PRESS RELEASE

REGULATED INFORMATION

INSIDE INFORMATION

Takeda and TiGenix announce that Cx601 (darvadstrocel) has received a positive CHMP opinion to treat complex perianal fistulas in Crohn's disease

- **First allogeneic stem cell therapy to receive positive CHMP opinion in Europe**
- **Cx601 offers potential new treatment option for patients who do not respond to current available therapies and are subject to numerous invasive surgeries[1]**

Osaka, Japan, December 15, 2017 and Leuven, Belgium, December 15, 2017, 13:10h CET – Takeda Pharmaceutical Company Limited (TSE: 4502) ("Takeda") and TiGenix NV (Euronext Brussels and NASDAQ: TIG) ("TiGenix") today announced that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA), in conjunction with the Committee for Advanced Therapies (CAT), has adopted a positive opinion recommending a marketing authorization (MA) for investigational compound Cx601 (darvadstrocel). Cx601 is expected to be indicated for the treatment of complex perianal fistulas in adult patients with non-active/mildly active luminal Crohn's disease, when fistulas have shown an inadequate response to at least one conventional or biologic therapy.[2] This recommendation marks the first allogeneic stem cell therapy to receive a positive CHMP opinion in Europe.

"Following today's news, physicians and surgeons in Europe can look forward to offering these Crohn's disease patients a novel and minimally invasive alternative treatment option in the future, which in clinical trials achieved higher combined remission and lower relapse rates* than the current standard of care," said Professor Julian Panés, Head of the Gastroenterology Department at the Hospital Clinic of Barcelona (Spain) and President of the European Crohn's and Colitis Organisation (ECCO). "Perianal fistulas are estimated to affect up to 28% of patients in the first two decades after Crohn's disease diagnosis and Cx601 offers new hope for those suffering from this severe and debilitating condition."

Cx601 was assessed by the CAT, the EMA's specialized scientific committee for Advanced Therapy Medicinal Products (ATMP), such as gene or cell therapies. The positive CHMP opinion was based on results from TiGenix's Phase III ADMIRE-CD pivotal trial. The ADMIRE-CD trial is a randomized, double-blind, controlled, Phase III trial designed to investigate the efficacy and safety of investigational compound Cx601.[3] 24-week results were published in *The Lancet* and showed that Cx601 achieved statistically significant superiority versus the control group in the primary efficacy endpoint of combined remission.[†,1] In addition, the rates and types of treatment related adverse events (non-serious and serious) and number of discontinuations due to adverse events were comparable between Cx601 and control arms, the most common of which were anal abscess and proctalgia.[1] Further follow-up data indicated that Cx601 maintained long-term remission of treatment refractory complex perianal fistulas in patients with Crohn's disease over 52 weeks.[4]

Dr. María Pascual, VP Regulatory Affairs and Corporate Quality at TiGenix, said, "We believe that this first approval recommendation for an allogeneic stem cell therapy in Europe reflects the maturity of our technology and its potential to offer new approaches for difficult to treat conditions. We have worked closely with the EMA and provided a robust data package from a well-designed clinical trial

* Relapse defined as reopening of any of the treated external openings with active drainage as clinically assessed, or development of perianal collection ≥2cm of the treated perianal fistula confirmed by centrally blinded pelvic MRI assessment in patients with clinical remission at any previous visit

† Combined remission defined as clinical assessment of closure of all treated external openings draining at baseline, despite gentle finger compression, and absence of collections >2cm confirmed by pelvic MRI

with challenging endpoints. In parallel, we will continue working hard to obtain regulatory approval in the U.S. and to develop Cx601 for additional indications, to fulfil our aim of allowing patients to benefit from the full potential of Cx601 across multiple geographies and diseases."

The opinion will now be referred to the European Commission with a decision anticipated in the coming months. An MA will allow Cx601 to be marketed in all 28 member states of the EU, plus Norway, Iceland and Lichtenstein.

