TiGenix and Takeda announce Alofisel® (darvadstrocel) receives approval to treat complex perianal fistulas in Crohn’s disease in Europe

- First allogeneic stem cell therapy to receive central marketing authorization approval in Europe
- Alofisel offers a new treatment option for patients who do not respond to current available therapies and may be subject to numerous invasive surgeries

Leuven, Belgium, March 23, 2018 and Osaka, Japan, March 24, 2018, 18:00h CET – TiGenix NV (Euronext Brussels and NASDAQ: TIG) (“TiGenix”) and Takeda Pharmaceutical Company Limited (TSE: 4502) (“Takeda”) today announced that the European Commission (EC) has approved Alofisel (darvadstrocel), previously Cx601, for the treatment of complex perianal fistulas in adult patients with nonactive/mildly active luminal Crohn’s disease, when fistulas have shown an inadequate response to at least one conventional or biologic therapy. Alofisel should be used after conditioning of fistula. This marks the first allogeneic stem cell therapy to receive central marketing authorization (MA) approval in Europe.

The European approval follows a positive opinion by the European Medicines Agency (EMA) Committee for Medicinal Products for Human Use (CHMP), in conjunction with the Committee for Advanced Therapies (CAT), in December 2017. The recommendation was based on results from TiGenix’s Phase III ADMIRE-CD pivotal trial, which showed that Alofisel achieved statistically significant superiority versus the control group in the primary efficacy endpoint of combined remission at 24 weeks, as well as further follow-up data that indicated Alofisel maintained long-term remission of treatment refractory complex perianal fistulas in patients with Crohn’s disease over 52 weeks.

“I am extremely excited about this approval, which brings allogeneic stem cell therapy one step closer to patients in Europe,” 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). “Alofisel offers a novel, minimally invasive and well tolerated alternative treatment option for patients with Crohn’s disease who do not respond to currently available therapies, and who have until now had limited treatment options available.”

“This approval of Alofisel reflects our deep understanding and recognized leadership in the development of allogeneic stem cells and our firm commitment to developing innovative therapies for medical needs,” said Dr. María Pascual, VP Regulatory Affairs and Corporate Quality at TiGenix. “We are pleased to offer the medical community an important new treatment option for patients with Crohn’s disease who do not respond to currently available therapies.”

Alofisel has been licensed to Takeda for the exclusive development and commercialization outside of the US. Receipt of the MA will trigger a milestone payment from Takeda to TiGenix of €15 million, and initiation of the process of transferring MA from TiGenix to Takeda.

“Today’s marketing authorization, the first for an allogeneic stem cell therapy, represents a positive advancement in the treatment of patients with complex perianal fistulas in Crohn’s disease,” said Dr. Asit Parikh, Head of Takeda’s Gastroenterology Therapeutic Area Unit. “We look forward to bringing this much needed treatment option to patients across Europe in the coming months.”

* 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
The receipt of MA from the EC is one of the conditions to completion of the tender offer announced by Takeda on January 5, 2018.

The consummation of the tender offer remains subject to other conditions, including the tender into the offer (in Belgium and the US), in aggregate, of a number of shares, warrants and American Depositary Shares that, together with all shares, warrants and American Depositary Shares owned by Takeda and its affiliates, represents or gives access to 85% or more of the voting rights represented or given access to by all of the outstanding shares, warrants and American Depositary Shares of TiGenix on a fully diluted basis as of the end of the initial acceptance period.

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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 Limited

Takeda Pharmaceutical Company Limited (TSE: 4502) is a global, research and development-driven pharmaceutical company committed to bringing better health and a brighter future to patients by translating science into life-changing medicines. Takeda focuses its R&D efforts on oncology, gastroenterology and neuroscience therapeutic areas plus vaccines. Takeda conducts R&D both internally and with partners to stay at the leading edge of innovation. Innovative products, especially in oncology and gastroenterology, as well as Takeda’s presence in emerging markets, are currently fueling the growth of Takeda. Approximately 30,000 Takeda employees are committed to improving quality of life for patients, working with Takeda’s partners in health care in more than 70 countries. For more information, visit https://www.takeda.com/newsroom/.

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.

* 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
TiGenix®’ lead product, Alofisel, successfully completed a European Phase III clinical trial for the treatment of complex perianal fistulas—a severe, debilitating complication of Crohn’s disease. 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 Alofisel 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. 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 Alofisel (darvadstrocel)
Alofisel 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. Alofisel 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 Alofisel showing a 44% greater probability of achieving combined remission compared to control (placebo).

