trizell's rights over Ovasave® in return for paying amounts which could reach €15 million including:

- a fixed €6 million, of which the Company has already paid €2 million upon signature on December 2, 2015. The balance is due on December 2, 2017 for €2 million and on December 2, 2018 for €2 million;
- a conditional €9 million on the future revenue generated by Ovasave®, which will be recognized if the contractual conditions are met.

Note 23: Related party transactions

Note 23.1: Compensation and director's attendance fees for executive corporate officers and members of the board of directors

The compensation presented below was granted to executive corporate officers and members of the board of directors during the periods shown:

In thousands of euros	12/31/2015	12/31/2014
Salaries and other short-term benefits	661	415
Probabilized cost of the stock options and warrants plans allocated during the financial year	588	1,432
Directors' attendance fees	70	30
Total	**1,319**	**1,878**

Salaries and other short-term benefits break down as follows:

In thousands of euros	2015 financial year		2014 financial year	
Name	Amount owed[1]	Amount due[2]	Amount owed[1]	Amount due[2]
François Meyer – Chairman of the board of directors (3)				
Fixed compensation (7)	82	82	60	60
Variable compensation (8)	0	0	0	28
Exceptional compensation	0	0	0	0
Director's attendance fees	0	0	0	0
Benefits in kind	0	0	0	0
Total	**82**	**82**	**60**	**88**
Stéphane Boissel – Chief Executive Officer (4)				
Fixed compensation (9)	186	186	0	0
Variable compensation (10)	17	0	0	0
Exceptional compensation	0	0	0	0
Director's attendance fees	0	0	0	0
Benefits in kind (11)	7	7	0	0
Total	**210**	**194**	**0**	**0**
Damian Marron – Chief Executive Officer (5)				
Fixed compensation (12)	60	60	184	184
Variable compensation (13)	0	46	46	22
Exceptional compensation (14)	211	211	15	15
Director's attendance fees	0	0	0	0
Benefits in kind	0	0	0	0
Total	**271**	**316**	**244**	**220**
Eric Pottier – Deputy Chief Executive Officer (6)				
Fixed compensation (15)	96	96	86	86
Variable compensation (16)	0	18	18	9
Exceptional compensation (17)	0	0	3	3
Director's attendance fees	0	0	0	0
Benefits in kind (18)	2	2	4	4
Total	**98**	**116**	**111**	**102**
Total	**661**	**708**	**415**	**410**

(1) For the financial year. Variable compensation owed for one financial year is paid in the next financial year.

(2) During the financial year.

(3) Mr. François Meyer held the office of Chairman and CEO of the Company until the meeting of the board of directors held on September 6, 2013, during which he resigned from his office as CEO. François Meyer still holds the office of Chairman of the board of directors.

(4) Mr. Stéphane Boissel was appointed CEO of the Company by the board of directors on April 27, 2015.

(5) Damian Marron was appointed CEO of the Company by the board of directors on September 6, 2013, a position from which he resigned on April 27, 2015.

(6) Mr. Eric Pottier was hired as Vice President Supply Chain on January 14, 2013 and was appointed Deputy Chief Executive Officer of the Company by the board of directors on January 22, 2013, a position from which he resigned on February 2, 2016.

(7) The board of directors' meeting held on September 6, 2013 set François Meyer's gross annual compensation at €60 thousand, covering his functions as Chairman, as well as his general management support function. The board of directors' meeting held on February 10, 2015 revalued and revised the apportionment of François Meyer's compensation to make a distinction between his compensation as

Chairman of the board of directors (€60 thousand gross per year) and the compensation for his specific mission (€24 thousand gross per year) effective February 1, 2015.

(8) There is no plan to pay François Meyer any variable compensation for his duty as the Chairman of the board of directors. The variable compensation he was paid in 2014 was related to his work as Chairman and CEO from 2013 up to the board of directors' meeting held on September 6, 2013, during which he resigned as CEO. It was approved by the board of directors of January 22, 2014 on a proposal from the nomination and compensation committee after the Company achieved 55% of its objectives in 2013.

(9) The Company entered into a management agreement with Stéphane Boissel following his appointment as the Company's CEO by the board of directors of April 27, 2015, with a view to determining the main terms and conditions of his duty as CEO. The signature of this management contract was authorized by the board of directors at its meeting held on April 27, 2015. Stéphane Boissel receives (i) a fixed annual compensation of €275,000, (ii) a variable compensation of 30% of the said fixed compensation, based on the attainment of annual targets fixed by the Company's board of directors and (iii) benefits in kind consisting of the payment of his business expenses, unemployment insurance and health and welfare protection, and a supplementary pension.

(10) Mr. Stéphane Boissel's variable compensation for 2015 was approved by the board of directors of February 3, 2016 on a proposal from the nomination and compensation committee after the Company achieved 20% of the objectives set by the management agreement of December 31, 2015.

(11) Mr. Stéphane Boissel's benefits in kind are, pursuant to the management agreement entered into with the Company on April 27, 2015, the provision of a vehicle and of unemployment insurance.

(12) On September 6, 2013, the board of directors set the fixed annual compensation allocated to Damian Marron at €180 thousand, to be paid pro rata according to his presence in the Company until December 2013 to take into account a transition period. Damian Marron's compensation was increased to €184 thousand by the board of directors on January 22, 2014, as part of the general increase policy for 2014. Damian Marron resigned as Chief Executive Officer effective April 27, 2015.

(13) Mr. Damian Marron's variable compensation was a maximum of €70 thousand conditional on the achievement of corporate targets defined and reviewed annually on the basis of proposal made by the nomination and compensation committee. The achievement of the 2013 and 2014 objectives was confirmed respectively by the board of directors on January 22, 2014, and March 10, 2015. No variable compensation was paid to Damian Marron for the 2015 financial year.

(14) In respect of the 2014 financial year, Damian Marron received an exceptional bonus granted by the board of directors' meeting held on May 22, 2014, upon the recommendation of the nomination and compensation committee in order to reflect his involvement in the Company's initial public offering process. Mr. Damian Marron received a severance package in respect of the 2015 financial year, in view of his departure and pursuant to the MiddleNext Code's recommendations.

(15) Mr. Eric Pottier does not receive any compensation as Deputy Chief Executive Officer. He is remunerated only for his position as Vice President Supply Chain and as a Qualified Person (*pharmacien responsable*).

(16) The board of director's meeting held on January 22, 2014 set Eric Pottier's variable compensation for 2014 at a maximum of €25 thousand, for 50% conditional upon attaining the corporate targets and for 50% conditional upon attaining his personnel targets, as defined and reviewed annually on a proposal from the nomination and compensation committee. The achievement of the 2014 targets was confirmed by the board of directors held on February 10, 2015. No variable compensation was paid to Eric Pottier for the 2015 financial year.

(17) In respect of the 2014 financial year, Eric Pottier received an exceptional bonus granted by the board of directors' meeting held on May 22, 2014, upon the recommendation of the nomination and compensation committee in order to reflect his involvement in the Company's initial public offering process.

(18) Mr. Eric Pottier's Benefits in kind relate to the provision of a vehicle.

The probabilized costs of the stock options and warrants plans allocated during the financial year to corporate officers break down as follows:

In thousands of euros	2015 financial year		2014 financial year	
Name	**Amount owed[1]**	**Amount due[2]**	**Amount owed[1]**	**Amount due[2]**
François Meyer – Chairman of the board of directors				
Probabilized cost of the stock option and warrants plans allocated during the financial year (3)	84	N/A	470	N/A
Total	**84**	**N/A**	**470**	**N/A**
Stéphane Boissel – Chief Executive Officer (4)				
Probabilized cost of the stock option and warrants plans allocated during the financial year (3)	451	N/A	N/A	N/A
Total	**451**	**N/A**	**0**	**N/A**
Damian Marron – Chief Executive Officer (5)				
Probabilized cost of the stock option and warrants plans allocated during the financial year (3)	0	N/A	809	N/A
Total	**0**	**N/A**	**809**	**N/A**
Eric Pottier – Deputy Chief Executive Officer				
Probabilized cost of the stock option and warrants plans allocated during the financial year (3)	19	N/A	111	N/A
Total	**19**	**N/A**	**111**	**N/A**
Marie-Yvonne Landel Meunier – Independent member				
Probabilized cost of the stock option and warrants plans allocated during the financial year (3)	0	N/A	42	N/A
Total	**0**	**N/A**	**42**	**N/A**
David Horn Solomon – Independent member (6)				
Probabilized cost of the stock option and warrants plans allocated during the financial year (3)	34	N/A	N/A	N/A
Total	**34**	**N/A**	**0**	**N/A**
Total	**588**	**N/A**	**1,432**	**N/A**

(1) For the financial year. Variable compensation owed for one financial year is paid in the next financial year.
(2) During the financial year.
(3) Share-based payments correspond to the probabilized cost of the stock options and warrants plans attributed to corporate officers during the financial year after deducting non-transferability discounts under the Shareholders' Agreement in force on the date of the allocation.
(4) Stéphane Boissel was appointed CEO of the Company by the board of directors on April 27, 2015.
(5) Damian Marron resigned as Chief Executive Officer with effect from April 27, 2015.
(6) David Horn Solomon was appointed independent member of the board of directors by the board of directors on March 30, 2015.

Directors' attendance fees break down as follows:

In thousands of euros	2015 financial year		2014 financial year	
Name	Amount owed[1]	Amount due[2]	Amount owed[1]	Amount due[2]
Marie-Yvonne Landel Meunier – Independent member				
Director's attendance fees	35	30	30	0
Total	**35**	**30**	**30**	**0**
David Horn Solomon – Independent member (3)				
Director's attendance fees	35	0	0	0
Total	**35**	**0**	**0**	**0**
Total	**70**	**30**	**30**	**0**

(1) For the financial year. Variable compensation owed for one financial year is paid in the next financial year.
(2) During the financial year.
(3) David Horn Solomon was appointed independent member of the board of directors by the board of directors of March 30, 2015, bringing the number of independent members of the board of directors to two. The same board of directors' meeting also revalued the directors' attendance fees allocated to each independent member of the board of directors.

Note 23.3: Miscellaneous

As at December 31, 2015, to the Company's knowledge, there was no management and/or financial link between its main suppliers and the members of its board of directors.

Note 24: Earnings per share

The basic earnings per share are calculated by dividing the net profit (loss) attributable to the Company's shareholders by the weighted average number of shares outstanding during the year.

The shareholders' meeting of March 7, 2014 recorded the 1-for-5 reverse stock split. According to IAS 33 "Earnings per share", the net profit / (loss) and the diluted earnings per share are presented with a retrospective adjustment of the share grouping for the periods presented, in order to be able to comparable them:

Net earnings par share	12/31/2015	12/31/2014
Net profit / (loss) (in thousands of euros)	(11,297)	(8,269)
Weighted average number of shares in circulation	12,289,456	10,560,913
Basic earnings par share (in euros)	**-0.92**	**-0.78**

Diluted earnings per share are calculated by dividing the net profit / (loss) attributable to the Company's shareholders by the following:

- the weighted average number of shares outstanding during the financial year;
- plus the number of shares that may result from the conversion of instruments giving deferred access to the share capital, as soon as such instruments have been issued.

The instruments giving deferred access to the share capital (warrants and stock options) are considered to be anti-dilutive as they result in higher earnings per share. As a result, diluted and basic earnings per share are identical.

Diluted earnings per share	12/31/2015	12/31/2014
Net profit / (loss) (in thousands of euros)	(11,297)	(8,269)
Weighted average number of potential shares*	13,760,045	11,757,317

** This weighted average number of potential shares takes into account the shares which could result from exercising the warrants and stock options, as soon as such instruments are issued.*

Note 25: Financial risk management

The main risks to which the Company is exposed are liquidity risk, currency risk, interest rate risk and credit risk.

Cash and cash equivalents constitute the principal financial instruments of the Company. These instruments are used to finance the Company's activities. It is the Company's policy not to use financial instruments for speculative purposes. The Company does not use derivative financial instruments.

