Press Release

Takeda Announces Topline Results of Phase 3 ADMIRE-CD II Trial of Alofisel® (darvadstrocel) in Complex Crohn's Perianal Fistulas

OSAKA, Japan, October 18, 2023, and CAMBRIDGE, Massachusetts, October 17, 2023 — Takeda (TSE:4502/NYSE: TAK) today announced that the Phase 3 ADMIRE-CD II study, assessing the efficacy and safety of Alofisel® (darvadstrocel) for the treatment of complex Crohn's Perianal Fistulas (CPF), did not meet its primary endpoint of combined remission at 24 weeks, based on topline data. The safety profile for darvadstrocel was consistent with prior studies and there were no new safety signals identified.

"While we are disappointed with this outcome, we recognize that medical research for difficult-to-treat conditions such as complex CPF remains challenging," said Chinwe Ukomadu, head of the GI & Inflammation Therapeutic Area Unit at Takeda. "We believe there are valuable lessons to learn from ADMIRE-CD II and are grateful to the patients and investigators who made this important research possible."

Full results of the study will be presented at a future medical meeting or published in a peer-reviewed journal.

Alofisel is approved in the European Union, Israel, Switzerland, Serbia, United Kingdom and Japan based on positive data from the previously completed ADMIRE-CD study.[1-6] The approval in Japan is also based on positive data from the Japanese study, Darvadstrocel-3002.[7] In addition, approximately 800 patients have been enrolled in INSPIRE, an ongoing, observational study of the real-world effectiveness and safety of Alofisel in patients with complex CPF.[8]

Takeda is continuing to assess the financial impacts of the study results, including impairment loss for intangible assets, on the fiscal quarter ended September 30, 2023. Any revisions to the consolidated forecast for the fiscal year ending March 31, 2024 (FY2023) will be announced during Takeda's second quarter earnings call, scheduled for October 26, 2023.

About Alofisel®

Alofisel® (darvadstrocel) is a dispersion of expanded allogeneic (or donor-derived), adipose-derived mesenchymal stem cells (eASC) for the treatment of complex CPF in adult patients with non-active or mildly active luminal Crohn's disease (CD).[1] It is the first allogeneic stem cell therapy to receive centralized marketing authorization approval in the European Union, and the first expanded human allogeneic adipose-derived mesenchymal stem cell therapy to be approved in Japan.[9,10]

Alofisel was previously investigated in a study called ADMIRE-CD - a randomized, double-blind, controlled, Phase 3 trial investigating the efficacy and safety of Alofisel for the treatment of complex perianal fistulas in 212 adult patients with non-active/mildly active luminal CD.[11,12] The study showed that a significantly greater proportion of patients in the Alofisel group, compared to the control group,

achieved the primary endpoint of combined remission at a 24 week follow-up (51.5% vs 35.6%; a difference of 15.8 percentage points; 97.5% CI 0.5-31.2; P =0.021), and this was maintained over 52 weeks (56.3% vs 38.6%; a difference of 17.7 percentage points; 95% CI 4.2-31.2; P =0.01).[11] Alofisel treatment had a similar safety profile compared to the control group and was well-tolerated over 52 weeks.[11]

Therapeutic Indications
Alofisel is approved in the European Union, Israel, Switzerland, Serbia and the United Kingdom for the treatment in adult patients with complex CPF with non-active/mildly active luminal Crohn's disease, when fistulas have shown an inadequate response to at least one conventional or biologic therapy.[1-5] Alofisel should be used only after conditioning of the fistulas.[1]

In Japan, Alofisel is indicated for the treatment of complex CPF in patients with non-active or mildly active luminal Crohn's disease.[6] This product is indicated for the treatment of patients who have shown an inadequate response to at least one existing medicinal treatment.[6]

Important Safety Information[1]

Contraindications
Hypersensitivity to the active substance, bovine serum or to any of the excipients.

Special warnings and special precautions for use
Alofisel may contain trace amounts of either gentamicin or benzylpenicillin and streptomycin. This should be considered in patients with known hypersensitivity to these classes of antibiotics. Local anesthesia is not recommended due to the unknown effect of local anesthetics on the injected cells.

The injection of any substance other than sodium chloride 9 mg/mL (0.9%) (e.g., hydrogen peroxide, methylene blue, iodine solutions or hypertonic glucose solutions) through the fistula tracts is not allowed before, during, or after the injection of darvadstrocel as this may compromise cell viability.

Alofisel is indicated for injection in the fistula tract tissue only. Alofisel must not be administered using a needle thinner than 22G. Thinner gauge needles can cause cell disruption during injection and may compromise cell viability.

As Alofisel is a living stem cell therapy, it cannot be sterilized, and therefore could contain potentially infected biological material, although the risk is considered to be low and controlled in the manufacturing process. Patients should be followed up for potential signs of infection after administration.

