TiGenix Business and Financial Update for the First Half 2017

(Conference call and webcast today at 15:00 CET)

Leuven (BELGIUM) – September 19, 2017, 07:00h CET – TiGenix NV (Euronext Brussels and NASDAQ: TIG), an advanced biopharmaceutical company focused on exploiting the anti-inflammatory properties of allogeneic, or donor-derived, stem cells to develop novel therapies for serious medical conditions, today reported its business and financial highlights for the six months’ ended June 30, 2017.

Key business and financial highlights for the first half of 2017 and post period events:

- Cx601 continued to reach significant value inflection points in Europe and the U.S.
  - Responses to the Day 180 LoOI submitted in September 2017. The Day 181 file for Cx601 falls within the first week of October, which may lead to a CHMP opinion in 2017
  - European Commission decision will trigger a payment of EUR 15.0 million from Takeda Pharmaceuticals upon marketing authorization
  - The Swiss Agency for Therapeutic Products (“Swissmedic”) accepted for review the file on Cx601 for the treatment of complex perianal fistulas in patients with Crohn’s disease
  - TiGenix obtained a commercial production license for its expanded manufacturing facility in Madrid to provide capacity for the potential initial European commercial roll out of Cx601. The expanded facility also secures manufacturing capacity for other pipeline products
  - The global pivotal Phase III trial to support a future U.S. registration for Cx601 formally launched in Europe and Israel in June 2017
  - TiGenix opened its U.S. headquarters at the epicenter of the Boston area biotech hub
  - Strengthened U.S. operations with two senior appointments: Dr Gregory Gordon, Head of Medical Department (US) and Annette Valles-Sukkar, Associate Director, Clinical Project
  - Cx601 delivered positive follow-up results at 104 weeks, confirming the long-term safety and efficacy profile

- Continued progress with pipeline
  - First patient enrolled in Phase I/II clinical trial of Cx611 for the treatment of severe sepsis
  - Phase I/II trial results of AlloCSC-01 in Acute Myocardial Infarction (AMI) announced

- Strong cash position at June 30, 2017 of EUR 56.5 million

“In the recent period, we have continued to make good progress towards bringing to market our lead product, Cx601, as an important new treatment option for patients suffering from a severe and debilitating complication of Crohn’s disease,” said Eduardo Bravo, CEO at TiGenix. “In Europe, we are now close to a CHMP opinion which may be received this year. Our partnership with Takeda and the preparations for European launch are progressing well. Looking beyond the European market, we successfully launched our global Phase III trial to support a future regulatory filing in the U.S. and continue to explore routes to accelerate access to the product for U.S. patients. With the progress for...
Cx601, its potential in new indications, and the continued advancement of our pipeline, we look forward to the coming months with great excitement.”

Business highlights for the first half 2017 and post-period events

Cx601 continued to reach major value inflection points


The submission of the responses to the CHMP Day 180 LoOI is part of the standard regulatory procedure, following which – on the so-called Day 181 – the European Medicines Agency (EMA) continues the review of a file after a clock stop.

The Day 181 for the Cx601 file falls within the first week of October, an approximate one month adjustment to the previously anticipated review calendar agreed with the EMA. TiGenix is confident it has provided detailed and clarifying responses to the CHMP, which may lead to a CHMP opinion in 2017.

The Company’s centralized European MA Application to the EMA was supported by the positive 24 and 52-week Phase III data from the ADMIRE-CD Phase III clinical trial. TiGenix is eligible to receive from Takeda a EUR 15.0 million milestone payment upon receipt of the MA.

In June, TiGenix, together with its partner Takeda, announced that the Swiss Agency for Therapeutic Products (“Swissmedic”) accepted for review the file on Cx601 to treat complex perianal fistulas in patients with Crohn’s disease. Cx601 was previously granted orphan drug status by Swissmedic in September 2016, recognizing the severe and debilitating nature of the disease. The Swissmedic filing submission included the Phase III ADMIRE-CD trial data for Cx601. The submission to Swissmedic represented a key milestone in the commercialization of Cx601 in Switzerland.