Note 25.1: Liquidity risk

Cash flow forecasts are produced by the finance department. Management uses these forecasts, which are regularly updated, to monitor the Company's cash requirements and ensure that there is sufficient liquidity available to cover its operating needs.

These forecasts take into account the Company's funding plans. Any surplus cash held by the Company is invested in short-term investment securities that are sufficiently liquid to meet the flexibility requirements set forth in the above-mentioned forecasts (see Note 2.7).

Note 25.2: Currency risk

As at December 31, 2015 the Company does not consider itself exposed to a foreign exchange rate risk as only a small part of its supplies are obtained outside the Eurozone and invoiced in foreign currency, mainly in American dollars, pounds Sterling, and Swiss francs.

In view of the insignificant amounts in currency positions, at this stage of the development of its business, the Company has not made any hedging arrangements to protect its business against fluctuations in exchange rates.

However, the Company cannot rule out the possibility that a significant increase in its business could leave it more exposed to currency risk. Should this occur, the Company would put in place an appropriate policy to hedge this risk. For the year ended December 31, 2015, the Company considers that a 10% variation in exchange rates in either direction would not have a material impact.

Note 25.3: Credit risk

The Company manages its cash and cash equivalents in a conservative manner. Cash and cash equivalents are cash and current financial instruments held by the Company (exclusively short-term investment securities that can be moved immediately).

In addition, credit risk relating to cash, cash equivalents and short-term financial instruments is not significant in view of the quality of the co-contracting financial institutions.

Note 24.4: Interest rate risk

The only interest rate risk exposure concerns investments of cash and cash equivalents. Given the current low rate of return on this type of investment, the Company believes that any 1% increase or decrease would have no material effect on its net income in light of the losses generated by its operating activities.

The Company does not have any variable-rate debt. Repayments on its debts are not subject to interest rate risk.

Note 26: Events subsequent to the reporting period

The following events occurred after the closing date:

- on January 25, 2016, the Company obtained the AMF's approval of the prospectus required to set up the optional PACEO® equity financing line with Société Générale signed on December 22, 2015. The Société Générale therefore subscribed for 1,150,000 share warrants, for an overall price of €115.

20.2 Statutory auditors' report on the financial statements prepared in accordance with the IFRS standards as adopted in the European Union for the financial year ended December 31, 2015

AUDIT CONSEIL EXPERTISE
Membre de PKF International

ERNST & YOUNG Audit

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

TxCell

Year ended December 31, 2015

Statutory auditors' report on the annual financial statements prepared in accordance with IFRS as adopted by the European Union

AUDIT CONSEIL EXPERTISE
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Commissaire aux Comptes
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TxCell

Year ended December 31, 2015

Statutory auditors' report on the annual financial statements prepared in accordance with IFRS as adopted by the European Union

To the members of the board of directors,

In our capacity as statutory auditors of TxCell and in accordance with your request in connection with your financial communication, we hereby report to you on the audit of the accompanying annual financial statements prepared in accordance with IFRS as adopted in the EU, for the year ended December 31, 2015.

The preparation of these annual financial statements is the responsibility of the board of directors. Our role is to express an opinion on these financial statements based on our audit.

We conducted our audit in accordance with professional standards applicable in France. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the annual financial statements are free from material misstatement. An audit involves performing procedures, by audit sampling and other means of testing, to obtain audit evidence about the amounts and disclosures in the annual financial statements. An audit also includes evaluating the appropriateness of accounting policies used and the reasonableness of accounting estimates made by management, as well as the overall presentation of the annual financial statements. We believe that the audit evidence we have obtained is sufficient and appropriate to provide a basis for our audit opinion.

In our opinion, the financial statements present fairly, in all material respects, the assets and liabilities and the financial position of the company at December 31, 2015 and the results of its operations for the year then ended in accordance with IFRS as adopted by the European Union.

Without modifying our opinion, we draw your attention to note 2.2 "Principle of going concern" to the annual financial statements which explains the financial situation of the company at December 31, 2015, as well as the proposed measures allowing the company to cover its cash requirements.

Marseille and Paris-La Défense, March 9, 2016

The statutory auditors
French original signed by

AUDIT CONSEIL EXPERTISE
Membre de PKF International

Guy Castinel

ERNST & YOUNG Audit

Cédric Garcia

20.3 Date of the most recent financial information

The latest financial information is presented in paragraph 20.1 of the *Document de Référence*. The previous information goes back to the financial year ended December 31, 2014 and is presented in the *document de référence* registered with the AMF on June 11, 2015 under the number R.15-049.

20.4 Interim financial reports

Not applicable.

20.5 Dividend policy

20.5.1 Dividends paid during the last three years

The Company has not made a profit and therefore has not distributed dividends since it was created.

20.5.2 Dividend policy

There are no plans to introduce a dividend payment policy in the short term on account of the Company's stage of development.

20.6 Court and arbitration proceedings

As at the date of the *Document de Référence*, to the best of the Company's knowledge, there are no government, court or arbitration proceedings pending or threatened that are likely to have, or have had in the last 12 months, a material impact on the Company's financial position, business or results.

20.7 Significant change in the financial or commercial position

As far as the Company is aware, there has been no significant change in the Company's financial and commercial position from December 31, 2015 up to the date of the *Document de Référence*.

21. ADDITIONAL INFORMATION

21.1 Share capital

21.1.1 Share capital amount

At the date of the *Document de Référence*, the Company's share capital amounts to €2,577,465.20 divided into 12,887,326 shares with a par value of €0.20 each. The Company's shares are entirely subscribed and fully paid up. The entire share capital consists of ordinary shares.

The change in the share capital and the number of outstanding shares over the financial year is described in paragraph 20.1.3 "Statement of changes in shareholders' equity" of the *Document de Référence* as well as in Note 10 "Equity".

21.1.2 Non-equity securities

None.

21.1.3 Acquisition by the Company of its own shares

The combined general shareholders' meeting held on April 21, 2016 authorized the board of directors, for a period of 18 months from the date of the meeting, to carry out a share buyback program pursuant to Article L. 225-209 of the French commercial code (*code de commerce*) and in compliance with the General Regulations of the AMF. This authorization has terminated the authorization granted by the combined shareholders' meeting of May 26, 2015 with the same purpose.

A maximum purchase price per share (excluding costs and commissions) was set at €20, with a total cap of €1,000,000. The maximum number of treasury shares shall not exceed 10% of the total number of outstanding shares of the Company.

During the financial year 2015, the share buyback program of the Company was used exclusively under the liquidity contract entered into with ODDO Corporate Finance.

As of December 31, 2015 the number of treasury shares held was 16,280 (versus 16,637 as of December 31, 2014) for a total of €110 thousand (versus €105 thousand as of December 31, 2014), representing 0.13% of the Company's share capital. The cash balance in the liquidity account at the same date amounted to €105 thousand (versus €81 thousand as of December 31, 2014). During the course of the financial year 2015, pursuant to such liquidity contract, 261,900 shares were bought at an average price of €7.2405, and 262,257 shares were sold at an average price of €7.2118. These treasury shares are recognized as a deduction from shareholders' equity in the financial statements prepared in accordance with IFRS.

21.1.4 Potential share capital

At the date of the *Document de Référence*, the securities giving access to the share capital are presented below:

21.1.4.1 Stock option subscription plans

Description of the plan	2014 T1 Options	2014 T2 Options	SB 2015 Options	2015 Options	TOTAL
Date of meeting	03/07/2014	03/07/2014	03/07/2014	03/07/2014	-
Date of the board of directors' decision	03/07/2014	03/07/2014	04/27/2015	04/27/2015	-
Total number of stock options authorized	2,400,000	2,400,000	2,400,000	2,400,000	-
Total number of stock options attributed	203,211	720,000	300,000	137,968	**1,361,179**
including number of stock options for corporate officers	*0*	*455,000*	*300,000*	*10,000*	***765,000***
Corporate officers concerned:					
Stéphane Boissel (3)	-	-	300,000	-	**300,000**
Damian Marron (4)	-	400,000	-	-	**400,000**
Eric Pottier (5)	-	55,000	-	10,000	**65,000**
Number of non-corporate-officer beneficiaries	20	30	0	64	
Option exercise start date	(1)	(2)	(3)	(2)	-
Option expiry date	03/07/2024	03/07/2024	04/27/2025	04/27/2025	-
Subscription price	5.58 €	5.58 €	5.56 €	5.56 €	-
Exercise methods	(1)	(2)	(3)	(2)	-
Total number of options subscribed	203,211	716,400	300,000	137,968	**1,357,579**
Cumulative number of canceled or voided stock options as at the date of the *Document de Référence*	-	300,573	-	30,000	**330,573**
Cumulative number of shares subscribed as at the date of the *Document de Référence*	50,168	11,093	-	-	**61,261**
Number of stock options outstanding as at the date of the *Document de Référence*	**153,043**	**404,734 (6)**	**300,000**	**107,968**	**965,745**
Total number of shares that can be subscribed by exercising the stock options outstanding as at the date of the *Document de Référence*	153,043	404,734 (6)	300,000	107,968	**965,745**

(1) All 2014 T1 Options are exercisable for a ten-year period, starting from their allocation by the board of directors. Should the beneficiary leave the Company he or she has, from the time he or she ceases to be an eligible beneficiary, six months to exercise the Options that would be exercisable at the date of leaving, after which the Options are void.

Notwithstanding the above, in case of a change of control of the Company, the board of directors will have the choice of deciding that any Option not exercised before the completion of such change of control will automatically be void.

(2) The 2014 T2 and the 2015 Options are exercisable by a third at the end of each year from their allocation by the board of directors, provided that the beneficiary is still an employee and/or corporate officer of the Company or one of its affiliates. Should the beneficiary leave the Company he or she has, from the time he or she ceases to be an eligible beneficiary, six months to exercise the Options that would be exercisable at the date of leaving, after which the Options are void.

Notwithstanding the above, in case of a change of control of the Company, all Options will immediately become exercisable by the beneficiary before the completion of such change of control, and the board of directors will have the choice of deciding that any Option not exercised before the completion of such change of control will automatically be void.

(3) Stéphane Boissel was appointed Chief Executive Officer of the Company by the board of directors on April 27, 2015. The SB 2015 Options can be exercised by a third at the end of each year from their allocation by the board and are subject to performance conditions, the fulfillment of which will be established by the board of directors, provided that Stéphane Boissel remains a corporate officer of the Company or one of its affiliates. Should he leave the Company, Stéphane Boissel has, from the time he ceases to be an eligible beneficiary, six months to exercise the SB 2015 Options that would be exercisable at the date of leaving, after which the Options are void.

Notwithstanding the above, in case of a change of control of the Company, all SB 2015 Options will immediately become exercisable by Stéphane Boissel before the completion of such change of control, and the board of directors will have the choice of deciding that any SB 2015 Option not exercised before the completion of such change of control will automatically be void.

(4) Mr. Damian Marron resigned from his position as Chief Executive Officer effective April 27, 2015.

(5) Mr. Eric Pottier resigned from his position as Deputy Chief Executive Officer effective February 2, 2016.

(6) The 2014 T2 Options outstanding at the date of the *Document de Référence* include the 133,333 Options held by Damian Marron, all of which are exercisable, and the 36,666 exercisable Options held by Eric Pottier, which must be exercised by the latter within six months of the date he ceases to be an eligible beneficiary, or will otherwise become void.

