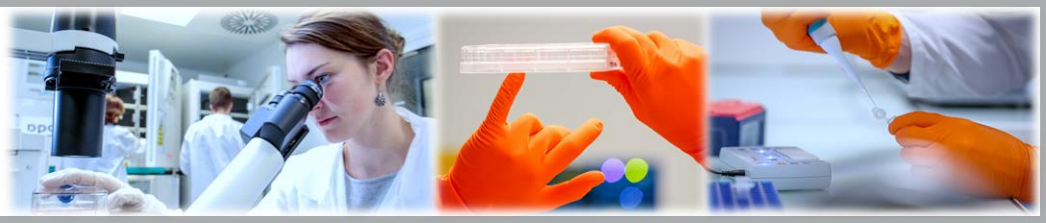


SHAREHOLDER NEWSLETTER #2
JULY 2017

CONTENTS

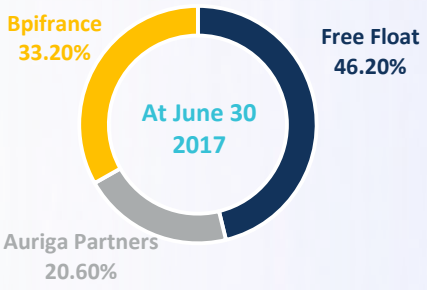
STOCK INFORMATION

TXCL LISTED EURONEXT — ELIGIBLE PEA PME

ISIN Code	FR0010127662
Total shares :	20,245,285
Capitalization	€41 M
Share price	€2.02
+ High/ + Low (12 months)	€4.12 – €1.73

Data at July 4, 2017

SHAREHOLDERS



To receive upcoming news and shareholder newsletters, please sign-up by sending us your email at txcell@newcap.eu

Stéphane Boissel, CEO

Dear shareholder,

I am pleased to present TxCell's second Shareholder Letter, notably with a special report on our CAR-Treg program in transplant rejection, in which we plan to initiate our first clinical study by the end of 2018. This could be the first time that any CAR-Treg candidate has been tested in humans, and could represent a major milestone for this exciting new class of therapeutics.

Additionally, we expect key preclinical results for several of our CAR-Treg programs by the end of this year. Due to our unique positioning in a growing field, we are convinced that preclinical results represent real value drivers. Indeed, since the identification of regulatory T cells in the 1990s, there has been an ever-increasing interest in these cells. Their therapeutic potential in the treatment of autoimmune and inflammatory diseases, as well as transplant rejection, has been established. Additionally, leading pharma and biotech companies have shown they understand the value of targeting this cell population, as evidenced by the recent acquisition, in-licensing, and option agreement announcements by Celgene, Novartis and Servier, respectively.

Our goal, therefore, is to obtain a clinical proof-of-concept for our CAR-Treg platform by 2020. We plan to develop CAR-Treg candidates in a number of autoimmune and inflammatory diseases beyond transplantation.

I hope you will enjoy reading this Shareholder Letter; thank you for your continued confidence and support.

François Meyer, Chairman and Head of Research

We have made major progress over the last twelve months and our CAR-Treg discovery platform is now fully functional. Our objective is to leverage this platform not only through our internal development programs but also through future pharma and biotech partnerships. To this end, we have strengthened our teams and optimized all of the steps necessary to produce and characterize CAR-Treg cells capable of specifically recognizing predefined antigens.

These steps include:

- optimizing the Chimeric Antigen Receptor (CAR) structure;
- optimizing the gene transfer step, which is used to introduce the CAR receptor into Treg cells transforming them into CAR-Tregs;
- performing in vitro characterization of the CAR-Treg cells obtained to ensure they have all the required characteristics.

The CAR-Treg cells thus obtained are then evaluated to determine efficacy. We select clinically-relevant animal models representative of autoimmune diseases or organ transplantation.

We look forward to discovering and sharing these critical scientific results with you in the coming months.