Cx601 has been licensed to Takeda for the exclusive development and commercialization outside of the U.S. Receipt of the MA will trigger a milestone payment from Takeda to TiGenix of €15 million. The companies have been working closely together to advance preparations for commercialization, with a potential start of the commercial launch by Takeda anticipated after MA is transferred from TiGenix to Takeda.

"Today's positive CHMP opinion is a crucial step to bringing a new treatment option to patients with complex perianal fistulas in Crohn's disease," said Dr. Asit Parikh, Head of Takeda's Gastroenterology Therapeutic Area Unit. "We would like to thank the scientific community and patients involved in the ADMIRE-CD trial for their support in helping us reach this important milestone. We remain committed to delivering innovative, therapeutic options for patients suffering from gastrointestinal disorders."

Complex perianal fistulas are considered one of the most disabling complications of Crohn's disease[5] and can cause intense pain[6] and swelling, infection and incontinence.[1] Despite available therapies and surgical advancements, they currently remain challenging for clinicians to treat[7] and have a significant negative impact on patient quality of life.[6]

Conference call and webcast

TiGenix will conduct a conference call on **December 18, 2017** at **15:00 CET / 09:00 ET**, which will also be webcast. To participate in the conference call, please call on the following numbers:

Confirmation Code: 9171070

London, United Kingdom:	+44 20 3427 1900
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Paris, France:	+33 1 76 77 2230
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The webcast can be followed live online via the link: https://edge.media-server.com/m6/p/o3msgui7

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Takeda's Commitment to Gastroenterology

Gastrointestinal (GI) diseases can be complex, debilitating and life-changing. Recognizing this unmet need, Takeda and our collaboration partners have focused on improving the lives of patients through the delivery of innovative medicines and dedicated patient disease support programs for over 25 years. Takeda aspires to advance how patients manage their disease. Additionally, Takeda is leading in areas of gastroenterology associated with high unmet need, such as inflammatory bowel disease, acid-related diseases and motility disorders. Our GI research & development team is also exploring solutions in celiac disease, advanced liver disease and microbiome therapies.

About Takeda Pharmaceutical Company

Takeda Pharmaceutical Company Limited is a global, R&D-driven pharmaceutical company committed to bringing better health and a brighter future to patients by translating science into life-changing medicines. Takeda focuses its research efforts on oncology, gastroenterology and central nervous system therapeutic areas. It also has specific development programs in specialty cardiovascular diseases as well as late-stage candidates for vaccines. Takeda conducts R&D both internally and with partners to stay at the leading edge of innovation. New innovative products, especially in oncology and gastroenterology, as well as its presence in emerging markets, fuel the growth of Takeda. More than 30,000 Takeda employees are committed to improving quality of life for patients, working with our partners in health care in more than 70 countries. For more information, visit http://www.takeda.com/news.

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, 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) and Cambridge, MA (USA). 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 adult Crohn's disease patients that have previously shown an inadequate response to at least one conventional therapy or biologic 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 and by the U.S Food and Drug Administration (FDA) in 2017. TiGenix completed a European Phase III clinical trial (ADMIRE-CD) in August 2015 in which both the primary endpoint and the safety and efficacy profile were met, with patients receiving Cx601 showing a 44% greater probability of achieving combined remission compared to control (placebo).[1] A follow-up analysis was completed at 52 weeks[4] 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.[1] Based on the positive 24 weeks Phase III study results, TiGenix submitted a Marketing Authorization Application to the European Medicines Agency (EMA). A global Phase III clinical trial (ADMIRE-CD II) 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 FDA through a special protocol assessment procedure (SPA) (clinicaltrials.gov; NCT03279081). ADMIRE-CD II 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. 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.

Forward-looking information

This press release 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 press release. 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.

References

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[5] Marzo M, Felice C, Pugliese D, *et al.,* Management of perianal fistulas in Crohn's disease: An up-to-date review. *World J Gastroenterol.* 2015; 21(5): 1394-1395.

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