21.1.4.2 Warrants ("BSA")

Description of the plan	BSA 04-11	BSA 03-14	BSA 05-14	BSA 03-15	BSA 05-16	TOTAL
Date of meeting	04/18/2011	03/07/2014	03/07/2014	03/07/2014	04/21/2016	-
Date of the board of directors' decision	-	03/07/2014	05/22/2014	03/30/2015	05/02/2016	-
Number of warrants authorized	698,289	2,400,000	2,400,000	2,400,000	500,000	-
Number of warrants issued	698,289	260,000	20,000	70,000	40,000	**1,088,289**
Number of warrants subscribed	698,289	260,000	20,000	70,000	-	**1,048,289**
Total number of shares that can be subscribed:	139,657 (1)	260,000	20,000	70,000	40,000	**529,657** (1)
including those which can be subscribed by corporate officers	*139,657*	*260,000*	*20,000*	*70,000*	-	***489,657***
Corporate officers concerned:						
François Meyer	139,657	260,000	-	50,000	-	**449,657**
Marie-Yvonne Landel Meunier	-	-	20,000	-	-	**20,000**
David Horn Solomon	-	-	-	20,000	-	**20,000**
Number of non-corporate-officer beneficiaries	-	-	-	-	-	-
Warrant exercise start date	10/18/2011	(2)	(3)	(5) (6)	(8)	-
Warrant expiry date	06/30/2016	03/07/2024	05/22/2024	03/30/2025	05/02/2026	-
Warrant issue price	0.03 €	0.28 €	0.30 €	0.30 €	0.28 €	-
Warrant strike price	0.55 €	5.58 €	5.94 €	5.97 €	5.57 €	-
Exercise methods (7)	(4)	(2)	(3)	(5) (6)	(8)	-
Cumulative number of canceled or voided warrants as at the date of the *Document de Référence*	122,032	-	-	-	-	**122,032**
Cumultive number of shares subscribed as at the date of the *Document de Référence*	-	-	-	-	-	-
Number of warrants outstanding as at the date of the *Document de Référence*	**576,257**	**260,000**	**20,000**	**70,000**	**40,000**	**966,257**
Total number of shares that can be subscribed by exercising the warrants outstanding as at the date of the *Document de Référence*	115,251 (1)	260,000	20,000	70,000	40,000	**505,251** (1)

(1) This number takes account of the reverse stock split of the Company's shares at a ratio of five existing shares for one new share decided by the shareholders' meeting held on March 7, 2014. It will therefore take five BSA 04-11 warrants to obtain one share.

(2) The BSA 03-14 warrants allocated to François Meyer are exercisable on the following schedule: (i) 200,000 BSA 03-14 are exercisable from the time they are subscribed, and (ii) 20,000 additional BSA 03-14 are exercisable at the end of each year from their allocation by the board of directors, provided in both cases that at the date of exercise the beneficiary is a corporate officer of the Company or has entered into a consultant contract with the Company.

(3) The BSA 05-14 warrants allocated to Marie-Yvonne Landel-Meunier can be exercised by a third at the end of each year from their allocation by the board of directors, subject to the beneficiary's continuous presence on the board of directors over the vesting period.

(4) All BSA 04-11 warrants are exercisable, provided that, at the exercise date, the beneficiary is a corporate officer of the Company or has entered into a consultant contract with the Company.

(5) The BSA 03-15 warrants allocated to David Horn Solomon can be exercised by a third at the end of each year from their allocation by the board of directors, subject to the beneficiary's continuous presence on the board of directors over the vesting period.

(6) The BSA 03-15 warrants allocated to François Meyer can be exercised by a third at the end of each year from their allocation by the board of directors, provided he is Chairman of the board of directors on the exercise date.

(7) In case of a change of control of the Company, all warrants allocated to any beneficiary will immediately become exercisable by such beneficiary before the completion of such change of control, and the board of directors will have the choice of deciding that any warrant not exercised before the completion of such change of control will automatically be void.

(8) The BSA 05-16 warrants have been allocated to the Scientific Advisory Board (SAB) members. The BSA 05-16 are all exercisable, provided that, at the exercise date, the beneficiary (i) is a member or observer of the board of directors of the Company or one of its affiliates, or (ii) has entered into a

consultant contract with the Company or one of its affiliates, or (iii) is a member of any committee implemented by the board of directors.

21.1.4.3Free shares (AGA)

Description of the plan	2016 AGA employees	2016 AGA management	TOTAL
Date of meeting	21/04/2016	21/04/2016	-
Date of the board of directors' decision	02/05/2016	02/05/2016	-
Total number of free shares authorized	750,000	750,000	-
Total number of free shares attributed	450,000	150,000	**600,000**
including number of free shares for corporate officers	-	*150,000*	***150,000***
Corporate officers concerned: Stéphane Boissel	-	150,000	**150,000**
Vesting date	(1)	(2)	-
End of the holding period	(3)	(3)	-
Cumulative number of shares subscribed as at the date of the *Document de Référence*	-	-	-
Cumulative number of canceled or voided free shares as at the date of the *Document de Référence*	-	-	-
Number of free shares outstanding as at the date of the *Document de Référence*	**450,000**	**150,000**	**600,000**

(1) The 2016 AGA employees are acquired by a third at the end of each year from their allocation by the board of directors, provided that the acquisition is subject to a condition of presence, and, for some employees, to performance conditions, linked to the realization of annual objectives by the beneficiary, as determined by the board of directors.

In case of a change of control of the Company, all AGA allocated to a beneficiary will immediately become acquired at the later of the two following date: (i) the first anniversary of the allocation date (the condition of presence is then lifted and the vesting period is completed with a holding period expiring on the second anniversary of the allocation date, i.e. on May 2, 2018) and (ii) the date of completion of the change of control (said date marking the end of the vesting period), if necessary extended by a holding period up to the second anniversary of the allocation date, i.e. on May 2, 2018.

(2) The 2016 AGA management are acquired by a third at the end of each year from their allocation by the board of directors, provided that the acquisition is subject to a condition of presence, and to performance conditions, linked to the realization of annual objectives by the beneficiary (i.e. financing, progess on research and development programs, signature of strategic partneships), as determined by the board of directors.

In case of a change of control of the Company, all AGA allocated to a beneficiary will immediately become acquired, at the same conditions as described in (1) above.

(3) The first third of the allocated free shares is subject to a one-year holding period from the date of acquisition, i.e. until May 2, 2018. No holding period was set for the two other thirds, subject to the provisions applicable in case of a change of control as described in (1) above.

21.1.4.4Other dilutive instruments

On December 22, 2015 the Company announced that it had entered into an optional equity financing line ("PACEO®") with Société Générale involving the issuance of up to 1,150,000 new shares over the 24 months following the subscription date of the warrants, using the delegation of authority granted to the board of directors under the 15th resolution of the combined general shareholders' meeting held on May 26, 2015.

On January 25, 2016 the Company obtained the AMF's visa on the prospectus required to set up the optional equity financing line (PACEO®) with Société Générale signed on December 22, 2015. On January 27, 2016 Société Générale subscribed for 1,150,000 warrants at a unit price of €0.0001, for a share premium impact of €115.

At the date of the *Document de Référence*, none of this equity financing line has been drawn down, and therefore 1,150,000 warrants are still outstanding. The Company is under no obligation to draw on this line.

21.1.4.5Summary of the dilutive instruments

At the date of the *Document de Référence*, the total number of shares that might be created by the exercise, or as appropriate the acquisition, of all the securities giving access to the Company's share capital granted and outstanding amounts to 3,220,996 new shares, representing about 20.00% of the fully diluted share capital.

21.1.5 Authorized capital

The resolutions relating to issuance approved by the extraordinary general shareholders' meeting held on April 21, 2016 are summarized below. The minutes of this shareholders' meeting are available on the Company's website: (www.txcell.com).

	Valid for / expiry	Maximum	Methods used to determine price
Authorization granted to the board of directors in order for the Company to purchase its own shares	18 months	€1,000,000 up to 10% of the share capital	10% of the share capital
Authorization granted to the board of directors in order to reduce the share capital by cancelling shares pursuant to the authorization to buy back the Company's own shares	18 months	10% of total share capital per 24-month period	10% of total share capital per 24-month period
Delegation of authority granted to the board of directors in order to increase the capital by issuing ordinary shares and/or any equity securities giving access to other equity securities or giving entitlement to the allocation of debt securities , and/or securities giving access to equity securities to be issued, with shareholders' preferential subscription right	26 months	€2,100,000 (1)	
Delegation of authority granted to the board of directors in order to increase the capital, immediately or in the future, by issuing ordinary shares or any equity securities giving access to other equity securities or giving entitlement to the allocation of debt securities, without shareholders' preferential subscription right and public offering	26 months	€2,100,000 (1)	(2)
Delegation of authority granted to the board of directors in order to increase the capital by issuing ordinary shares and/or any equity securities giving access to other equity securities or giving entitlement to the allocation of debt securities, and/or any securities giving access to equity to be issued, without shareholders' preferential subscription right through an offer to qualified investors or a limited circle of investors referred to in article L. 411-2 II of the French monetary and financial code (*code monétaire et financier*)	26 months	€520,000 (1) up to 20% of share capital per 12-month period	(2)
Delegation of authority granted to the board of directors in order to increase the capital by issuing ordinary shares or any securities without shareholders' preferential subscription right to a category of persons underwriting to subscribe the Company's securities issued pursuant to the exercise of an equity line	18 months	€520,000 (1)	(3)
Authorization grantedto the board of directors, in the event of an issue of shares or any securities giving access to the capital without shareholders' preferential subscription right, in order to set the issue price up to 10% of the share capital and within the limitations provided by the general shareholders' meeting	26 months	up to 10% of share capital per 12-month period	(4)
Delegation of authority granted to the board of directors in order to increase the number of shares to be issued pursuant to a capital increase with or without a preferential subscription right	26 months	up to 15% of the initial issue (1) (5)	Same price as initial issue
Delegation of authority granted to the board of directors in order to issue ordinary shares and securities giving access to the Company's capital, in the event of a public exchange offer by the Company including an exchange component	26 months	€2,100,000 (1)	

	Valid for / expiry	Maximum	Methods used to determine price
Delegation of power granted to the board of directors in order to issue Company's ordinary shares or securities giving access by any means, immediately or in the future, to Company's ordinary shares, up to 10% of the capital, in compensation for contributions in kind involving third-party companies' equity securities or securities giving access to their share capital outside a public exchange offer	26 months	€260,000 up to 10% of the existing share capital on the date of the transaction under consideration (1)	
Delegation of authority granted to the board of directors in order to increase the capital by incorporation of premium, reserves, profits and other funds	26 months	€ 480,000	
Authorization granted to the board of directors in order to grant stock options	38 months	500,000 shares (6)	(7)
Authorization granted to the board of directors in order to allot free shares to be issued or purchased by the Company	38 months	750,000 shares up to 10% of the share capital (6)	
Delegation of authority granted to the board of directors in order to issue and allocate warrants to (i) observers (*censeurs*) and members of the Company's board of directors in office on the date of the warrants' allocation, who are not employees or managers of the Company or any of its subsidiaries, (ii) persons who entered with the Company into a services or consultant contract or (iii) members of any committee that have been set up or that might be set up by the board of directors, who are not employees or managers of the Company or any of its subsidiaries	18 months	500,000 shares (6)	(8)

(1) These amounts are not cumulative. The cumulative maximum nominal amount for capital increases was set by the shareholders' meeting at €2,450,000.

(2) The issue price of the shares shall be at least equal to the weighted average share price over the last three trading days preceding the day on which it is set minus, where applicable, the legally authorized discount (i.e. currently 5%) and adjusted if there are differences in the dates from which the shares earn dividends, provided that the issue price of the securities giving access to the Company's capital is such that the sum received immediately by the Company plus, where applicable, the sum which it may receive subsequently, is, for each share issued as a result of the issuance of these securities, at least equal to the issue price defined above.

(3) The issue price of the shares shall be at least equal to the volume-weighted average price over the last three trading days preceding the day on which it is set, minus a maximum discount of 20%, taking into account as the case may be the date from which the shares earn dividends, provided (i) that in the case of an issue of securities giving access to the capital, the issue price of the shares that might result from the exercise, conversion or exchange of such securities may, at the discretion of the board of directors, be set by reference to a mathematical formula defined by the board and applicable to the issue of such securities subsequently (e.g. at the time of exercise, conversion or exchange), in which case the aforementioned maximum discount may be calculated, if the board of directors deems it appropriate, as of the date such formula is applied (and not at the date where the issue price is set) and (ii) that the issue price of the securities giving access to the capital, if any, issued under this delegation will be such that the funds, if any, immediately received by the Company, plus those that it might receive at the time of the exercise or conversion of said securities, is, with regard to each share issued consequent to the issue of these securities, at least equal to the aforementioned minimum amount.