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FOCUS: GRAFT REJECTION IN SOLID ORGAN TRANSPLANTATION, A MAJOR HEALTH ISSUE

CAR-Tregs, an innovation against graft rejection

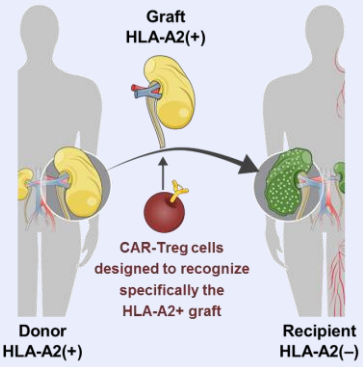
Transplant rejection remains one of the major challenges of organ transplantation today, and is a significant unmet medical need. Improvements in the management of chronic rejection are needed, specifically in the area of side effect management, where treatments have been known to cause *de novo* malignancies, infections, etc.

Regulatory T cells (Tregs), in their natural environment, are essential for the induction and maintenance of immune tolerance. CAR-Tregs have recently demonstrated efficacy in *in vivo* transplantation models in mice[1] and could lead to CAR-Treg-based therapies with numerous advantages, including:

- specificity towards the graft, without direct impact on other organs,
- local inhibition of inflammation,
- tolerance induction, i.e. potential cellular persistence, which could favor graft maintenance in the long term.

Unlike immunosuppressors, which reduce the patient's overall immune defenses, regulatory T cells could provide a way to re-educate the patient's immune system to tolerate the graft.

TxCell's approach in transplantation



Our objective is therefore to induce immune tolerance specifically to the graft.

To do this, we genetically modify regulatory T cells allowing them to recognize the graft and only the graft. These modified cells are called CAR-Tregs. They are designed to be activated solely at the graft level to elicit two effects which are intrinsic to regulatory T cells:

- an anti-inflammatory effect,
- a tolerance induction effect.

KEY FIGURES (US & EUROPE)

>60,000 solid organ transplant procedures performed per year[2,3]

>160,000 patients on waiting lists[4]

RISK OF ORGAN REJECTION

Kidney transplant: only **50% graft survival** at 10 years[5]

Lung transplant: **mortality rates of 40-55%** at 5 years[6]

IMMUNOSUPPRESSION MARKET

Global market: **$5.1 Bn**[7]

Average cost of treatment in the US: **$10k to $14k** per patient per month

Dr. Megan Levings, *Professor, Department of Surgery, University of British Columbia*

Could you please describe your role in the TxCell-UBC collaboration?

We are working hard to complete the preclinical proof-of-concept data package that will be needed to develop the clinical protocol. My role is to review with my staff the design of experiments and the data generated. We have many different ideas for exciting experiments we would like to pursue, so my role is also to prioritize to make sure we stay focused on specific goals.

Transplant rejection is a major public health issue, what is your approach to tackle this problem?

My lab is focused on finding ways to harness the natural ability of the immune system to turn off unwanted immune responses. If we can find a way to use CAR-Tregs to stop the rejection of transplanted organs it would be a revolution in this area of medicine.

Why do you think that CAR-Tregs have the potential to address this issue efficiently?

CAR-Tregs are designed to reproduce the way the immune system normally works more effectively in comparison to previous approaches, which used unmodified Tregs. By genetically engineering the cells, we can be certain that all the cells have the precise properties we desire.

Why did you choose to work with TxCell, and how do you see your progress after this first year of collaboration?

My lab published the first ever proof-of-concept with human CAR-Tregs in a transplantation model, in March 2016[1].

With TxCell, we had a mutual interest in driving CAR-Treg technology to a clinical application. The first year has been a lot of hard work for the team, but I am very happy with how far we have come and the whole lab is very motived to work on this project because they can see how close we are to the clinical application of this innovative technology.

If you were to formulate a dream, what would that be?

That engineering Tregs with CARs is truly the solution to transplantation tolerance!