Alofisel should only be administered by specialist physicians experienced in the diagnosis and treatment of conditions for which darvadstrocel is indicated.

Patients treated with Alofisel must not donate blood, organs, tissues and cells for transplantation.

The traceability requirements of cell-based therapy medicinal products must apply.

Fertility, Pregnancy & Lactation

No data is available from the use of Alofisel in pregnant women. Alofisel is not recommended during pregnancy and in women of childbearing potential who are not using contraception. As a precautionary measure, darvadstrocel is not recommended for administration during breast-feeding.

Adverse reactions include: Common (≥1/100 to <1/10): anal abscess, proctalgia, anal fistula and procedural pain. Conditioning of fistulas has been associated with proctalgia and procedural pain.

For EU audiences, please see the Summary of Product Characteristics (SmPC) for Alofisel®

Please consult with your local regulatory agency for approved labeling in your country.

Takeda in Gastroenterology
We believe that gastrointestinal (GI) and liver diseases are not just life-disrupting conditions, but also diseases that can impact a patient's quality of life.[13,14] Beyond a fundamental need for effective treatment options, we understand that improving patients' lives also depends on their needs being recognized. [13,14] With nearly 30 years of experience in gastroenterology, Takeda has made significant strides in addressing GI patient needs with treatments for inflammatory bowel disease (IBD), acid-related diseases, short bowel syndrome (SBS) and motility disorders. We are making significant strides toward closing the gap on new areas of unmet needs for patients who have celiac disease, alpha-1 antitrypsin-associated liver disease and Crohn's disease, among others. Together with researchers, patient groups and others, we are working to advance scientific research and clinical medicine in GI.

About Takeda
Takeda is focused on creating better health for people and a brighter future for the world. We aim to discover and deliver life-transforming treatments in our core therapeutic and business areas, including gastrointestinal and inflammation, rare diseases, plasma-derived therapies, oncology, neuroscience and vaccines. Together with our partners, we aim to improve the patient experience and advance a new frontier of treatment options through our dynamic and diverse pipeline. As a leading values-based, R&D-driven biopharmaceutical company headquartered in Japan, we are guided by our commitment to patients, our people and the planet. Our employees in approximately 80 countries and regions are driven by our purpose and are grounded in the values that have defined us for more than two centuries. For more information, visit www.takeda.com.

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The companies in which Takeda directly and indirectly owns investments are separate entities. In this press release, "Takeda" is sometimes used for convenience where references are made to Takeda and its subsidiaries in general. Likewise, the words "we", "us" and "our" are also used to refer to subsidiaries in general or to those who work for them. These expressions are also used where no useful purpose is served by identifying the particular company or companies.

Forward-Looking Statements

This press release and any materials distributed in connection with this press release may contain forward-looking statements, beliefs or opinions regarding Takeda's future business, future position and results of operations, including estimates, forecasts, targets and plans for Takeda. Without limitation, forward-looking statements often include words such as "targets", "plans", "believes", "hopes", "continues", "expects", "aims", "intends", "ensures", "will", "may", "should", "would", "could", "anticipates", "estimates", "projects" or similar expressions or the negative thereof. These forward-looking statements are based on assumptions about many important factors, including the following, which could cause actual results to differ materially from those expressed or implied by the forward-looking statements: the economic circumstances surrounding Takeda's global business, including general economic conditions in Japan and the United States; competitive pressures and developments; changes to applicable laws and regulations, including global health care reforms; challenges inherent in new product development, including uncertainty of clinical success and decisions of regulatory authorities and the timing thereof; uncertainty of commercial success for new and existing products; manufacturing difficulties or delays; fluctuations in interest and currency exchange rates; claims or concerns regarding the safety or efficacy of marketed products or product candidates; the impact of health crises, like the novel coronavirus pandemic, on Takeda and its customers and suppliers, including foreign governments in countries in which Takeda operates, or on other facets of its business; the timing and impact of post-merger integration efforts with acquired companies; the ability to divest assets that are not core to Takeda's operations and the timing of any such divestment(s); and other factors identified in Takeda's most recent Annual Report on Form 20-F and Takeda's other reports filed with the U.S. Securities and Exchange Commission, available on Takeda's website at: https://www.takeda.com/investors/sec-filings-and-security-reports/ or at www.sec.gov. Takeda does not undertake to update any of the forward-looking statements contained in this press release or any other forward-looking statements it may make, except as required by law or stock exchange rule. Past performance is not an indicator of future results and the results or statements of Takeda in this press release may not be indicative of, and are not an estimate, forecast, guarantee or projection of Takeda's future results.

Medical Information

This press release contains information about products that may not be available in all countries, or may be available under different trademarks, for different indications, in different dosages, or in different strengths. Nothing contained herein should be considered a solicitation, promotion or advertisement for any prescription drugs including the ones under development.

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