(4) Within the limit of 10% of the Company's capital (as at the date of the transaction) every 12 months, the board of directors may waive the pricing requirements set forth by the aforementioned delegations

and set the issue price of the ordinary shares and/or issued securities giving immediate or future access to the Company's capital, as follows:

- the issue price of the ordinary shares will be at least equal to the volume-weighted average share price over the last three trading days prior to its determination minus, where appropriate, a maximum discount of 20%, it being specified that it can under no circumstances be less than the par value of a share of the Company on the date of issuance of such shares;
- the issue price of the securities giving access to the Company's capital will be such that the sum received immediately by the Company plus, if any, that which it may receive subsequently, is, for each share issued as a result of the issuance of these securities, at least equal to the issue price specified in the paragraph above.

(5) 15% or any other fraction that may be determined by the applicable regulations.

(6) These amounts are not cumulative. The overall cap for the authorized issuances is 1,200,000 shares.

(7) The purchase or subscription price per share will be set by the board of directors as of the day the option is granted within the limits set by law and this delegation and shall under no circumstances be inferior to ninety-five per cent (95%) of the average share price over the twenty trading days prior to the date of the board's decision to grant the options, rounded up to the next euro cent, or, in the case of purchase options, inferior to 80% of the average purchase price of the Company's treasury shares, rounded up to the next euro cent.

(8) The issue price of a warrant will be determined by the board of directors as of the day such warrant is issued based on the warrant's specific terms and conditions and will be at least equal to 5% of the volume-weighted average price on Euronext Paris over the last five (5) trading days preceding the grant date of such warrant by the board. The exercise price will be set by the board of directors at the date the warrants are allocated and shall be at least equal to the weighted average price over the twenty trading days prior to the date of the board's decision to grant the warrants.

21.1.6 Information about the capital of any member of the group which is under option or agreed conditionally or unconditionally to be put under option

To the best of the Company's knowledge, there is no option, nor any conditional or unconditional agreement providing for such an option, on the Company's capital.

21.1.7 History of the share capital

21.1.7.1 Changes in the share capital

The Company was registered with the French trade and companies register on April 12, 2001, with an initial capital of €38,112.

As of December 31, 2012 the share capital amounted to €1,336,799.20 consisting of 33,419,980 shares of €0.04 par value.

The table below presents a summary of the changes in the share capital from that date until the date of the *Document de Référence*.

Date of the transaction	Nature of the transaction	Number of shares issued or cancelled	Nominal amount (in €)	Issue or contribution premium (in €)*	Cumulative nominal amount of share capital (in €)	Total cumulative number of shares outstanding	Par value (in €)
08/02/2013	Capital increase by exercise of $BSA_{Tranche\ 2}$	5,882,353	235,294.12	2,764,705.91	1,572,093.32	39,302,333	0.04
02/20/2014	Capital increase by exercise of $BSA_{Tranche\ 2}$	2	0.08	0.94	1,572,093.40	39,302,335	0.04
03/07/2014	1-for-5 reverse stock split	-31,441,868	-	-	1,572,093.40	7,860,467	0.20
04/14/2014	Conversion of bond issues	627,239	125,447.80	3,374,545.82	1,697,541.20	8,487,706	0.20
04/14/2014	Initial Public Offering	2,903,226	580,645.20	15,619,355.88	2,278,186.40	11,390,932	0.20
05/09/2014	Oversubscription	268,833	53,766.60	1,446,321.54	2,331,953.00	11,659,765	0.20
07/11/2014	Exercise of 2014 Options	3,250	650.00	17,485.00	2,332,603.00	11,663,015	0.20
07/15/2015	Exercise of 2014 Options	54,203	10,840.60	291,612.14	2,343,443.60	11,717,218	0.20
07/24/2015	Private placement	1,166,300	233,260.00	7,697,580.00	2,576,703.60	12,883,518	0.20
11/19/2015	Exercise of 2014 Options	3,808	761.60	20,487.04	2,577,465.20	12,887,326	0.20

*Excluding the allocation of issue fees

21.1.7.2Changes in the distribution of the capital and voting rights over the past three financial years

Shareholder	*Situation as of December 31, 2013*	*Situation as of December 31, 2014*		*Situation as of December 31, 2015*	
	% of capital and voting rights (2)	*% of capital*	*% of voting rights*	*% of capital*	*% of voting rights*
Auriga Partners	37.50%	33.55%	33.60%	30.36%	30.40%
Bpifrance Investissement	35.58%	30.41%	30.45%	27.52%	27.55%
Bpifrance Participations	0.00%	12.45%	12.46%	11.26%	11.28%
Seventure Partners	19.74%	15.32%	15.35%	8.48%	8.50%
Other shareholders holding less than 5%	7.19%	8.13%	8.15%	22.25%	22.28%
Treasury shares (1)	0.00%	0.14%	0.00%	0.13%	0.00%
TOTAL	100.00%	100.00%	100.00%	100.00%	100.00%

(1) Shares held as part of a liquidity contract, without voting rights

(2) The percentage of voting rights is identical to the percentage of capital in the absence of own shares

To the Company's best knowledge there is no significant difference in the distribution of the existing capital and the corresponding voting rights at the date of the *Document de Référence*.

21.2 Act of incorporation and bylaws

21.2.1 Corporate purpose (Article 3 of the Company's bylaws)

The Company's direct and indirect purpose, in France and abroad, is as follows:

- to carry out, on its behalf or on behalf of third parties, any research, development and study operation and to develop production and marketing processes for pharmaceutical products;
- to file or grant patents and licenses directly or indirectly related to its activities;
- and, more generally, any economic, legal, financial, civil or commercial transaction of any kind whatsoever, that may be directly or indirectly related to the corporate purpose or any similar, related or supplementary purpose.

21.2.2 Provisions of the bylaws or other documents relating to members of the Company's administrative and management bodies

21.2.2.1Board of directors

The Company is governed by a board composed of individuals and legal entities; the number of members is determined by the ordinary general shareholders' meeting, within the limits set forth by the law.

At the time of their appointment, legal entities must designate an individual to act as their permanent representative on the board of directors. The term of office of the permanent representative will be identical to the term of office of the legal entity he/she represents. When a legal entity dismisses its permanent representative, it must designate a replacement immediately. These rules also apply in the event of the death or resignation of the permanent representative.

Members of the board of directors will be appointed for a six-year term of office. The office of a member of the board of directors will expire at the close of the ordinary general shareholders' meeting convened to vote on the financial statements for the previous financial year and held in the year in which the member of the board of directors' term of office is due to expire.

Members of the board of directors may be re-elected. They may be removed from office at any time by decision of the general shareholders' meeting.

In the event one or more seats on the board of directors fall vacant due to death or resignation, the board of directors may make provisional appointments between two general shareholders' meetings.

Any appointments made by the board pursuant to the previous paragraph are subject to the ratification of the next ordinary general shareholders' meeting.

If they are not ratified, the decisions and actions already taken by the board will nevertheless remain valid.

In the event the number of the members of the board of directors falls below the minimum set by law, the remaining members must immediately convene an ordinary general shareholders' meeting in order to appoint the necessary number of members of the board of directors.

A company employee may be appointed to the board. However, his or her contract of employment must correspond to a genuine position. In this case, an appointment to the board will not result in the termination of the person's employment contract.

No more than one-third of the members of the board of directors in office can be bound to the Company by a contract of employment.

No more than one-third of the members of the board of directors in office can be aged over 75. In the event this threshold is crossed during their terms, the eldest board member will be deemed to have resigned automatically at the close of the next general shareholders' meeting.

21.2.2.2Observers (*censeurs*)

The ordinary general shareholders' meeting may appoint observers of the board on the basis of proposals made by the board of directors. The board of directors may also appoint observers directly, subject to ratification of the appointment by the next general shareholders' meeting.

No more than five observers, who form a panel may be appointed. They are selected solely on the basis of their skills and expertise.

They are appointed for a six-year term of office, expiring at the close of the ordinary general shareholders' meeting convened to vote on the financial statements for the previous financial year.

The panel of observers examines matters submitted to it by the board of directors or its Chairman, for their consideration. Observers attend the board of directors' meetings and take part in the deliberations in an advisory capacity only; without their absence affecting the validity of these deliberations.

They are convened to attend board meetings under the same conditions as the other board members.

The board of directors may remunerate the observers out of the directors' attendance fees allocated to the board of directors by the general shareholders' meeting.

21.2.2.3Meetings of the board of directors

The board of directors meets as often as the Company's interest requires.

The members of the board of directors are convened to its meetings by the Chairman. Notice of a meeting may be given by any method, orally or in writing.

The Chief Executive Officer can also ask the Chairman to convene a meeting of the board of directors, with regard to a specific agenda.

Moreover, members of the board of directors representing at least one-third of the total number of members of the board can also validly convene a meeting. In that case, they must specify the agenda to be discussed.

If the Company has a works council (*comité d'entreprise*), the members of this council, appointed in accordance with the French labor code (*code du travail*), must be convened to attend all meetings of the board of directors.

Board meetings will be held at the head office or at any other location in France or abroad.

At least one half of the total members must be present for the board to validly deliberate.

Decisions of the board of directors will be adopted by a majority of the votes; in the event of a tie, the Chairman of the meeting will not have a casting vote.

Internal rules that may be adopted by the board of directors may provide, in particular, that for purposes of calculating the quorum and majority any member of the board of directors who attend a board meeting via videoconferencing or telecommunication methods that comply with by the applicable regulations will be deemed present. This provision does not apply to the decisions listed in Articles L.232-1 and L.233-16 of the French commercial code (*code de commerce*).

Each member of the board of directors will receive the necessary information to perform his or her duties and may request any documents he or she considers useful.

Any member of the board of directors may grant a power of attorney to another member to be represented at a board meeting, by means of a letter, telegram, telex, fax, e-mail or any other electronic method; however, a member of the board of directors can only hold one proxy per meeting.

Copies of or excerpts from minutes of the board of directors' meetings are validly certified by the Chairman of the board of directors, the Chief Executive Officer, any member of the board of directors acting temporarily as Chairman or any person duly empowered to this effect.

21.2.2.4General Management

The general management of the Company is carried out, under the board's responsibility, either by the Chairman of the board of directors or by another individual appointed by the board of directors and bearing the title of Chief Executive Officer.

The Chief Executive Officer is vested with the broadest powers to act in the Company's name in all circumstances. He exercises his authority within the limits of the Company's purpose and subject to the authority expressly granted by law to the shareholders' meeting and to the board of directors.

He represents the Company in its relations with third parties. The Company will be bound by the Chief Executive Officer's actions that fall outside the scope of the Company's purpose, unless it can establish that the third party knew that the action fell outside of the scope thereof or that the third party could not have been unaware of the fact, given the circumstances; the mere publication of the bylaws not being sufficient to constitute such proof.

The Chief Executive Officers may not be over 65 years old. If the Chief Executive Officer reaches this age limit, he will be deemed to have resigned de facto. However, his term of office will be extended until the next board of directors' meeting, at which the new Chief Executive Officer will be appointed.

He may be removed from office by the board of directors at any time. Removal from office without just and serious cause may give rise to the payment of compensation unless the Chief Executive Officer also holds office as Chairman of the board of directors.

The board of directors will decide, by a majority of the votes of the members of the board of directors present or represented, between the two forms of general management referred to in the first paragraph of this section.

The shareholders and third parties are informed of this choice under the legal and regulatory conditions.

The board of directors' decision will remain in effect until it decides otherwise or, at the discretion of the board of directors, for a period corresponding to the Chief Executive Officer's term of office.

When the general management of the Company is carried out by the Chairman of the board of directors, the provisions applying to the Chief Executive Officer will apply to him.