Also in June, TiGenix formally launched the global pivotal phase III clinical trial for Cx601 for the treatment of complex perianal fistulas in patients with Crohn’s disease, which is designed to support a future regulatory filing for Cx601 in the U.S. The first investigator meeting was held on June 8 and June 9 in Rome, Italy, and brought together more than 60 leading gastroenterologists, colorectal surgeons and study co-ordinators from 30 confirmed clinical trial sites across Belgium, Czech Republic, Italy, Poland and Spain. Similar investigator meetings are planned to take place in Europe (EU), Israel, the United States and Canada from the fourth quarter of 2017.

The global pivotal Phase III trial is a randomized, double-blind, placebo-controlled study designed to confirm the efficacy and safety of a single administration of Cx601 for the treatment of complex perianal fistulas in Crohn's disease patients. The trial design is similar to the European Phase III ADMIRE-CD trial for Cx601, with an identical primary endpoint. In January 2017, the U.S. Food and Drug Administration (FDA) agreed to the design of the protocol for the global Phase III trial, and confirmed that a future U.S. Biologics License Application (BLA) could be filed based on the study results at week 24, instead of week 52, from a broader patient population than the initial Special Protocol Assessment (SPA) formally endorsed in August 2015. With these adjustments, the trial should benefit from an expedited recruitment process, leading to shorter timelines, an earlier filing, and the possibility of an earlier approval in the U.S.

In parallel, TiGenix continues to explore further expedited pathways to accelerate the submission and review process for its future BLA in the United States.

In June, TiGenix opened its U.S. headquarters in Cambridge, Massachusetts. Establishing U.S. operations is a significant step for TiGenix and will support its strategic goal of developing and commercializing Cx601 in the U.S. TiGenix’ U.S. operations are based at the Cambridge Innovation Center in Kendall Square, at the epicenter of the Boston-area biotech hub. TiGenix has since strengthened its U.S. operations with two senior appointments: Dr Gregory Gordon, Head of Medical Department (U.S.) and Annette Valles-Sukkar, Associate Director, Clinical Project.
In September, TiGenix obtained a license for the commercial production of expanded adipose-derived stem cells (eASCs) at its expanded manufacturing facility in Madrid. The manufacturing license follows an inspection by the Spanish Medicines Agency (AEMPS), and provides production capacity for the potential initial European commercial roll out of Cx601. The expanded facility will also provide sufficient capacity for the manufacturing of other pipeline products under development by TiGenix, including Cx611.

Throughout the period, TiGenix has continued to communicate the positive results from the ADMIRE-CD Phase III clinical trial. In March, TiGenix announced positive follow-up results at 104 weeks, confirming the long-term safety and efficacy profile of Cx601 for the treatment of complex perianal fistulas for Crohn’s disease patients.

The 52-week results have also been presented at a number of important international conferences including the 12th Congress of the European Crohn’s and Colitis Organisation (ECCO) in February and at the 2017 Digestive Disease Week (DDW) annual meeting, one of the most prestigious congresses in gastroenterology (GI), in May 2017.

Alongside the DDW presentation, TiGenix hosted a key opinion leader (KOL) event, where leading experts in the GI field met to discuss the unmet medical need in treating complex perianal fistulas. The clinical data of Cx601 was reviewed at the meeting and further insight was provided into why Cx601 has the potential to become a breakthrough therapy in the management of complex perianal fistulas in patients with Crohn’s disease.

Underlining TiGenix’ commitment to the treatment of this debilitating condition, the Company has entered into partnerships with the largest patient advocacy groups focused on Crohn’s disease and ulcerative colitis. In the United States, TiGenix has joined the Crohn’s and Colitis Foundation’s President’s Corporate Circle, and in Europe, TiGenix has signed a sponsorship agreement with the European Federation of Crohn’s and Ulcerative Colitis Associations (EFCCA). The Company will work with both organizations to broaden the understanding and awareness of complex perianal fistulas in Crohn’s disease.

**Progress with pipeline**

Beyond Cx601, TiGenix continues to advance its pipeline of allogeneic products.

Cx611 is TiGenix’ potential first-in-class, intravenous, allogeneic (or donor derived) stem cell therapy intended for the treatment of severe sepsis, a major cause of mortality in the developed world. A Phase Ib/Ia (SEPCELL) clinical trial for Cx611 for the treatment of severe sepsis in community-acquired pneumonia (CAP) was launched in the second half of 2016 and the first patient was dosed in January 2017. Data is expected to be available in 2019 and we believe that Cx611 represents a highly innovative potential treatment for this indication.