In October 2016, TxCell signed a strategic collaboration

with the University of British Columbia (UBC) in Canada to develop CAR-Tregs in organ transplantation and launch a first-in-man study by the end of 2018, which could be a world premiere.

[1] *MacDonald KG, Hoeppli RE, Huang Q, Gillies J, Luciani DS, Orban PC, Broady R, Levings MK. J Clin Invest. 2016, 126(4):1413-1424.*
[2] *US Department of Health & Human Services. 'More than 30,000 transplants performed annually for first time in United States' January 9, 2016.*
[3] *European Commission, Journalist workshop on organ donation and transplantation, November 26, 2014.*
[4] *UNOS, European Commission.*
[5] *Gondos A , Döhler B, Brenner H, Opelz G. Kidney graft survival in Europe and the United States: strikingly different long-term outcomes. Transplantation. 2013 Jan 27;95(2):267-74.*
[6] *Hartert M, Senbaklavaci O, Gohrbandt B, Fischer BM, Buhl R, Vahl CF. Lung transplantation: a treatment option in end-stage lung disease. Dtsch Arztebl Int 2014; 111(7): 107–16.*
[7] *Organ Transplant Immunosuppressant Drugs Market, Transparency Market Research 2015.*

TECHNOLOGY: HOW ARE CAR-TREG CELLS MADE?

Portrait: Pierre Heimendinger, Vice-president Pharmaceutical Development at TxCell

Former Head of Pharmaceutical Development at Transgene SA, Pierre Heimendinger, PharmD., has been in charge of the development and optimization of TxCell's manufacturing processes since the end of 2015.

Can you tell us about the role of your Pharmaceutical Development team?

Our role is to develop an 'industrial' manufacturing and control process. We start from the work done by the cellular engineering team and transform the process from a purely 'research' grade process into one that conforms with Good Manufacturing Practice (GMP). Unlike research scientists, who work with very small amounts of cells, we start with a volume of blood product comparable to that to be drawn from the patients in the clinic. We optimize each step of the manufacturing process, one by one, with the goal of ensuring the safety, quality and efficacy of the final drug product.
To achieve this, we use closed systems as much as possible to avoid any external contamination. We also try to minimize the duration of each step to optimize the total length of the manufacturing process so that we have an end product composed of cells that are as active biologically as possible. In parallel, we are careful to control all costs, whether they are related to personnel or supplies, to ensure the economic viability of the product for its potential future commercialization.

Beyond the manufacturing of the product itself, we also set up the whole production chain, from the patient's collection up to the quality control tests. In particular, it is essential to ensure that the starting material is collected under the right conditions so that we can then produce good quality CAR-Treg cells.
Finally, we also oversee the transfer of technology to third-party Contract Manufacturing Organizations that will be in charge of producing the clinical batches. We educate them on how to perform our process by reproducing very precisely each step as we have developed it.

What will Lentigen bring to the production process and why have you decided to outsource this step?

Lentigen brings specific expertise in the manufacture of GMP lentiviral vectors. Internally, we can produce lentiviral vectors at a 'research' grade but we do not have the capacities to produce them in GMP conditions. Lentigen has already produced such vectors for pharmaceutical industry leaders, which gives us guarantees in terms of product safety.