In accordance with Article 706-43 of the French code of criminal procedure (*code de procédure pénale*), the Chief Executive Officer may validly delegate authority to any person of his choice to represent the Company in criminal proceedings brought against it.

On the basis of a proposal made by the Chief Executive Officer, the board of directors may appoint one or more individuals to assist the Chief Executive Officer, as Deputy Chief Executive Officer.

In agreement with the Chief Executive Officer, the board of directors defines the scope and duration of the powers conferred upon the Deputy Chief Executive Officers. The board of directors sets their compensation. When a Deputy Chief Executive Officer is also a member of the board of directors, his term of office may not exceed his term as member of the board.

With respect to third parties, the Deputy Chief Executive Officers have the same powers and authority as the Chief Executive Officer, including, in particular, the power to engage in legal proceedings.

No more than three Deputy Chief Executive Officers may be appointed.

The Deputy Chief Executive Officer(s) may be removed from office by the board of directors at any time, on the basis of the proposal made by the Chief Executive Officer. Any removal from office without just and serious cause may give rise to the payment of compensation.

Deputy Chief Executive Officers must not be aged over 65. If a Deputy Chief Executive Officer reaches this age limit he will be deemed to have resigned automatically. However, his term of office will be extended until the next board of directors' meeting, at which a new Deputy Chief Executive Officer may be appointed.

When the Chief Executive Officer ceases to perform or is prevented from performing his or her duties, the Deputy Chief Executive Officers will remain in office and continue to perform their duties until a new Chief Executive Officer is appointed, unless the board of directors decides otherwise.

21.2.3 Rights, privileges and restrictions attached to the Company shares

21.2.3.1Form of shares

Fully paid up shares may be held in registered or in bearer form, as chosen by each shareholder, subject, however, to the legal provisions relating to the mandatory form of shares held by certain specific individuals or legal entities. Shares that have not been fully paid up must be held in registered form.

Shares are recorded in individual accounts in accordance with the terms and conditions set out in the applicable laws and regulations.

Ownership of shares issued in registered form results from their registration in an account in the shareholder's name.

21.2.3.2Voting rights

The voting rights attached to shares are proportional to the fraction of the capital they represent and each share shall give right to at least one vote. The bylaws expressly exclude any mechanism that would grant

a double voting right to shares having been registered in the same shareholder's name for at least two years.

21.2.3.3Rights to dividends and profits

Each share entitles its holder to a share of the Company assets, profits and liquidation surplus in proportion to the number of shares issued and outstanding, and their par value.

Whenever it is necessary to hold a certain number of shares, whether preferential or not, or securities in order to exercise a given right, the shareholders or holders of the securities must personally arrange to group together the necessary number of shares or securities.

At least five percent (5%) must be drawn from the profits for the financial year, after deduction of prior losses, if any, and charged to a reserve account named "legal reserve". This deduction is no longer required once the legal reserve has reached one-tenth of the share capital.

The available earnings comprises the profits for the financial year, minus the prior losses and the deduction described in the previous paragraph, plus retained earnings.

If the financial statements for the financial year, as approved by the general shareholders' meeting, show the existence of available earnings, the shareholders may resolve to charge the amount to one or more reserve accounts, for which it will determine the allocation and use, to carry it forward as retained earnings or to distribute it as a dividend.

After noting the existence of available reserves, the shareholders may decide to distribute amounts drawn from these reserves. In such a case, the resolution must expressly indicate the reserve accounts from which the funds will be drawn. However, dividends are drawn in priority from the available earnings for the financial year.

The terms of payment of dividends are determined by a general shareholders' meeting or, failing that, by the board of directors.

However, the dividends must be paid within nine months of the end of the financial year.

The general meeting convened to vote on the financial statements for the financial year may grant each shareholder, for all or part of the dividend being distributed, the option of receiving payment of the dividend in cash or in shares.

Likewise, the ordinary general shareholders' meeting, voting in accordance with the conditions set out in Article L.232-12 of the French commercial code, may grant the shareholders an interim dividend and the option, for all or part of this interim dividend, between receiving payment of the interim dividend in cash or in shares.

21.2.3.4Dividend limitation period

Dividends that remain unclaimed for a period of five years after payment date revert to the State (Article L.1126-1 of the French general code of property owned by public bodies – *code général de la propriété des personnes publiques*).

21.2.3.5Preferential subscription rights

The Company's shares carry a preferential subscription right to capital increases, in accordance with the conditions set out in the French commercial code.

21.2.3.6Limitations placed on voting rights

The bylaws do not place any limitations on the voting rights attached to the shares.

21.2.3.7Identifiable bearer shares

At any time, at its own expense, and in accordance with the applicable legislation and regulations, the Company may ask any authorized body to provide it with the name, or the company name in the case of legal entities, nationality and address of each of the holders of securities immediately or subsequently entitling to voting rights in the Company's general shareholders' meetings, as well as the number of securities held by each of them and any restrictions that may apply to the securities.

21.2.3.8 Acquisition of treasury shares

Please refer to paragraph 21.1.3 of the *Document de Référence*.

21.2.4 Methods for modifying shareholders' rights

As set out in the Company's bylaws, the shareholders' rights may only be modified by the shareholders at an extraordinary general shareholders' meeting.

21.2.5 General shareholders' meetings

21.2.5.1 Holding of shareholders' meetings

General shareholders' meetings are convened and held in accordance with the conditions laid down by law.

If the Company wishes to send convening notices electronically rather than by post, it must first obtain the consent of the relevant shareholders, who must give the Company their e-mail address.

Meetings are held at the registered office or at any other location specified in the convening notice.

The right to attend general shareholders' meetings is governed by the applicable laws and regulations and is, in particular, conditional upon the registration of the shares in the name of the shareholder or of the intermediary registered to act on the shareholder's behalf by midnight (Paris time) two business days prior to the general shareholders' meeting, either in the registered share accounts kept by the Company or in the bearer share accounts held by the authorized intermediary.

Any shareholder who does not personally attend a meeting can choose one of the following three options, in accordance with the terms and conditions set out in the laws and regulations:

- appoint a proxy in accordance with the terms and conditions set out in the laws and regulations;
- vote by post; or
- send a blank proxy form to the Company.

The board of directors may arrange for the shareholders to attend and vote at shareholders' meetings via videoconferencing facilities or any other telecommunication method allowing them to be identified, in accordance with the terms and conditions set out in the applicable laws and regulations. If the board of directors decides to make use of this ability for a given shareholders' meeting, this decision will be specified in the meeting notice and/or the convening notice. Shareholders attending general shareholders' meetings via videoconferencing facilities or another telecommunication method referred to above, as the board of directors may decide, will be deemed to be present at the meeting for the purpose of calculating the quorum and the majority.

General shareholders' meetings are chaired by the Chairman of the board of directors or, in his absence, by the Chief Executive Officer, by a Deputy Chief Executive Officer provided he is a member of the board, or by a member of the board specifically delegated for that purpose by the board. Failing that, the general shareholders' meeting elects its Chairman.

The scrutineers' (*scrutateurs*) functions are performed by the two shareholders present at the general shareholders' meeting who hold the largest number of votes, and who accept these duties. The officers of the meeting appoint a secretary, who need not be a shareholder.

An attendance sheet is kept in accordance with applicable law.

When an ordinary general shareholders' meeting is held on first call, shareholders may validly deliberate only if the shareholders present or represented hold at least one-fifth of the shares with voting rights. When an ordinary general shareholders' meeting is held on second call, shareholders may validly deliberate regardless of the number of shareholders present or represented.

At ordinary general shareholders' meetings, resolutions are adopted by a majority of the shareholders present or represented.

When an extraordinary general shareholders' meeting is held on first call, shareholders may validly deliberate only if the shareholders present or represented hold at least one-quarter of the shares with voting rights. When an extraordinary general shareholders' meeting is held on second call, shareholders may validly deliberate only if the shareholders present or represented hold at least one-fifth of the shares with voting rights.

At extraordinary general shareholders' meetings, resolutions are adopted by a majority of two-thirds of the shareholders present or represented.

Copies of or excerpts from the minutes of general shareholders' meetings are validly certified by the Chairman of the board of directors, a member of the board acting as Chief Executive Officer, or the secretary of the shareholders' meeting.

21.2.5.2Powers of shareholders' meetings

Ordinary and extraordinary general shareholders' meetings exercise their respective powers in accordance with the conditions laid down by law.

21.2.6 Provisions enabling to delay, defer or prevent a change of control

The Company's bylaws do not contain any provisions enabling to delay, defer or prevent a change of control.

21.2.7 Ownership disclosure thresholds set in the bylaws

The Company's bylaws do not provide for ownership threshold crossing declarations besides those required by law and regulations.

21.2.8 Specific provisions governing variations in capital

The Company's bylaws do not contain any specific provisions governing variations in its capital.

21.3 Pledge of Company assets or shares

At the date of the *Document de Référence*, the Company has not pledged any shares or assets.

22. KEY CONTRACTS

22.1 Licence agreement with INSERM

On January 30, 2006, the Company signed a licence agreement with INSERM concerning patent families owned by INSERM (PTXC2) or jointly owned by INSERM and the Company (PTXC1 and PTXC5) and the related know-how. The relevant agreement was amended on December 9, 2013 and on December 31, 2014 (please refer to paragraph 11.3.1 of the *Document de Référence*).

Under the agreement, INSERM granted the Company exclusive worldwide rights to develop, manufacture and market (directly or through its subsidiaries or sub-licensee) products and processes using the relevant patents and related know-how in the field of cell therapy for chronic autoimmune and/or inflammatory diseases (the "Products").

The agreement was entered into for a term to expire at the latest of the following two dates: the date on which the last patent expires or becomes invalid, or the end of a ten-year period from the first market launch of a Product.

The agreement further provides that, in the event the Company develops and markets Products, it will pay to INSERM a series of lump sum amounts conditional on achievement of milestones reached in terms of the development, regulatory process and the first anniversary of the market launch. As at the date hereof, the total future payments for all indications can amount to €889 thousand. Note that €76 thousand was already paid on October 17, 2013 in view of the success of the first trial. In the event the Company or its subsidiaries market(s) the Products, the Company will also be required to pay royalties to INSERM based on a percentage of the sales (net of various charges, tax and discounts) for the Products.

However, in the event the Company grants a sublicense to a third party allowing it to develop and market Products, the amounts to be paid to INSERM by the Company will be calculated as a percentage of the amounts received by the Company from the third party because of the development and marketing of the Products. A payment of € 90 thousand has already been made under the sublicense agreement entered into with Ferring International Center and transferred to Trizell Holding SA entitled "Collaboration, option, development and licence agreement", which has been terminated by an agreement dated December 2, 2015 (please refer to paragraph 22.2 below).

22.2 Termination agreement of the Collaboration, option, development and licence agreement with Ferring International Center (as transferred to Trizell Holding SA)

On December 12, 2013, the Company and Ferring International Center ("Ferring") entered into a Collaboration, option, development and licence agreement under which Ferring has an option to obtain an exclusive, worldwide licence for the development, manufacture and marketing of Ovasave® for the treatment of inflammatory bowel diseases, including Crohn's disease and ulcerative colitis.

By way of a deed entitled "Assignment and novation" with effect on December 31, 2014, Ferring transferred all rights and obligations under the Collaboration, option, development and licence agreement to the benefit of Trizell Holding SA ("Trizell"), a company also controlled by the Dr. Frederik Paulsen Foundation.

