

## TiGenix starts Phase I trial of Cx611 in severe sepsis

**Leuven (BELGIUM) – 10 December, 2014 –TiGenix NV (Euronext Brussels: TIG), an advanced biopharmaceutical company focused on developing and commercialising novel therapeutics from its proprietary platform of allogeneic, expanded adipose-derived stem cells in inflammatory and autoimmune diseases, announced today that the first subject has been entered into its Phase I trial of Cx611 in severe sepsis.**

Cx611 is an intravenously-administered product of allogeneic expanded adipose-derived stem cells (eASC's). The product will enter Phase II of clinical development for early rheumatoid arthritis next year, and this study marks the start of its development for patients with severe sepsis. This trial is a proof of principle study and is designed to demonstrate the efficacy of Cx611 in healthy volunteers challenged with a bacterial endotoxin (lipopolysaccharide) which elicits an inflammatory response inducing sepsis-like clinical symptoms. The trial is a placebo-controlled dose-ranging study (3 doses of eASC's) in which 32 healthy male volunteers will be randomised to receive Cx611 or placebo in a ratio of 3:1. Primary endpoints will be vital signs and symptoms, laboratory measures and functional assays of innate immunity.

“The mortality rate for patients with severe sepsis is over 50%”, said Dr Marie Paule Richard, Chief Medical Officer of TiGenix. “We believe that by adding Cx611 to the current standard of care, TiGenix can reduce this grave loss of life. TiGenix expects to complete the trial by the third quarter of 2015, and then to follow up with a Phase II trial of Cx611 as an add-on therapy to the standard of care in patients with severe sepsis.”

### **For more information:**

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### **About Cx611**

*Cx611 is an intravenously-administered product of allogeneic expanded adipose-derived stem cells (eASC's). TiGenix is currently developing Cx611 for patients with early rheumatoid arthritis and for patients with severe sepsis. For the first of these two indications, in 2013 TiGenix reported positive 6-month safety data from its Phase IIa study of Cx611 in refractory rheumatoid arthritis, as well as a first indication of therapeutic activity using standard outcome measures and biologic markers of inflammation for at least three months after dosing. The multicentre, randomised, double-blind, placebo-controlled Phase IIa trial enrolled 53 patients with active refractory rheumatoid arthritis (mean time since diagnosis 15 years), under treatment with at least one non-biologic disease-modifying anti-rheumatic drug (DMARD), who failed to respond to at least two biologic drugs (mean previous treatment: 3 or more DMARDs and 3 or more biologic drugs). The study design was based on a three-cohort dose-escalating protocol. For both the low and medium dose regimens, 20 patients received active treatment versus 3 patients on placebo; for the high dose regimen, 6 patients received active treatment versus 1 on placebo. Patients were dosed at Days 1, 8, and 15 and were followed up monthly over a six-month period. Follow-up consisted of a detailed monthly work-up of all patients, measuring all pre-defined parameters. The aim was to evaluate the safety, tolerability and optimal dosing over the full 6 months of the trial, as well as exploring therapeutic activity. Only one patient suffered serious adverse events that led to a discontinuation of treatment. All other side effects were mild and transient indicating that eASCs are well tolerated and associated with an*

overall acceptable safety profile. Measured clinical activity scores were ACR20<sup>1</sup>, ACR50<sup>1</sup>, ACR70<sup>1</sup>, EULAR<sup>2</sup> response rates, and the disease activity score, DAS28<sup>3</sup>. To gain a first insight into therapeutic activity, these parameters were evaluated every month for six months. Patients receiving Cx611 had higher ACR scores, a better EULAR response, and higher DAS28 scores than patients receiving placebo over three months, and a sustained benefit over six months. The Company is currently working with clinical experts to complete a protocol for a randomised, double-blind, comparative Phase II study to test the efficacy of Cx611 in patients exhibiting substantial disease activity of rheumatoid arthritis despite treatment with methotrexate and corticosteroids, but unexposed to a biological drug. Recruitment for the proposed study could start in the third quarter of 2015 and TiGenix would expect final results to be available by the first half of 2017. In severe sepsis, as well as additional animal model testing, TiGenix has started a randomised, placebo-controlled trial to test the mechanism of action of Cx611 in healthy volunteers challenged with a bacterial endotoxin (lipopolysaccharide), a potent pro-inflammatory constituent of the outer membrane of Gram-negative bacteria, which elicits an inflammatory response inducing sepsis-like clinical symptoms. TiGenix expects to complete this study by the third quarter of 2015 and then to follow up with a phase II trial of Cx611 as an add-on therapy to the standard of care in patients with severe sepsis.

<sup>1</sup> ACR 20 means a 20% improvement in tender or swollen joint counts as well as 20% improvement in at least three of the following five criteria: patient assessment, physician assessment, erythrocyte sedimentation rate, pain scale and functional questionnaire. The ACR50 and ACR70 categories adhere to the same criteria, but for 50% and 70% improvement, respectively.

<sup>2</sup> EULAR, European League Against Rheumatism

<sup>3</sup> DAS28, Disease Activity Score 28 joint count

## About TiGenix

TiGenix NV (Euronext Brussels: TIG) is an advanced biopharmaceutical company focused on developing and commercialising novel therapeutics from its proprietary platform of allogeneic, or donor-derived, expanded adipose-derived stem cells, known as eASCs, in inflammatory and autoimmune diseases. Two products from this technology platform are currently in clinical development. Cx601 is in Phase III for the treatment of complex perianal fistulas in Crohn's disease patients. Cx611 is in Phase IIb for early rheumatoid arthritis, and in Phase Ib for severe sepsis. TiGenix also developed ChondroCelect, an autologous cell therapy product for cartilage repair of the knee, which was the first Advanced Therapy Medicinal Product (ATMP) to be approved by the European Medicines Agency (EMA). From June 2014, the marketing and distribution rights of ChondroCelect have been exclusively licensed to Sobi for the European Union (except for Finland, where it is distributed by the Finnish Red Cross Blood Service), Norway, Russia, Switzerland and Turkey, and the countries of the Middle East and North Africa. TiGenix is headquartered in Leuven (Belgium) and has operations in Madrid (Spain). For more information, please visit [www.tigenix.com](http://www.tigenix.com)

## Forward-looking information

This document may contain forward-looking statements and estimates with respect to the anticipated future performance of TiGenix and the market in which it operates. Certain of these statements, forecasts and estimates can be recognised by the use of words such as, without limitation, "believes", "anticipates", "expects", "intends", "plans", "seeks", "estimates", "may", "will" and "continue" and similar expressions. They include all matters that are not historical facts. Such statements, forecasts and estimates are based on various assumptions and assessments of known and unknown risks, uncertainties and other factors, which were deemed reasonable when made but may or may not prove to be correct. Actual events are difficult to predict and may depend upon factors that are beyond the Company's control. Therefore, actual results, the financial condition, performance or achievements of TiGenix, or industry results, may turn out to be materially different from any future results, performance or achievements expressed or implied by such statements, forecasts and estimates. Given these uncertainties, no representations are made as to the accuracy or fairness of such forward-looking statements, forecasts and estimates. Furthermore, forward-looking statements, forecasts and estimates only speak as of the date of the publication of this document. TiGenix disclaims any obligation to update any such forward-looking statement, forecast or estimates to reflect any change in the Company's expectations with regard thereto, or any change in events, conditions or circumstances on which any such statement, forecast or estimate is based, except to the extent required by Belgian law.