In March 2017, TiGenix announced the top-line results for the Phase I/II (CAREMI) study of AlloCSC-01 in Acute Myocardial Infarction (AMI). CAREMI was the first-in-human clinical trial with the primary objective being safety and evaluating the feasibility of an intracoronary infusion of AlloCSCs in patients with AMI and left ventricular dysfunction treated within the first week post-AMI. CAREMI was not powered to establish efficacy, therefore no conclusion was drawn on the secondary efficacy endpoints.

All safety objectives of the study were met. No mortality or major cardiac adverse events (MACE) were found at 30 days meeting the primary endpoint of the study. In addition, neither mortality nor MACE were found at 6 months or 12 months follow-up. Of particular relevance to this allogeneic approach, no immune-related adverse events were recorded at one-year follow-up. A larger reduction in infarct size was found in one pre-specified subgroup associated with poor long-term prognosis which represents more than half of the patient population of the randomization phase of the study. This findings revealed valuable insight, and provided a specific direction for potential studies in a targeted subset of high-risk patients.
Financial highlights for the first half 2017

During the first half of 2017, total revenues amounted to EUR 0.6 million compared to EUR 0.9 million to the same period in 2016. This slight decrease is related to the reduction in royalties and other operating income following the Company’s decision to withdraw the market authorization for ChondroCelect in July 2016 and terminate the agreements with Sobi.

In the first half of 2017 we have continued to progress significantly in our pipeline. In line with our expectations as we advance our clinical programs, research and development expenses for the first half of 2017 amounted to EUR 16.6 million, compared to EUR 9.7 million for the same period in 2016, mainly attributable to clinical activities in connection with the launch of our global pivotal Phase III trial to support a future filing for Cx601 in the US, and launch of the Phase Ib/IIa clinical trial for Cx611 in severe sepsis.

General and Administrative expenses in the first half of 2017 slightly increased and amounted to EUR 4.4 million, compared to EUR 4.3 million for the same period in 2016.

As a result of the above, the operating loss for the first half of 2017 amounted to EUR 20.5 million compared to EUR 13.1 million during the same period in 2016.

The net financial expense of the first six months of 2017 amounted to EUR 5.7 million, compared to a net financial income of EUR 3.7 million during the same period in 2016. This primarily relates to a non-
cash item; the change in the fair value (non-cash) of the embedded derivative on the convertible bonds issued in March 2015 (in line with the increase in share price during the period).

Primarily as a result of the planned increase in the research and development expenses associated with the progress in our clinical development activities and the non-cash change in net financial expense described above, the loss for the first half 2017 amounted to EUR 26.2 million, compared to EUR 9.4 million for the same period in 2016 (which was positively affected by a non-cash fair value gain).

At the end of June 2017, the Company had cash and cash equivalents of EUR 56.5 million, compared to EUR 78.0 million at the beginning of the year. This is in line with our expectations and is mainly due to the net cash used in operating activities during the first half 2017.

Outlook for the coming periods:

- 2H 2017 – Cx601 CHMP opinion
- 2H 2017 – Plan on new indications for Cx601
- 1H 2018 – EUR 15.0 million milestone potential payment by Takeda on EU approval decision
- 1H 2018 – Takeda to launch Cx601 in EU markets
- 1H 2018 – Cx601 IND and start of recruitment in U.S. centers

Interim financial statements

The interim financial statements for the first half of 2017 will be available as of Wednesday 20 September 2017 in the investor section of the TiGenix website, http://www.tigenix.com

Conference call and webcast presentation

TiGenix will conduct a conference call on 19 September 2017, at 15:00 CET / 09:00am ET, which will also be webcast. To participate in the conference call, please call on the following numbers to participate:

Confirmation Code: 1049542

London, United Kingdom: +44(0)20 3427 1917
New York, United States of America: +1 212 444 0896
Paris, France: +33(0)1 70 48 01 66
Brussels, Belgium: +32(0)2 404 0662
Madrid, Spain: +34 91 114 6581
Amsterdam, Netherlands: +31(0)20 721 9158

The webcast can be followed live online via the link: http://edge.media-server.com/m/p/naozpxws

The press release and the webcast slide presentation will be made available on the TiGenix website. A replay of the webcast will be available on the website shortly after the live webcast has finished.

For more information

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About TiGenix

TiGenix NV (Euronext Brussels and NASDAQ: TIG) is an advanced biopharmaceutical company developing novel therapies for serious medical conditions by exploiting the anti-inflammatory properties of allogeneic, or donor-derived, expanded stem cells.