Following this transfer, the Collaboration, option, development and licence agreement was subject to an amendment (the "Development Agreement") entered into between the Company and Trizell with effect on March 30, 2015. This Development Agreement provides for the financing, by Trizell, of certain research and development activities related to Ovasave® conducted by the Company, in anticipation of the possible exercise of the option by Trizell. On December 2, 2015, the Company and Trizell entered into an agreement, governed by English law, terminating the Collaboration, option, development and licence agreement and the Development Agreement. Under this agreement, Trizell waives the option granted to its benefit to obtain a worldwide exclusive license on development, manufacture and marketing of Ovasave® for the treatment of inflammatory bowel diseases, including Crohn's disease

and ulcerative colitis. Trizell also transfers to the Company intellectual property rights which it could own, as well as Ferring, on Ovasave®. In return, the Company undertook to pay to Trizell, over several years, certain amounts either as lump sums or based on the revenues generated by the products initially covered by the Collaboration, option, development and licence agreement, for a minimum global amount of € 6 million and a maximum amount of € 15 million, as follows:

- a lump sum payment of € 2 million payable at the signing of the contract, being specified that the first payment was made in December 2015;
- two lump sum payments of € 2 million payable at the second (December 2017) and third anniversaries (December 2018) of the signing of the contract, within the aggregate limit of € 15 million;
- royalties equal to a specific percentage of revenues arising from Ovasave®, within the overall limit of € 15 million.

22.3 Exclusive option agreement granted by Yeda Research and Development Company Ltd.

On June 30, 2015, the Company entered into an exclusive option agreement with Yeda Research and Development Company Ltd. ("Yeda"), the valorization and technology transfer arm of the Weizmann Institute of Sciences, based in Rehovot, in Israel.

Governed by Israeli law, this agreement grants to the Company an exclusive right to exercise the option, during 12 months, which allows it to negotiate the terms of an exclusive and worldwide license on the invention made by Pr. Zelig Eshhar and its team, from the Weizmann Institute of Sciences, on redirected genetically engineered T regulatory cells (CAR-Treg) and their use in treating autoimmune and inflammatory diseases, as well as the PCT patent application number WO 2008/095141, and the related patent applications to develop, manufacture and market the products for the treatment of autoimmune and/or inflammatory diseases (the "Product").

The European patent application number EP2126054 entitled "*redirected genetically modified regulator T cells and their use in the ending of autoimmune and inflammatory diseases*" has received a notification of intention to grant by the European Patent Office, on April 25, 2016. Nonetheless, the U.S. patent application number 12525270, covering in substance the same invention is still under review: an official letter has been issued on December 29, 2015 for which a reply must be sent by June 29, 2016.

In the event that the option is exercised by the Company, i.e., before June 30, 2016, the parties will have 90 days to negotiate exclusively and in good faith the terms of a license.

In the absence of exercise of the option by the Company, Yeda will be free to negotiate with any other third party.

In the event that the option is exercised by the Company, but the negotiations of the terms of the license do not succeed in the allotted time, Yeda will be free to negotiate with any other third party; however, it will not be able to conclude a license agreement with a third party at financial conditions less favorable to it than those finally offered to it by the Company for a period of 6 months.

A Memorandum of Understanding was signed on October 28, 2015 in order to define the key terms of the license agreement if it were to be concluded following a possible exercise of the option by the Company.

As a result, the license, if it were to be concluded, would be exclusive, worldwide, with the right for the Company to grant sub-licenses or assign its rights conferred under the agreement to a third party without obtaining the prior consent of Yeda. It would be concluded for a period up to the later of the following two dates: the date on which exists no valid claim of a patent or patent application subject of the agreement, or expiration of a period of 12 years from the first marketing of a Product in each relevant country.

This license would be granted in consideration of various payments by the Company to the benefit of Yeda, and in particular at the stage of the negotiations of (i) annual fixed license fees, (ii) amounts/fees reflecting the use and defense, by the Company and/or its sub-licensees, of the patents, and (iii) lump sums subject to the achievement of milestones related to the development of the Product.

Patents and patent applications covered by the license agreement would remain managed by Yeda, with consultation of the Company at each stage of the examination process, while the costs of management and maintenance in force of such tights would be borne by the Company.

The Company may terminate the agreement at any time before the first marketing of a Product, with 3-months' notice. Yeda could terminate the agreement in case of contractual failure by the Company, if not cured within a period specified for this purpose.

Upon termination of the license, if it were to be concluded, the Company would grant a non-exclusive, perpetual, worldwide license, without payment of any fee and, with the right to grant sublicenses, to Yeda on improvements developed by the Company as part of the license (if any) and necessary for the manufacture and/or marketing of Products.

In case termination of the license occurs after a failure by the Company, the sub-licensee of the latter may, under certain conditions, assume the rights of the Company by entering into a license agreement directly with Yeda.

The Memorandum of Understanding and the potential license agreement are subject to English law.

22.4 Agreement for the supply of clinical research services with SGS Belgium NV, SGS Life Science Services division

On January 31, 2014, the Company outsourced to SGS Belgium NV, SGS Life Science Services division (SGS), a Contract Research Organisation (CRO), the operational conduct of the Phase IIb trial of Ovasave® pursuant to a Clinical Research Services Agreement governed by Belgian law.

The services SGS undertakes to supply are regulatory CTA (Clinical Trial Application) preparation and submission, qualification and monitoring hospitals of the clinical trial, the management of clinical data, statistics and pharmacovigilance, in compliance with good clinical practice as defined by the European Union and the ICH. The Company sponsors and funds the trial, monitors the project advancement, is responsible for manufacturing the products and supplies the batches to be used for the trial.

All results obtained in the course of the clinical trial will remain the sole property of the Company, and no additional payments will be made to SGS in this respect.

In addition to the usual cases for termination, the Company can terminate the agreement at any time with 30 days prior notice. In the event of termination, the Company will be required to pay SGS a fixed amount of compensation, unless termination is due to the withdrawal of the authorisation to carry out the Phase IIb clinical trial of Ovasave® or the occurrence of a serious adverse event during the trial (including unsatisfactory analysis results).

SGS's liability is limited to twice the total amount of the study budget for any direct loss or damage (excluding serious negligence, intentional error or failure to comply by SGS with its obligations, in particular regarding the confidentiality of data or the property of results and inventions). SGS will not be liable for any indirect loss or damage.

SGS is only entitled to unilaterally terminate the agreement in the event of a material breach by TxCell that is not cured within 30 days, or in the event of liquidation or a similar event.

22.5 Services agreement with Cell Therapy Catapult Services Limited

On March 30, 2015, the Company entered into a services agreement governed by English law with Cell Therapy Catapult Services Limited ("Catapult") for the development and industrialization of the Ag-Treg products production process of the Company (Ovasave®, Col-Treg and others). The outsourced project should enable the Company to have an automated and industrialized process in line with the needs and production standards for Phase III clinical trials and the marketing stage in 2018.

Any intellectual property rights and know-how specific to Ag-Tregs, including Ovasave®, developed under the services agreement will be the property of the Company, without additional payment to Catapult.

In addition to the usual events of termination, the Company may terminate the agreement at any time upon 90 days prior written notice. In case of termination, the Company will be required to pay Catapult any reasonable and unavoidable cost or fees payable by the latter to third parties in connection with the services, covered by the agreement, provided that the amount due to Catapult may not be higher than the amount paid under the services agreement.

Catapult's liability is limited to the total amount paid under the agreement for any damages, excluding any indirect damage or loss of opportunity (within the limit of what is allowed by the applicable law).

22.6 Services agreement with MaSTherCell

On December 3, 2015, the Company and MaSTherCell SA (Manufacturing Synergies for Therapeutic Cells) entered into a framework agreement for a period of 5 years for manufacturing autologous antigen-specific type 1 regulatory T cells, products from the ASTrIA platform (the "Products"), including Ovasave® and Col-Treg. Under this framework agreement governed by English law, the Company undertakes to outsource exclusively to MaSTherCell the manufacturing of Products in Europe (the EU and EFTA) until December 3, 2020. However, this exclusivity remains subject to exceptions (in particular in case of lack of agreement on the quantity and the price of the Product, under a license granted by the Company on a Product or if MaSTherCell was not able to manufacture the quantities required by the Company).

The framework agreement supersedes and invalidates any previous agreement between the two parties, including the memorandum of understanding dated July 27, 2015.

22.7 Services agreement with PCT

On March 9, 2016, the Company entered into an agreement with PCT LLC ("PCT"), a subsidiary of Caladrius Biosciences, Inc., pursuant to which PCT undertakes to carry out a preliminary strategic assessment of existing manufacturing process of the Company, set up for its ASTrIA platform (the "Services").

The agreement was concluded for an initial period expiring on December 31, 2016; however, each party may terminate it by 30 days prior written notice to the other party. It may also be terminated earlier or renewed by mutual agreement of the parties.

The Company may terminate the agreement in case of failure by PCT to comply with its contractual obligations and to cure such default within 30 days following the receipt of a notification.

Under the contract, PCT receives a fixed financial compensation calculated on the estimated number of hours needed to perform the services under the agreement. In addition, the agreement provides that PCT may charge overtime with the prior consent of the Company.

Under terms of this agreement, each party keeps the ownership or control of its former intellectual property rights (and related rights). PCT grants the Company a perpetual, worldwide, royalty-free and non-exclusive license on its former intellectual property rights relating to items used in the delivery of services and necessary for the Company to develop, manufacture, make manufacture, use, sale, offer for sale, export and import its products. This license includes the right for the Company to grant sublicenses to its affiliated companies and third parties which manufacture such products for the Company or which receive them under license from the Company.

The intellectual property rights (and related rights) relating to the deliverables, developments, improvements and other results obtained and made in the context of the agreement belong to the Company, including the rights to any improvements relating to items covered by the former intellectual property rights of PCT. On the latter, the Company grants PCT (for itself and its affiliated companies and their clients) a perpetual, worldwide, royalty-free, non-exclusive, non-assignable and non-sub-licensable right for use in connection with other products than those covered by the agreement.

The rights and obligations of the parties under the agreement may be assigned by either party to the benefit of any third party, subject to the prior written consent of the other party.

The agreement is subject to the laws of New York and provides that any dispute between the parties may be brought to any federal or state court located in the County or the State of New York as PCT may elect.

22.8 Collaboration agreement with Ospedale San Raffaele

A collaboration agreement (the "Agreement") was entered into between the Company and Ospedale San Raffaele S.R.L., ("OSR") on April 22 2016, mainly dedicated to research and development of chimeric antigen receptor engineered regulatory T cell (CAR-Treg) therapy products for the treatment of immune-mediated inflammatory diseases (excluding cancer and infectious disease).

The collaboration includes a development part focused on the non-clinical development of CAR-Treg cells for the treatment of Lupus Nephritis ("Development Program"), and a research part on the design and biology of other chimeric antigen receptors for use in Treg cell products addressing other autoimmune indications ("Research Program").

In addition, a steering committee, established by the parties, may select additional research and/or development programs ("Additional Program") (together with the Research Program and the Development Program, the "Collaboration Program").

In consideration for the performance by OSR of the activities allocated to it, the Company will pay to OSR a fixed amount every 6 months until 6 months after second anniversary of the effective date (i.e., October 22, 2018) (under the Research Program) and a fixed amount after the achievement of each milestone (under the Development Program).

Each party to the Agreement remains the sole owner of its background intellectual property rights (the "Background IP"), and of the foreground intellectual property rights relating to the results it identified, developed, generated or conceived solely in the performance of the Agreement (the "Foreground IP"). The intellectual property rights protecting any result identified, developed, generated or conceived by both parties in the performance of the Agreement shall be jointly owned by the parties (50/50) (the "Joint Foreground IP").

The Company is in charge of preparing, filing, prosecuting, defending (including actions challenging the ownership or validity of the rights but excluding actions against third parties infringers) and maintaining any patent or patent application claiming any Foreground IP and/or Joint Foreground IP, in the name of the relevant owner(s) at its costs (including the cost of damages awarded against TxCell and its sub-licensees in connection with any such actions).

Each party grants to the other, to the extent necessary to perform its obligations under the Agreement, a non-exclusive, fully paid-up, non sub-licensable and non-transferable license under its Background IP, Foreground IP and the Joint Foreground IP.

