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Press release

## **TxCell and Inserm collaborate to develop new CAR-Tregs in transplantation and multiple sclerosis**

### **Expansion of TxCell's CAR-Treg platform to develop novel proprietary population of CD8+ regulatory T cells**

**Valbonne, France and Nantes, France, May 2, 2017, 5.45pm CEST – TxCell SA (FR0010127662 – TXCL),** a biotechnology company developing innovative, personalized cellular immunotherapies using regulatory T cells (Treg) to treat severe inflammatory and autoimmune diseases as well as transplant rejection, and **Inserm Transfert**, on behalf of Inserm (French public organization dedicated to human health) and the Nantes University (Nantes, France), today announce the signature of a R&D collaboration agreement. This collaboration agreement complements the December 2016 exclusive worldwide licensing agreement pertaining to a new subset of Treg cells originated in one of the Inserm laboratories.

The agreement announced today covers R&D activities to take place between TxCell and the Center for Research in Transplantation and Immunology (CRTI), a center of excellence in the field of transplantation and immunology. The CRTI is a research unit (UMR 1064) affiliated to both Inserm and to the Nantes University. TxCell and the CRTI will collaborate on the development of Chimeric Antigen Receptor (CAR) engineered CD8+Treg cells (CAR-Tregs). These comprise a proprietary Treg cell population expressing the CD8 marker (CD8+ Tregs). The collaboration will concentrate on the treatment of transplant rejection and autoimmune diseases, specifically focusing on multiple sclerosis. In addition, TxCell and the CRTI will develop a manufacturing process to enable clinical proof-of-concept studies.

The collaboration will expand TxCell's research efforts, which were focusing so far on engineered CD4+ Treg cells, to explore the therapeutic potential of engineered CD8+ Treg cells in parallel. These CD8+ Tregs are non-cytotoxic and display a unique and highly immunosuppressive mechanism of action, mediated through the release of cytokines with anti-inflammatory and tolerogenic properties<sup>1,2</sup>.

The transplantation arm of the collaboration announced today complements the ongoing collaboration between TxCell and the University of British Columbia (UBC) in Vancouver,

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<sup>1</sup> Bézie S, Picarda E, Ossart J, Tesson L, Usal C, Renaudin K, Anegon I, Guillonneau C. IL-34 is a Treg-specific cytokine and mediates transplant tolerance. *J Clin Invest.* 2015 Oct 1;125(10):3952-64.

<sup>2</sup> Picarda E, Bézie S, Venturi V, Echasserieau K, Mérieau E, Delhumeau A, Renaudin K, Brouard S, Bernardeau K, Anegon I, Guillonneau C. MHC-derived allopeptide activates TCR-biased CD8+ Tregs and suppresses organ rejection. *J Clin Invest.* 2014 Jun;124(6):2497-512.

Canada. Since October 2016, TxCell and UBC have been working together on the development of a CAR-Treg-based cellular immunotherapy to prevent graft rejection in the context of Solid Organ Transplantation (SOT). The TxCell-UBC collaboration is focused on CAR-Treg cells made from CD4+ Treg cells.

*“TxCell is now benefiting from the CRTI’s expertise on these novel CD8+ Treg cells in addition to the intellectual property secured in December 2016,”* said François Meyer, Head of Research of TxCell. *“Evaluating CAR-CD8+Treg cells in preclinical models of transplantation and autoimmune diseases to confirm their therapeutic potential will continue to push development in key target markets for TxCell.”*

*“This collaboration with TxCell will help us set in concrete the clinical development of innovative therapies based on CAR-CD8+Treg cells. We look forward to evaluating with TxCell the potential of these specific CAR-Tregs in the treatment of graft rejection and multiple sclerosis,”* said Dr. Carole Guillonnet, CRNS scientist and co-director of the CRTI team number 2.

*“TxCell’s expertise in the industrial development of CD4+ Treg cells will be a major asset to move towards a potential use in the clinic of the CD8+ Treg cells we have identified,”* added Dr. Ignacio Anegón, INSERM scientist and co-director of the CRTI team number 2. *“This TxCell-CRTI collaboration represents a robust synergy between translational immunotherapy scientists and an experience biotech company.”*

In December 2016, TxCell gained exclusive worldwide rights to two patent families covering the new type of CD8+ Tregs for all autoimmune diseases and transplantation-related disorders. The CRTI team has already demonstrated the efficacy of these CD8+ Tregs in a number of preclinical models of inflammation, including heart allograft, human skin transplant rejection and graft-versus-host disease (GvHD) in mice with humanized immune systems<sup>3</sup>. In these models, the administration of CD8+ Treg cells has been shown to prevent the occurrence of skin graft rejection and GvHD, respectively.

In addition to the background intellectual property already in-licensed in December 2016, TxCell now also has an exclusive option on programs and products developed under the collaboration agreement announced today.

Financial terms of the agreement have not been disclosed.

**About CRTI** – <http://www.itun.nantes.inserm.fr/>

The Center for Research in Transplantation and Immunology (CRTI) is a research unit (UMR 1064) affiliated to Inserm and Nantes University. The CRTI research programs and organization rely on the definition of common scientific objectives, the development of translational

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<sup>3</sup> Guillonnet C, Hill M, Hubert FX, Chiffolleau E, Hervé C, Li XL, Heslan M, Usal C, Tesson L, Ménoret S, Saoudi A, Le Mauff B, Josien R, Cuturi MC, Anegón I. CD40lg treatment results in allograft acceptance mediated by CD8CD45RC T cells, IFN-gamma, and indoleamine 2,3-dioxygenase. J Clin Invest. 2007 Apr;117(4):1096-106

research, sharing of resource, technical platforms development and research development towards clinical and industrial applications.