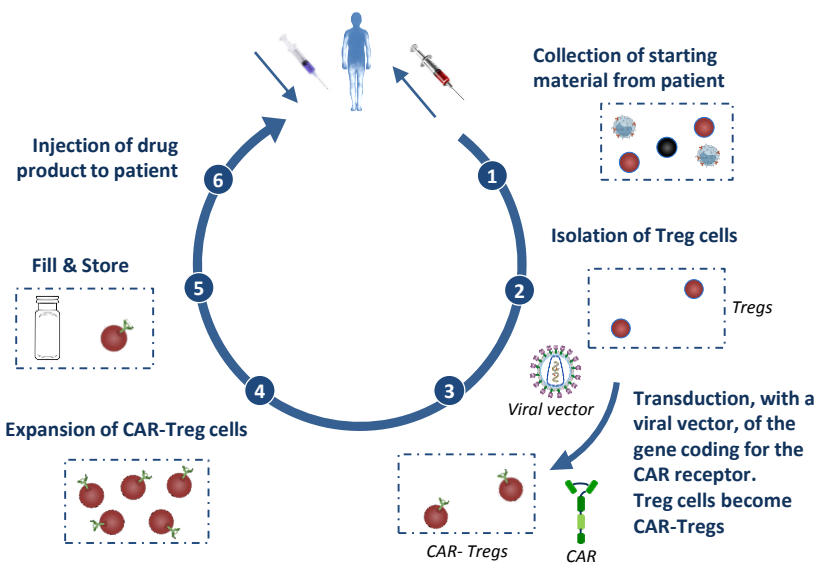
Which methods to you use to produce the CAR-Tregs and what are the challenges to industrialize this production?

We use a combination of existing production tools (e.g. machines to sort or wash cells) together with specific tools developed in collaboration with manufacturers.
Indeed, we are pioneers in cellular immunotherapy based on regulatory T cells and we work on rare cell populations. As a result, we need to develop cell sorting tools adapted specifically to our cells.
One of the challenges is to be able to isolate those populations of rare cells with a good yield and a very good purity, under GMP conditions. The production process we develop must be short, economically viable and robust, i.e. reproducible and reliable whatever the quality of the starting material, which can vary, depending on the condition of the patient.

What are your key next steps?

The second half of 2017 will be a period of intense activity, with the planned selection of our second CMO for the production of the final pharmaceutical product, the finalization of our CAR-Treg manufacturing and control process, and the start of technology transfer to the selected CMO. We need to finalize all this so that we ready for the launch of the first CAR-Treg clinical study by the end of 2018.

Main steps of CAR-Treg manufacturing



TXCELL'S RESEARCH ORGANIZATION

TxCell's research department includes three main teams: the ***Cell Engineering*** team, which develops the "CAR" receptor, the ***Preclinical*** team which is in charge of the evaluation of CAR-Treg cells in animal models and finally the ***Pharmaceutical Development*** Team led by Pierre Heimendinger. Overall, 36 scientists work in three units, which represent approximately 80% of the Company's staff.

WHAT IS A VIRAL VECTOR?

Transferring genes using viral vectors involves use of a virus to introduce genes into cells in order to modify those cells genetically. This method is used in gene therapy as well as in cell therapy when cells are modified before being injected to the patients. Several types of viruses can be used as vectors, including retroviruses and lentiviruses. For its transplantation program, TxCell has decided to use a lentivirus. This is the same type of vector used to manufacture CAR-T cells in oncology. CAR-T cells have already been used in clinical trials and are likely to be launched commercially in oncology applications in the United States in 2017.

TxCell selected Lentigen Technology, Inc. to produce the HLA-A2 CAR lentiviral vector in its most advanced program.

Lentigen Technology Inc. a Miltenyi Biotec Company

Teaching regulatory T cells to treat your disease

QUESTIONS FROM SHAREHOLDERS

Why did you choose to issue new shares with warrants attached for the capital increase completed in February 2017? What should I do with my warrants?

By attaching warrants to the new shares, shareholders have been offered an additional opportunity to participate in the future development of TxCell by further increasing their financial participation in the company at predefined conditions. With a maturity of one year (i.e. February 26, 2018) 4 warrants will entitle holders to subscribe to 3 new shares in return for payment of the subscription price of 2.60 euros per new share. These warrants can also be traded on the market (ISIN code FR0013231792). The proceeds from the exercise of all the warrants would allow TxCell to fund its operations up to the IND approval (targeted for late 2018) for the first-ever clinical study a CAR-Treg worldwide. If warrants are not exercised or sold by February 26, 2018 (included), they will become null and void.

What is the newsflow in the coming months?

TxCell aims to be the first company to initiate a clinical trial with a CAR-Treg, by the end of 2018.