During a specific period (the "Option Period"), each party grants to the other a non-exclusive, worldwide, royalty-free, irrevocable, sub-licensable (except for OSR), license under the Foreground IP, the Background IP and the Joint Foreground IP, for the purposes of research and development in relation to CAR-Treg products for the treatment or prevention of any immune-mediated inflammatory disease indication (excluding cancer and infectious disease) in humans or animals (the "Field"). During such Option Period, the Company benefits from an exclusive option to obtain a license in relation thereto, under predetermined terms and conditions, aimed (notably) at enabling the Company to develop, manufacture and commercialize products.

Should the Company elect not to exercise the option to obtain such a license during the Option Period, the Company must notify OSR of its decision so that both parties may have a non-exclusive and royalty free right to use the Foreground IP and Joint Foreground IP, for all purposes within the Field.

If the Company does not exercise its option, each party grants to the other a non-exclusive, worldwide, royalty-free (except for OSR), perpetual, irrevocable, sub-licensable license under the Foreground IP

and Joint Foreground IP, as well as on OSR Background IP (with respect to the Company) for (i) research and development purposes, within the Field, with respect to the Company and (ii) all purposes, within the Field, with respect to OSR.

Each party grants to the other a non-exclusive, worldwide, royalty-free (except for OSR), perpetual, irrevocable, sub-licensable license under the Foreground IP and Joint Foreground IP (excluding the NGFR-spacer patents with respect to the Company), for all purposes outside the Field.

The Agreement may be terminated at any time by mutual consent. In addition, the Company may terminate the Research Program and the Development Program by notification to the steering committee and subject to 60 days prior written notice to OSR, provided that such termination may not take effect until after the expiry of a 12 months period following April 22, 2016. In this case, the Company will be liable to OSR for expenditure and costs irrevocably and reasonably incurred by OSR under the Research Programme on the date of termination and which exceed the amounts already paid by the Company, and reciprocally.

The Agreement will continue until terminated in accordance with the following provisions:

- mutual agreement of the Parties at any time;
- expiry of 6 month period following the completion or termination of all programs within the Collaboration Program; or
- failure by one party to comply with its contractual obligations and to cure such default within a 60 days period following the receipt of a notification from the other party.

Subject to written notice to the other party, either party may assign and transfer all of its rights and obligations under the Agreement to any person to which it transfers all or substantially all of its assets or business to which the Agreement relates, provided that the assignee undertakes to the other party to be bound by, and perform the, obligations of the assignor under the Agreement.

The Agreement is governed by English law and the courts of England and Wales shall have exclusive jurisdiction to resolve any claim arising from it.

22.9 Partnership agreement with l'Etablissement Français du Sang Bourgogne Franche-Comté

Please refer to paragraph 8.1 of the *Document de Référence*.

23. INFORMATION PROVIDED BY THIRD PARTIES, DECLARATIONS OF EXPERTS AND DECLARATIONS OF INTERESTS

23.1 Designation of experts

None.

23.2 Designation of third parties

None.

24. PUBLIC DOCUMENTS

The following documents (or a copy of these documents) can be consulted while the *Document de Référence* remains valid:

- the Company's bylaws;
- all reports, letters and other documents and historical financial information;
- assessments and statements prepared by any expert at the Company's request that are partially reproduced or referred to in the *Document de Référence*;
- the financial information included in the *Document de Référence*; and
- the internal regulations of the board of directors.

In accordance with Article 28 of the European regulation No.809/2004/EC of April 29, 2004, the following information is incorporated by reference in the *Document de Référence*:

- the annual financial statements prepared in accordance with IFRS for the financial year ended December 31, 2014, and the corresponding statutory auditors' report, presented in paragraph 20.1 and 20.2 of the *document de référence* registered with the AMF on June 11, 2015 under number R.15-049;
- the annual financial statements prepared in accordance with IFRS for the financial year ended December 31, 2013, and the corresponding statutory auditors' report, presented in paragraph 20.1 and 20.2 of the *document de base* registered with the AMF on March 13, 2014 under number I.14-008;
- chapter 9 – Review of results and financial position – and chapter 10 – Liquidity and capital resources – of the *document de référence* registered with this AMF on June 11, 2015 under number R.15-049;
- chapter 9 – Review of results and financial position – and chapter 10 – Liquidity and capital resources – of the *document de base* registered with this AMF on March 13, 2014 under number I.14-008.

All of the legal and financial documents relating to the Company that must be made available to the shareholders in accordance with the applicable regulations can be consulted at the Company's head office.

The *Document de Référence*, the *document de référence* registered with the AMF on June 11, 2015 under number R.15-049 and the *document de base* registered with the AMF on March 13, 2014 under number I.14-008 may also be consulted on the Company's website (www.txcell.com) and on the AMF's website (www.amf-france.org).

25. INFORMATION ON EQUITY INTERESTS

As at December 31, 2015, the Company has no equity interests in any other companies.

26. APPENDIX

26.1 Statutory auditors' report on the financial statements and financial statements prepared in accordance with French GAAP for the financial year ended December 31, 2015

[INTENTIONALLY OMITTED]

27. GLOSSARY

A

Adalimumab: therapeutic monoclonal antibody marketed since 2003 as Humira, that can bind tumor necrosis factor alpha (TNF-α) to block TNF-α-dependent inflammatory processes.

Allogenic: concerns tissues and cells in individuals of the same species but a different line.

Aminosalicylates: class of anti-inflammatory drugs that act by inhibiting the production of pro-inflammatory molecules such as arachidonic acid.

ANSM: Agence Nationale de Sécurité du Médicament/*National Health Products Safety Agency*

Antibody: an antibody is a complex protein used by the immune system to specifically detect and neutralize pathogens.

Antigen: an antigen is a natural or synthetic macromolecule, recognized by antibodies or immune system cells and that can cause an immune response.

Anti-TNF: drug that blocks TNF-α-dependent inflammatory processes.

APC: the role of antigen-presenting cells is to present parts of self and non-self to lymphocytes in order to trigger a specific immune response. They may be monocytes or macrophages, B lymphocytes and dendritic cells.

Asepsis: prevention of contamination of a zone or a surface by foreign micro-organisms (bacteria, parasites, etc.).

ATMP: Advanced Therapy Medical Products: industrially manufactured products used for gene therapy and cell therapy, obtained by tissue or cell engineering.

ATP: adenosine-5'-triphosphate is the molecule that uses hydrolysis to provide the energy required for biochemical metabolic reactions of all known organisms.

Auto-antigen: a normal constituent of the body that is attacked by the immune system in autoimmune diseases.

Autoimmune uveitis: a uveitis with no infectious cause. Uveitis is a rare inflammatory disease of the eye. Uveitis is classified anatomically according to the principal site of the inflammation, i.e. anterior, intermediate, posterior or pan-uveitis.

Autoimmunity: results from the defective installation or maintenance of self-tolerance. Autoimmune diseases result from hyperactivity of the immune system when exposed to substances or tissues normally present in the organism.

Autologous: concerns cells and tissues of the same individual.

B

B lymphocytes: also called B cells (the "B" from the bursa of Fabricius in chicks in which they were first discovered), they are responsible for the production of antibodies. When antibodies bind to antigens on the surface of a micro-organism, this causes the death of the micro-organism in question. The process by which B lymphocytes protect the body is called humoral immunity because B cells release antibodies into body fluids (called humors).

Biological: a biological drug is obtained from a biological substance, for example vaccines or drugs obtained from human blood and plasma.

Biomarker: a measurable biological characteristic related to a normal or abnormal process. In medicine, a biomarker can be used for screening (search for a disease in a population), diagnosis (characterization of a disease in an individual), response to medical treatment, relapse after treatment, and toxicity of a molecule.

Biosimilar: biosimilar drugs are produced by biotechnology and whose patent has expired. The regulatory status of biosimilar drugs differs from that of "ordinary" generic drugs because of the difference in the manufacturing process between a biosimilar drug and its generic version. Even though the final substance is the same, its molecular complexity is such that the manufacturing process may affect the final product. Biosimilar drugs are therefore judged to be "similar" but not identical to biotechnology-produced drugs already on the market.

Biotherapies: the term biotherapies covers gene therapies (gene transfer, intervention on genes), cell therapies (manipulation of stem cells or differentiated cells), tissue therapies (grafts of living tissues), different types of immunotherapy, some innovative pharmacotherapies (biological drugs from substances in the human body), the use of biomaterials, the use of viruses (phagotherapy), etc.

C

Cachexia: cachexia is a severe weakening of the body (weight loss, muscular atrophy, etc.) related to severe malnutrition. Cachexia is not a disease itself but rather the symptom of another disorder.

Calprotectin: faecal calprotectin is a small protein whose normal value varies with age. It is secreted primarily by polynuclear neutrophil white blood cells inside the intestinal tract and is eliminated in the faeces. Its increase is the sign of an intestinal inflammation.

CAT: Committee for Advanced Therapies: the committee of the European Medicines Agency (EMA) that assesses the quality, safety and efficacy of advanced therapy medical products (ATMP) and that monitors scientific developments in this area.

CDAI: Crohn's Disease Activity Index: a measure of the activity of Crohn's disease. This index is used as a standard in all French and international clinical trials and by regulatory authorities. If the CDAI is < 150 the patient is in remission, if it is between 150 and 450 the patient's Crohn's disease is active and if it is > 450 the disease is severe. A reduction of ≥ 100 points of the CDAI during therapy enables the patient to be placed in the group of responders. The CDAI is a set of weighted sub-scores calculated over one week. It includes the number of liquid or very soft stools, the intensity of abdominal pain, general wellbeing, other aspects related to the pathology such as the presence of fistulas, arthritis, uveitis, etc., taking anti-diarrhoea drugs, the presence or absence of an abdominal mass, packed cell volume and patient weight.

Cell mediation: cell mediation is the name given to a specific immune reaction involving cells such as effector T lymphocytes.

Cell therapy: this therapy aims to treat an organ or an organism by providing cells, occasionally modified, to replace or support dysfunctional cells.

Chemokines: these chemoattracting cytokines are a family of small proteins, most of which are soluble. Their most well known function is attraction (chemotactism) and the control of the activation state of immune system cells.

CHMP: Committee for Medicinal Products for Human Use

Chondrocytes: cells composing cartilage.

CIID: Chronic inflammatory intestinal diseases, as their name indicates, covers diseases related to chronic inflammation of the intestine.

Clinical anamnesis (case history): the general medical history of the patient and the course of the disorder or disease in question that is entered in the patient's medical file. This is the first step in the diagnosis procedure.

Closed system: system that guarantees asepsis.

CMO: Contract Manufacturing Organisation. A company that provides the pharmaceutical industry with complete drug development services, in particular for manufacturing drugs.

Collagen type II: a fibrillar protein in all joints of the body and in the vitreous body of the eye.

Corticosteroids: hormones (also called corticoids) that are produced by the adrenal glands, located above the kidneys, in the part of the gland called the adrenal cortex. Corticosteroids can be synthesized in the laboratory and used therapeutically, in which case we speak of corticotherapy. Corticosteroids affect the body's metabolic reactions, have an anti-inflammatory action that combats inflammations, and also has immunosuppressive activity, in other words reducing the body's defence reactions, sometimes desired in certain autoimmune diseases.

CRO: Contract Research Organisation. A company that offers support to the pharmaceutical, biotechnology and medical devices sectors, in the form of contractual research subcontracting.

Crohn's disease: this is one of the chronic inflammatory intestinal diseases (CIID). It is often characterized by chronic diarrhoea, abdominal pain, anorexia, fever and musculoskeletal malformations. Patients suffer from recurrent episodes with variable degrees of remission. Crohn's disease may cause serious symptoms, often accompanied by the appearance of fistulas.

CRP: C-Reactive Protein is a marker of acute inflammation. Its quantity increases very rapidly in the course of an inflammatory process and enables a differential diagnosis between certain pathologies.

Curative: signifies that the process, effect or product is used to cure a disease.

Cytokines: soluble cellular signalling substances synthesized by immune system cells or other cells and/or tissues, remotely acting on other cells to regulate and control their activity and function.

Cytotoxicity: the property of a chemical or biological agent to harm cells, in some cases leading to their destruction.

