

European Patent Office issues key patent to TiGenix for expanded adipose-derived stem cell compositions

Leuven (BELGIUM) – 22 January, 2015 –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 European Patent Office (EPO) has issued European Patent EP2292736 relating to an adipose-derived stem cell composition. The patent is entitled “Identification and isolation of multipotent cells from non-osteochondral mesenchymal tissue”. The claims of the granted patent cover both a specified population of expanded adipose-derived multipotent cells and their therapeutic uses, as well as pharmaceutical compositions of such cells.

TiGenix is developing injectable products from its proprietary platform of allogeneic expanded adipose-derived stem cells (eASCs) for inflammatory and autoimmune diseases. Cx601 is a solution of allogeneic eASCs for local injection currently in Phase III of clinical development for the treatment of complex perianal fistulas in patients with Crohn’s disease. Clinical results from the on-going European Phase III trial are expected in the third quarter of 2015, and, if positive, may allow the company to file for Marketing Authorisation in Europe. Cx611 is an intravenously-administered product of allogeneic eASCs, which TiGenix is currently developing for patients with early rheumatoid arthritis and for patients with severe sepsis.

“This European patent further strengthens our intellectual property position in the field of expanded adipose-derived stem cell compositions and their therapeutic uses”, said Wilfried Dalemans, Chief Technical Officer of TiGenix. “The grant of this patent advances our leading position in bringing adipose-derived stem cell therapeutics to patients.”

The issuance of this patent reinforces TiGenix’s intellectual property portfolio of 24 patent families which now includes 14 granted patents related specifically to its eASC platform. The pending and granted patents in TiGenix’s intellectual property portfolio include patent families that are directed to its eASC platform; and more specifically, to eASC compositions and therapeutic applications as well as to cell therapy delivery mechanisms and other eASC technology improvements.

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About Cx601

Cx601 is a suspension of allogeneic expanded adipose-derived stem cells (eASCs) delivered locally through intra-lesional injection. Cx601 is being developed for the treatment of perianal fistulas in Crohn’s disease patients. Crohn’s disease is a chronic inflammatory disease of the intestine and patients can suffer from complex perianal fistulas for which there is currently no effective treatment. In 2009, the European Commission granted Cx601 orphan designation for the treatment of anal fistulas, recognising the debilitating nature of the disease and the lack of treatment options. In a Phase II clinical trial, Cx601 showed efficacy at 24 weeks in 56% of treated fistula tracts, which is more than two times higher than the current standard of care (TNF inhibitors). Efficacy was measured as the complete closure and re-epithelisation of the fistula being treated with an absence of drainage. Additionally, 69.2% of patients demonstrated a reduction in the number of initially draining tracts. The trial also confirmed the safety of the use of allogeneic stem cells for the treatment of perianal fistula. Based on these results, TiGenix sought scientific advice from the

European Medicines Agency (EMA) on the future development path of Cx601. TiGenix then initiated a randomised, double-blind, placebo-controlled Phase III trial in Europe and Israel designed to comply with the requirements laid down by the EMA. 'Madrid Network', an organisation within the Autonomous Region of Madrid which helps companies to grow through high-technology innovation, issued a soft loan to help finance this Phase III study. The programme is funded by The Secretary of State for Research, Development and Innovation (Ministry of Economy and Competitiveness) within the framework of the INNTEGRA plan. This pivotal study is intended to enable filing for marketing authorisation in Europe and to serve as a key supportive study in filing for approval in other territories, including the US. The study's primary endpoint is remission of the fistulous disease, defined as 100% healing of the tracts. The trial has a first complete analysis of results at 24 weeks, with a follow-up analysis to be performed at 52 weeks post-treatment. Evaluation of healing includes both clinical assessment and MRI confirmation (lack of abscesses larger than 2 cm²). Recruitment of the whole sample of patients was completed in the fourth quarter of 2014. The first clinical report is expected to be available in the third quarter of 2015. With positive results, TiGenix intends to submit a request for marketing authorisation with the EMA early in 2016. TiGenix is preparing to develop Cx601 for the US market. The company has filed for a Special Protocol Assessment (SPA) by the Food and Drug Administration (FDA) to ensure that the design of a new Phase III study to be conducted in the US is aligned with the FDA's requirements for the future approval of Cx601. The company intends to appoint a contract manufacturing organisation (CMO) in the US with whom it will then begin the transfer of technology to enable production of Cx601 in the US.

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 ACR20¹, ACR50¹, ACR70¹, EULAR² response rates, and the disease activity score, DAS28³. 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.

¹ 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.

² EULAR, European League Against Rheumatism

³ 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

Forward-looking information

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