By the end of 2017, TxCell also expects to generate new preclinical proof-of-concept data for its CAR-Treg programs. These notably include the transplant rejection program, an area with a commercial opportunity estimated at over $5 billion. These data would represent the first proof-of-concepts of TxCell's new technology platform, before expanding to other autoimmune and inflammatory diseases.

We hear a lot about CAR-T, what's the difference with TxCell CAR-Treg?

Both CAR-T and CAR-Treg are technologies that make use of genetically engineered immune system cells. The difference is in the type of cells that is used. CAR-T cells use "killer" cells, for example, to destroy cancer cells; whereas TxCell uses regulatory T-cells to control the body's immune response, which, when excessive, is at the root of autoimmune disease or graft rejections. In essence, CAR-Tregs could be to autoimmune diseases and transplantation what the famous CAR-T cells are to oncology.

TXCELL IN THE PRESS

Feb. 6, 2017 **TxCell : 11 M€ pour les CAR-Tregs**

BIOTECHFINANCES

« Seule sur les cellules Tregs spécifiques d'antigènes […] Ce focus sur les CAR-Treg intervient suite au recentrage stratégique opéré par TxCell."

Feb. 22, 2017 **First-Ever CAR-Treg Trial gets Funding Boost in France**

LABIOTECH.eu

"TxCell […] is developing CAR-Treg, a unique version of this technology with the potential of being applied to several big indications."

ANALYST COVERAGE

Firm	Analyst	Date	Recommendation
INVEST SECURITIES	M. Descoutures	July 4, 2017	Buy
ODDO BHF	S. Malafosse	Dec. 9, 2016	Neutral
SOCIETE GENERALE Corporate & Investment Banking	D. Le Louët	June 1st, 2017	Sell
EDISON	J. Savin	March 14, 2017	NA
LIFESCI CAPITAL	J. Isaacson	March 14, 2017	NA

RECENT INDUSTRY NEWS – TREG AND CELL THERAPY

January 2017: **DELINIA, INC.**, a U.S.-based private company developing treatment for autoimmune diseases acting through *in vivo* Treg stimulation, was acquired by U.S. giant **CELGENE**. The transaction included an upfront payment of $300 million and additional milestone payments of up to $475 million.

April 2017: **PARVUS**, a Canadian company, signed an exclusive worldwide licensing agreement with **NOVARTIS** for Navacim, its type 1 diabetes program. The program is based on nanoparticles inducing the *in vivo* formation and expansion of Tregs to restore immune tolerance. Financial terms of the agreement have not been disclosed but include Novartis taking an equity investment in Parvus.

May 2017: **ILTOO PHARMA**, a French company, signed an exclusive licensing option agreement with **SERVIER** for its drug-candidate, ILT-101, targeting the treatment of autoimmune diseases. ILT-101 is composed of low-dose IL-2 to restore the balance between regulatory T cells and effector T cells. Under terms of the option agreement, Servier will be required to make a decision in 2018, following completion of the phase 2 study currently underway in lupus. Servier paid ILTOO an upfront payment of €8 million. The agreement also provides for milestone payments of up to €200 million, as well as double-digit royalties on future sales.

The first two CAR-T products, developed by Novartis and Kite Pharma, could be launched in the US in 2017 and confirm the potential of CAR-based cellular therapies.

CAR-T cells are genetically-modified effector T cells targeting a predefined antigen, generally in the oncology field. The two most advanced products are CTL019 (tisagenlecleucel) from Novartis, for the treatment of relapsed or refractory acute lymphoblastic leukemia in children and young adults, and KITE-C19 (axicabtagene ciloleucel) from Kite Pharma for the treatment of aggressive, relapsed or refractory forms of non-Hodgkin's lymphoma. CTL019 and KTE-C19 both target the CD19 antigen. These products are currently under review by the US FDA, which is expected to make a decision by the end of 2017. Regulatory approval would represent a transformational event for the industry in which TxCell operates.