D

Desmogleins: Desmogleins are proteins from the Cadherin family comprising DSG1, DSG2, DSG3 and DSG4 (often named desmogleins 1-4). Desmogleins play a role in the function of desmosomes (area where a cell plasma membrane adhere to an adjacent cell) that establish tight links between epithelial cells.

E

Effector T lymphocytes: also called effector T cells ("T" for thymus because they terminate maturation in the gland), they are responsible for what is called "cell immunity" by destroying cells recognized as being infected.

EMA: European Medicines Agency is a European Community agency created in 1995. It evaluates, coordinates and supervises the development of new drugs for human and veterinary use in the European Union.

Enterobacteria: one of the most important families of bacteria, in terms of both quantity (more than 40 genera) and quality. It comprises many, highly ubiquitous genera frequently encountered in infectious pathologies as well as bio-industries.

Entocort® or budesonide: a glucocorticosteroid with anti-inflammatory action.

Enzyme: an enzyme is a protein macromolecule that is a biological catalyst, i.e. it facilitates a biochemical reaction with no change to non-catalyzed products.

F

FDA: Food and Drug Administration. American agency that regulates foods and medicines and is empowered to authorize the distribution and commercialization of drugs in the United States, including those manufactured abroad.

Fistulizing: fistulizing Crohn's disease means that the patient has one or several fistulas, a medical term for an abnormal channel between two organs, causing the circulation of fluids into an organ for which they are not normally destined.

G

GCP: Good Clinical Practice, promoted by the International Conference of Harmonisation (ICH) dealing with technical requirements for the registration of drugs for human consumption. It describes an international standard for ethics applied in human clinical trials.

Gene therapy: a therapeutic strategy involving the introduction of genes in the cells or tissues of a patient to treat a disease.

Gevokizumab: gevokizumab (or XOMA 052) is a monoclonal antibody directed against the beta fraction of interleukin 1, a cytokine involved in inflammatory responses.

GMP: Good Manufacturing Practice is a concept of quality assurance. GMPs are established by the European Commission and EU member states for the development of quality procedures and are applicable to drugs manufactured for human or veterinary use.

H

Helper T lymphocytes: also called T helper or Th, they are a cell type that differs from other T lymphocytes, are not cytotoxic and act only as intermediaries of the immune response. They proliferate only when they are bound to certain pathogenic antigens to activate other cell types that act more directly on the response, explaining why they are called T lymphocyte "helper cells".

Hemorrhagic rectocolitis: hemorrhagic rectocolitis is an inflammatory intestinal disease whose effects are inflammation and the formation of lesions in the walls of the large intestine (colon) and rectum. It is a chronic and autoimmune disorder.

Hepatocytes: cells of the liver conducting a large number of metabolic functions.

Homeostasis: the capacity of a system (open or closed) to maintain its operating equilibrium.

HSP: Heat shock proteins in general are responsible for preventing damage to proteins in response to elevated body temperatures.

I

IBDQ: Inflammatory Bowel Disease Questionnaire. A questionnaire to assess the quality of life of patients. It is used as a standard in all French and international clinical trials and by regulatory authorities. It is calculated over two weeks and is composed of 32 questions covering four areas: digestive symptoms, systemic signs, emotional state and effects on social life.

ICH: International Conference on Harmonisation. An organisation of health authorities and the pharmaceutical industry (Western Hemisphere, Europe, Asia) that prepares regulatory standards to follow for the development of new drugs.

IDMC: Independent Data Monitoring Committee. A committee responsible, on one hand, for periodically assessing the clinical trial’s progress, safety data and efficiency critical results and, on the other hand, for making recommendations to the sponsor advising him whether to pursue, to modify or to interrupt a trial.

Ileocaecal: part of the digestive tract between the extremity of the ileum (third and final part of the small intestine) and the caecum (first part of the large intestine).

Immune system: the immune system is a biological system composed of a coordinated set of elements for recognition and defence, which differentiates between "self" and "non-self". Whatever is recognized as non-self is attacked, including pathogens such as viruses, bacteria, parasites, etc.

Immunity adjuvant: inorganic or organic compounds used to boost the immune response in the context of a therapeutic process (in particular used with vaccines).

Immunity: concept concerning the immune system (see immune system).

Immunogenicity: the potential of an antigen to induce an immune response.

Immunomodulator: qualifies a treatment that stimulates or inhibits immune system reactions.

Immunosuppressant: qualifies a treatment that prevents the body's immune response.

Immunotherapy: a treatment involving the administration of substances (that may be of biological origin, in particular in the case of cell immunotherapies) that stimulate or inhibit the body's immune defences to combat a variety of diseases.

IND: Investigational New Drug. The IND program of the FDA is how a pharmaceutical company obtains permission to send an experimental drug abroad (generally to clinical investigation centers for clinical trials) before applying for a marketing authorization for the drug.

Infectious pathogen: an agent responsible for an infectious disease.

Infliximab: therapeutic monoclonal antibody marketed as Remicade®, capable of binding tumor necrosis factor alpha (TNF-α) to block TNF-α-dependent inflammatory processes.

Inhibitor: something that slows or opposes a given process.

Integrins: cell adhesion receptors. They are transmembrane proteins in which one extremity generally interacts with proteins of the extracellular matrix exterior to the cell, and whose other extremity interacts with intracellular constituents, in particular signalling molecules that control the migration, survival, proliferation and differentiation of cells.

Interleukins (IL): interleukins are a group of cytokines whose name was coined because the first observations seemed to show that they were expressed by white blood cells. It was subsequently found that interleukins are produced by a wide variety of tissues and cells. Even though they were classed under this terminology for reasons of facility, they are totally unrelated in terms of biochemical similarities and functions. The number they bear reflects only their chronological order of discovery.

Islets of Langerhans: islets of Langerhans cells are endocrine cells (producing hormones) clustered in pancreatic structures called islets.

L

Lymphatic system: composed of lymphocytes and a system of vessels transporting these cells in the lymphatic fluid or lymph.

Lymphocytes: one type of white blood cells with a major immune function to defend the body against aggressions by external microbial agents. They are produced in the bone marrow and circulate *via* the bloodstream and lymph vessels.

Lymphoma: a cancer of the lymphatic system that develops at the expense of lymphocytes, cells that play an essential role in immune defence reactions.

M

MA: Marketing Authorisation (product licence) required to market a therapeutic product.

Macrophages: white blood cells arising from the transformation of monocytes. They are localized in tissues that could be the site of infections or the accumulation of debris to eliminate (liver, lungs, lymph nodes, spleen, etc.). Macrophages have three main functions: phagocytosis (ingestion of bacteria, yeasts, cell debris, etc. for their destruction); secretion activity (cytokines, etc.); cell cooperation (they are antigen-presenting cells in relation to lymphocytes). They therefore are key players in natural immunity because they phagocytise non-specific elements. They are attracted to the site of an inflammation by chemotactism.

Matrix products: products from the matrix of an organism (material [or tissue] containing more specialized structures).

Mesenchymal stem cells: mesenchymal stem cells (MSC) are an example of "adult" tissues or stem cells. They are pluripotent, meaning that they can give rise to several specialized cell types in the body, but not all types (in comparison to totipotent cells). MSCs can produce different specialized cells in

skeletal tissues, for example they can differentiate (or specialize) into cartilaginous cells (chondrocytes), bone cells (osteoblasts) and fat cells (adipocytes).

Methotrexate: methotrexate is an anti-metabolite used to treat certain cancers and autoimmune diseases. An anti-metabolite is a chemical substance that prevents the use of a metabolite, another substance that is part of the normal metabolism of an organism. The presence of anti-metabolites may have toxic effects on cells such as stopping growth and cell division.

Monoclonal antibodies: monoclonal antibodies are antibodies that recognize only one type of epitope (one chemical group) in a given antigen.

Monocytes: white blood cells that can be transformed to macrophages or dendritic cells.

MRI: magnetic resonance imaging. A medical imaging technique for obtaining non-invasive 2D or 3D views of the interior of the body with relatively high contrast resolution.

Multiple sclerosis: multiple sclerosis (MS) is a chronic, autoimmune, neurological disease of the central nervous system. Its clinical signs result from the demyelination of nerve fibers of the brain, spinal cord and optic nerve.

Myelin: an essential fatty membrane that insulates every nerve in the brain and spinal cord, just like plastic insulation on electric wires. Myelin is a protein complex indispensable for the propagation of nerve impulses. Partial or total destruction inevitably causes nerve conduction to occur at a slower rate or be lost, causing neurological disorders.

N

Natalizumab: natalizumab is a selective inhibitor of adhesion molecules. It binds to the α4 sub-unit of human integrins. The trade name of this selective immunosuppressor is Tysabri®.

Natural killer cells (NK): cells of the natural immunity of mammals. They can lyse foreign cells independently of the antigen. In particular, they produce chemical substances that destroy cancer cells.

O

Open label: investigators, researchers and patients of a clinical trial or part thereof are aware of the treatment being administered.

Orphan disease: a disease with no effective treatment. Most orphan diseases are rare.

Orphan drug: the orphan drug designation is a regulatory status granted by regulatory bodies to drugs developed for the treatment of rare diseases.

Ovalbumin: an essential protein of egg white.

P

Pemphigus vulgaris: designates rare autoimmune diseases, in other words due to the antibodies of an organism attacking its own cells. These pathologies concern the skin and mucous membranes.

Pharmacokinetics: this discipline determines the post-administration fate of an active substance (drug) in the body over time.

Placebo: a preparation physically identical to that tested but lacking the active substance.

Polynuclear neutrophil: a type of white blood cell arising in the bone marrow that defends the body against foreign bodies such as yeasts or bacteria.

Protein therapy: treatment with proteins.

R

Randomisation: a method of distribution used in clinical trials, based on random selections.

Rare disease: a disease with a low prevalence, between 1/1,000 and 1/200,000 according to national definitions.

Regenerative medicine: regenerative medicine creates functional living tissues to replace those of damaged tissues or organs. Regeneration may be *in situ* by the stimulation of damaged organs or in the laboratory *in vitro* (major progress for organ transplant issues). The use of stem cells is a major feature of regenerative medicine.

Regulator T lymphocytes: also called Tr, Treg or suppressor T lymphocytes, they are a sub-population of T lymphocytes with the property of inhibiting the proliferation of other effector T lymphocytes. They are required to maintain immunological tolerance and therefore participate in maintaining homeostasis of the immune system.

S

Single gene disorders: these phenomena occur when a mutation causes the modification or absence of only one gene.

Stem cells: undifferentiated cells that can give rise to specialized cells by cell differentiation and can maintain their number by proliferation in the body (auto-renewal) or indefinitely in culture.

Steroids: this term refers to steroid hormones (see corticosteroids).

Systemic: this term signifies that the treatment administered reaches its target *via* the bloodstream. It is the opposite of a local treatment.

T

Terminal ileum: third and last part of the small intestine.

Thiopurines: anti-metabolic drugs often used to treat ulcerative colitis and Crohn's disease.

Tolerance: in immunology, tolerance is the absence of an immune response to an antigen.

Tumorigenicity: the ability of normal cells to become cancerous.

U

Ustekinumab (Stelera): a monoclonal antibody directed against interleukins 12 and 23 (via a common sub-unit), developed as a drug.

V

Vaccination: a process involving the introduction of an external agent (the vaccine) in a living organism in order to create a positive immune reaction against an infectious disease. The active substance of a vaccine is an antigen intended to stimulate the body's natural defences (the immune system). In parallel, the primary immune reaction enables the antigen in question to be "memorized" so that in the course of a genuine contamination in the future, acquired immunity can be activated more rapidly.

Vedolizumab: a monoclonal antibody directed against integrin α4β7 that is currently being tested for chronic intestinal inflammatory diseases. It is a selective immunosuppressant.

W

Wiskott-Aldrich syndrome: an immune deficiency. It is a genetic disease resulting from a mutation of the WAS gene in the secondary X chromosome.

X

Xenogenic: from another species. A xenograft for example is the transplant of body tissue between two different animal species.