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). 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 Alofisel 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 Alofisel 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 and statements regarding the expected consummation of the tender offer, which involves a number of risks and uncertainties, including the satisfaction of closing conditions for the tender offer, the possibility that the transaction will not be completed, the impact of general economic, industry, market or political conditions, and the other risks and uncertainties discussed in TiGenix’s public filings with the SEC, including the “Risk Factors” section of TiGenix’s Form 20-F filed on April 6, 2017, as well as the tender offer documents to be filed by Takeda and the solicitation/recommendation statement to be filed by TiGenix. 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 TiGenix’s control. Therefore, actual results, the financial condition, performance, timing 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. Takeda and TiGenix disclaim any obligation to update any such
forward-looking statement, forecast or estimates to reflect any change in TiGenix’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.

This communication constitutes communication within the scope of article 31 and 33 of the Belgian Law of April 1, 2007 on public takeover bids.

**Prospectus and Response Memorandum**

Following its approval by the Financial Services and Markets Authority (“FSMA”), the prospectus (including the acceptance form and the response memorandum) will be available free of charge by telephone (+32 (0)2 433 41 13). An electronic version of the prospectus (including the acceptance form and the response memorandum) will also be available on the websites of BNP Paribas Fortis SA/NV (www.bnpparibasfortis.be/epargneretplacer (French and English) and www.bnpparibasfortis.be/sparenenbeleggen (Dutch and English)), Takeda (http://www.takeda.com/newsroom) and TiGenix (http://tigenix.com/takeda-takeover-bid).

**Disclaimer**

The tender offer for the outstanding shares, warrants and American Depositary Shares has not yet commenced. This communication is for informational purposes only and does not constitute an offer to purchase securities of TiGenix nor a solicitation by anyone in any jurisdiction in respect of such securities, any vote or approval. If Takeda decides to proceed with an offer to purchase TiGenix’s securities through a public tender offer, such offer will and can only be made on the basis of an approved offer document by the FSMA and tender offer documents filed with the U.S. Securities and Exchange Commission (“SEC”), which holders of TiGenix’s securities should read as they will contain important information. This communication is not a substitute for such offer documents. Neither this communication nor any other information in respect of the matters contained herein may be supplied in any jurisdiction where a registration, qualification or any other obligation is in force or would be with regard to the content hereof or thereof. Any failure to comply with these restrictions may constitute a violation of the financial laws and regulations in such jurisdictions. Takeda, TiGenix and their respective affiliates explicitly decline any liability for breach of these restrictions by any person.

**Important Additional Information for U.S. investors**

The voluntary public takeover bid described herein has not yet commenced. This communication is for informational purposes only and is neither a recommendation, an offer to purchase nor a solicitation of an offer to sell any securities of TiGenix.

At the time the voluntary public takeover bid is commenced, security holders of TiGenix are urged to read the offer documents which will be available at www.sec.gov. At the time the voluntary public takeover bid is commenced, it shall be comprised of two separate offers — (i) an offer for all ordinary shares issued by TiGenix (the “Ordinary Shares”) and warrants to acquire Ordinary Shares in accordance with the applicable law in Belgium, and (ii) an offer to holders of TiGenix’s American Depositary Shares issued by Deutsche Bank Trust Company Americas acting as depositary (“ADSs”), and to holders of Ordinary Shares who are resident in the U.S. in accordance with applicable U.S. law (the “U.S. Offer”).

The U.S. Offer will only be made pursuant to an offer to purchase and related materials. At the time the U.S. Offer is commenced, Takeda will file, or cause to be filed, a tender offer statement on Schedule TO with the SEC and thereafter, TiGenix will file a solicitation/recommendation statement on Schedule 14D-9, in each case with respect to the U.S. Offer.

Holders of ADSs and Ordinary Shares subject to the U.S. Offer who wish to participate in the U.S. Offer, are urged to carefully review the documents relating to the U.S. Offer that will be filed by Takeda with the SEC since these documents will contain important information, including the terms and conditions of the U.S. Offer. Holders of ADSs and Ordinary Shares subject to the U.S. Offer who wish to participate in the U.S. Offer, are also urged to read the related solicitation/recommendation statement on Schedule 14D-9 that will be filed with the SEC by TiGenix relating to the U.S. Offer since it will contain important information. You may obtain a free copy of these documents after they
have been filed with the SEC, and other documents filed by TiGenix and Takeda with the SEC, at the SEC’s website at www.sec.gov. Investors and security holders may also obtain free copies of the solicitation/recommendation statement on Schedule 14D-9 and other documents filed with the SEC by TiGenix at www.tigenix.com. In addition to the offer and certain other tender offer documents, as well as the solicitation/recommendation statement, TiGenix files reports and other information with the SEC. You may read and copy any reports or other information filed by TiGenix at the SEC Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the Public Reference Room. TiGenix’s filings at the SEC are also available to the public from commercial document-retrieval services and at the website maintained by the SEC at www.sec.gov.

YOU SHOULD READ THE FILINGS MADE BY TAKEDA AND TIGENIX WITH THE SEC CAREFULLY BEFORE MAKING A DECISION CONCERNING THE U.S. OFFER.

References

2 Data on file