Main research areas are immunology, transplantation, autoimmune diseases, regenerative medicine and genetics with the aim in the long term of: (i) improving graft survival in transplanted patients thanks to novel biomarkers and immuno-intervention strategies, (ii) implementing these new tools in other clinical conditions such as IMIDs and (iii) developing alternative solutions for replacement of organs and tissues.

The CRTI UMR1064 and the clinical departments of Clinical Immunology, Nephrology and Urology at the Nantes teaching hospital together form the Institute of Transplantation-Urology-Nephrology (ITUN). The kidney and pancreas transplantation program of the ITUN ranks among the best in France and Europe.

**About Inserm & Inserm Transfert – <http://www.inserm-transfert.fr>**

Founded in 2000, Inserm Transfert SA is the private subsidiary of the French National Institute of Health and Medical Research (Inserm). Inserm Transfert is dedicated to technology and knowledge transfer of Inserm's laboratories innovations, from scouting of invention disclosure to industrial partnership.

Founded in 1964, the French National Institute of Health and Medical research (Inserm) is a public science and technology institute that supports more than 300 laboratories across France and include nearly 15,000 researchers, engineers, technicians, post-doctoral fellow, students... Inserm is the only French public research institute to focus entirely on human health and that positions itself on the pathway from research laboratory to the bed of the patient in a multidisciplinary approach. Inserm is a core member of the National Alliance for Life and Health Sciences (Aviesan), founded in April 2009.

**About TxCell – [www.txcell.com](http://www.txcell.com)**

TxCell is a biotechnology company that develops platforms for innovative, personalized T cell immunotherapies for the treatment of severe inflammatory and autoimmune diseases with high unmet medical need. TxCell is targeting a range of autoimmune diseases (both T-cell and B-cell-mediated) including Crohn's disease, lupus nephritis, bullous pemphigoid and multiple sclerosis, as well as transplant rejection.

TxCell is the only clinical-stage cellular therapy company fully dedicated to the science of regulatory T lymphocytes (Tregs). Tregs are a recently discovered T cell population for which anti-inflammatory properties have been demonstrated. Contrary to conventional approaches based on non-specific polyclonal Tregs, TxCell is exclusively developing antigen-specific Tregs. This antigen specificity may either come from genetic modifications with Chimeric Antigen Receptor (CAR) or from pre-existing Treg cell T-Cell Receptor (TCR). TxCell is developing two

proprietary technology platforms, ENTriA, which is composed of genetically-engineered Tregs, and ASTriA, which is composed of non-modified naturally antigen-specific Tregs.

Based in Sophia-Antipolis, France, TxCell is listed on Euronext Paris and currently has 46 employees.

## Next events

### Financial and business conferences

May 3	Investment for Advanced Therapies Summit	London (UK)
May 22-23	BioEquity Europe 2017	Paris (FR)
May 30	Gilbert Dupont 15 <sup>th</sup> Annual Healthcare Conference	Paris (FR)
June 6-9	Jefferies Global Healthcare Conference	New York (US)
June 9	Kepler Cheuvreux Biotech Day	Paris (FR)
June 19-22	BIO International Convention	San Diego (US)

### Scientific and medical conferences

May 3-6	International Society for Cellular Therapy (ISCT) Annual Meeting	London (UK)
May 10-13	American Society of Gene and Cell Therapy (ASGCT) Annual Meeting	Washington (US)
May 30-31	Phacilitate's inaugural Special Interest Group: Automation	Edinburgh (UK)
June 1-2	22 <sup>e</sup> congrès Nantes Actualités Transplantation (NAT)	Nantes (FR)

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## Forward-Looking Statements - TxCell

This press release contains certain forward-looking statements relating to the business of TxCell, which shall not be considered *per se* as historical facts, including TxCell's ability to develop, market, commercialize and achieve market acceptance for specific products, estimates for future performance and estimates regarding anticipated operating losses, future revenues, capital requirements, needs for additional financing. In addition, even if the actual results or development of TxCell are consistent with the forward-looking statements contained in this press release, those results or developments of TxCell may not be indicative of their in the future.

In some cases, you can identify forward-looking statements by words such as "could," "should," "may," "expects," "anticipates," "believes," "intends," "estimates," "aims," "targets," or similar words. Although the management of TxCell believes that these forward-looking statements are reasonably made, they are based largely on the current expectations of TxCell as of the date of this press release and are subject to a number of known and unknown risks and uncertainties and other factors that may cause actual results, performance or achievements to be materially different from any future results, performance or achievement expressed or implied by these forward-looking statements. In particular, the expectations of TxCell could be affected by, among other things, uncertainties involved in the development of the Company's products, which may not succeed, or in the delivery of TxCell's products marketing authorizations by the relevant regulatory authorities and, in general, any factor that could affect TxCell capacity to commercialize the products it develops, as well as, any other risk and uncertainties developed or identified in any public documents filed by TxCell with the AMF, included those listed in chapter 4 "Risk factors" of the 2016 *document de référence* (registration document) approved by the AMF on April 26, 2017 under number R.17-024. In light of these risks and

uncertainties, there can be no assurance that the forward-looking statements made in this press release will in fact be realized. Notwithstanding the compliance with article 223-1 of the General Regulation of the AMF (the information disclosed must be “accurate, precise and fairly presented”), TxCell is providing the information in these materials as of this press release, and disclaims any intention or obligation to publicly update or revise any forward-looking statements, whether as a result of new information, future events, or otherwise.