TiGenix’ lead product, Cx601, has successfully completed a European Phase III clinical trial for the treatment of complex perianal fistulas - a severe, debilitating complication of Crohn’s disease. Cx601 has been filed for regulatory approval in Europe and a global Phase III trial intended to support a future U.S. Biologic License Application (BLA) started in 2017. TiGenix has entered into a licensing agreement with Takeda, a global pharmaceutical company active in gastroenterology, under which Takeda acquired the exclusive right to develop and commercialize Cx601 for complex perianal fistulas outside the U.S. TiGenix’ second adipose-derived product, Cx611, is undergoing a Phase I/II trial in severe sepsis – a major cause of mortality in the developed world. Finally, AlloCSC-01, targeting acute ischemic heart disease, has demonstrated positive results in a Phase I/II trial in acute myocardial infarction (AMI). TiGenix is headquartered in Leuven (Belgium) and has operations in Madrid (Spain). For more information, please visit http://www.tigenix.com.

About Cx601

Cx601 is a local administration of allogeneic (or donor derived) expanded adipose-derived stem cells (eASCs) for the treatment of complex perianal fistulas in Crohn’s disease patients that have previously failed conventional therapy. Crohn’s disease is a chronic inflammatory disease of the intestine and complex perianal fistulas are a severe and debilitating complication for which there is currently no effective treatment. Cx601 was granted orphan drug designation by the European Commission in 2009. TiGenix completed a European Phase III clinical trial (ADMIRE-CD) in August 2015. The 24-week data were published in the Lancet and showed both the primary endpoint and the safety and efficacy profile were met. A follow-up analysis was completed at 52 weeks and 104 weeks post-treatment, confirming the sustained efficacy and safety profile of the product. The 24-week results of the Phase III ADMIRE-CD trial were published in The Lancet in July 2016. Based on the positive 24 weeks Phase III study results, TiGenix submitted a Marketing Authorization Application to the European Medicines Agency (EMA) and a CHMP opinion is expected in 2017. A global Phase III clinical trial intended to support a future U.S. Biologic License Application (BLA) started in 2017, based on a trial protocol that has been agreed with the Food and Drug Administration (FDA) through a special protocol assessment procedure (SPA). In July 2016, TiGenix entered into a licensing agreement with Takeda, a global pharmaceutical company active in gastroenterology, under which Takeda acquired exclusive rights to develop and commercialize Cx601 for complex perianal fistulas in Crohn’s patients outside of the U.S.

About Cx611

Cx611 is an intravenous administration of allogeneic expanded adipose-derived stem cells (eASCs) for the treatment of severe sepsis. Sepsis is a life-threatening complication of infection leading to systemic inflammation and organ failure and is the leading cause of death in the developed world. In May 2015, TiGenix completed a Phase I sepsis challenge trial (CELLULA) that demonstrated a favorable safety and tolerability profile for Cx611. Based on the results of this study, TiGenix launched a Phase I/II clinical trial (SEPCELL) in 2016 evaluating Cx611 for the treatment of severe sepsis secondary to community-acquired pneumonia (sCAP) in patients who require mechanical ventilation and/or vasopressors. The first patient was dosed in January 2017 and data is expected in 2019. The trial has received funding from the European Union’s Horizon 2020 research and innovation programme under grant agreement No 681031 and is being carried out through the SEPCELL consortium, which gathers six partners from four European countries. See www.sepcell.eu for more information.

About AlloCSC-01

AlloCSC-01 is an intracoronary administration of allogeneic cardiac stem cells for the treatment of ischemic heart disease. A phase I/II clinical trial (CAREMI) evaluating AlloCSC-01 in Acute Myocardial Infarction (AMI) met its primary endpoint with no mortality or major cardiac adverse events (MACE) found after 30 days of treatment. No mortality or MACE were found at 6 or 12 months follow-up and there were no immune-related adverse events at 12 months follow-up. The CAREMI trial has benefitted
from the support of the CAREMI consortium (Grant Number 242038, http://www.caremiproject.eu/) funded by the Seventh Framework Programme of the European Commission under the coordination of the Centro Nacional de Investigaciones Cardiovasculares (CNIC) and the Centro Nacional de Biotecnología and the participation of research institutions and companies from nine EU countries.
