TiGenix

REGULATED INFORMATION
PRESS RELEASE

Safety and tolerability of Cx611 confirmed in Phase I sepsis challenge trial

Leuven (BELGIUM) – 28 May, 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 results of its Phase I sepsis challenge trial of Cx611 confirm safety and tolerability.

"The results of this Phase I proof of principle study demonstrate the favorable safety and tolerability profile of Cx611, which is consistent with our previous study in patients with rheumatoid arthritis" said Dr Marie Paule Richard, Chief Medical Officer of TiGenix. "No serious adverse events were reported with any of the three doses tested. With respect to anti-inflammatory activity, no significant effect of Cx611 on the lipopolysaccharide-induced symptoms could be detected."

"The timeframe of this particular lipopolysaccharide challenge model in healthy volunteers might have been too short to allow Cx611 to exert its therapeutic effect" said Dr Wilfried Dalemans, Chief Technical Officer of TiGenix. "Compared to this challenge model, patients suffering from severe sepsis display a much higher level and persistence of inflammation that is expected to provide the necessary signals for the activation of Cx611 and thereby positively interfere with the underlying inflammatory process." TiGenix, along with its Clinical Advisory Board, is further analysing the data to incorporate them into its future developments.

Cx611 is an intravenously-administered product of allogeneic expanded adipose-derived stem cells (eASCs). Its efficacy in significantly reducing mortality has been demonstrated in several animal models of sepsis through a combination of reduced inflammation, production of anti-microbial effectors, and increased phagocytosis. This Phase I trial was a proof of principle study designed to demonstrate the safety and the ability of Cx611 in modifying the inflammatory response in healthy volunteers challenged with a bacterial endotoxin. The trial was a placebo-controlled, parallel group study in which 32 healthy male volunteers were randomised to receive Cx611 (at 3 doses) or placebo in a ratio of 3:1 and followed for 24 hours.

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About Cx611

Cx611 is an intravenously-administered product of allogeneic expanded adipose-derived stem cells (eASCs). 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[1], ACR50[1], ACR70[1], EULAR[2] response rates, and the disease activity score, DAS28[3]. 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 fourth quarter of 2015 and TiGenix would expect final results to be available by the end of 2017.

[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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