May 31, 2023

Company Name: AnGes Inc.
Presentative: Ei Yamada, President & CEO

# Notice of Marketing Approval Application for HGF Gene Therapy Product Collategene®

AnGes announced that it has today submitted a marketing approval application to the Ministry of Health, Labour and Welfare for its HGF (*1) Gene Therapy Product Collategene® for Intramuscular Injection 4mg (Collategene®) with a view to lifting the terms.

Collategene® was granted conditional and time-limited marketing approval in March 2019 for the indication, efficacy or performance (*2) of the improvement of leg ulcers in chronic arterial occlusion and was launched by Mitsubishi Tanabe Pharma Corporation in September of the same year. AnGes has decided to apply for the lifting of the conditions because the results of the use-results comparison survey of the post-marketing approval condition assessment, which has been conducted since the launch, confirmed the reproducibility of the clinical trial results of the previous application.

This is the first marketing approval application for a product that received conditional and time-limited approval under the early approval system introduced in the revised Pharmaceutical Affairs Law of 2014.

For details regarding Collategene®, please see the attached document.

The impact of this change on our consolidated earnings forecast for the fiscal year ending December 2023 is immaterial. We plan to promptly announce any further events that should be disclosed in the future.

*1: HGF (Hepatocyte Growth Factor) was discovered in Japan in 1984 as a growth factor in the liver, which is the organ with the highest regenerative capacity, and found to play a major role not only in the liver but also in the formation and regeneration of various organs and tissues in the body, including blood vessels, lymphatic vessels and nerves.

*2: Improvement of ulcers in chronic arterial occlusion (arteriosclerosis obliterans and Buerger's disease) in which revascularization is difficult due to insufficient effect of standard drug treatment

AnGes Inc.
Mitsubishi Tanabe Pharma Corporation

# AnGes filed for approval of its HGF gene therapy product Collategene® for the first time since the introduction of the conditional/time-limited authorization system for regenerative medicine products

On May 31, 2023, AnGes (Head Office: Ibaraki, Osaka, Japan, President: Ei Yamada, hereinafter "AnGes") filed a new marketing application with the Ministry of Health, Labour and Welfare for its HGF (*1) gene therapy product Collategene® for Intramuscular Injection 4mg (hereinafter "Collategene®") for the treatment of leg ulcers in chronic arterial occlusion (*2).

Collategene® received conditional and time-limited marketing approval in March 2019. Regenerative medicine products approved with conditions and time limits are subject to a new application for approval based on the results of the evaluation of the conditions of approval within the approval period. If this application is approved, this will be the first product to receive approval for the lifting of conditions after the introduction of the conditional and time-limited approval system for regenerative medicine products.

Collategene® is a mainstay project that AnGes has been working on since its founding and has received conditional and time-limited marketing approval as the world's first therapeutic product using plasmid DNA technology for the treatment of leg ulcers in chronic arterial occlusion in Japan. Collategene® is the first gene therapy product in Japan launched by Mitsubishi Tanabe Pharma Corporation (Head Office: Chuo-ku, Osaka, Japan; Representative Director: Akihiro Tsujimura, hereinafter "MTPC") in September 2019.
The conditions for approval of Collategene® are as follows:

① Collategene® should be used in a facility where wound management is performed by multiple departments under the supervision of a physician with sufficient knowledge and experience in the treatment of severe chronic arterial occlusion.
② Post-marketing condition evaluation should be conducted in all patients using Collategene® during the period until the new marketing application for Collategene® is filed after the conditional and time-limited approval.

and the deadline is five years.
With the aim of lifting the conditions, AnGes and MTPC conducted a confirmatory study to evaluate the post-marketing approval conditions and completed patient enrollment for the target number of cases in December 2021.

AnGes and MTPC will provide a new treatment option for ulcers of chronic arterial occlusive disease for which revascularization is difficult to perform, thereby contributing to improving the QOL of patients with critical limb ischemia.

*1: HGF (Hepatocyte Growth Factor) was discovered in Japan in 1984 as a growth factor in the liver, which is the organ with the highest regenerative capacity, and found to play a major role in the formation and regeneration of not only the liver but also various organs and tissues in the living body, including blood vessels, lymphatic vessels and nerves.

*2: Improvement of ulcers in chronic arterial occlusion (arteriosclerosis obliterans and Buerger's disease) in which revascularization is difficult due to insufficient effect of standard drug treatment

<About AnGes>

AnGes was founded in December 1999 with the goal of developing drugs by applying the angiogenic action of the HGF (Hepatocyte Growth Factor) gene. Based on advanced technologies to create next-generation biopharmaceuticals, such as gene therapy and therapeutic vaccines, our company's goal is to contribute to the improvement of people's lives and medical standards by developing innovative medicines for diseases for which there is no cure, as well as intractable and rare diseases.

To achieve this goal, in the first quarter of 2023, our company completed patient enrollment for the expected number of patients in the Phase II clinical trial of Collategene® in the United States and is currently following up. In addition, in Israel, our partner company Kamada filed an application for marketing approval of Collategene® and is currently under review. As described above, AnGes will seek to expand the sales area of Collategene® in Japan, as well as in the United States, Israel and Europe, and will also explore the development of new indications for the drug.

< About Mitsubishi Tanabe Pharma Corporation >

Mitsubishi Tanabe Pharma Corporation (MTPC), the pharma arm of Mitsubishi Chemical Group (MCG), is one of the oldest pharmaceutical companies in the world, founded in 1678, and focusing on ethical pharmaceuticals. MTPC is headquartered in Doshomachi, Osaka, the birthplace of Japan’s pharmaceutical industry. MCG has positioned health care as its strategic focus in its management policy, “Forging the future”. MTPC sets the MISSION of “Creating hope for all facing illness”. To that end, MTPC is working on the disease areas of central nervous system, immuno-inflammation, diabetes and kidney, and cancer. MTPC is focusing on “precision medicine” to provide drugs with high treatment satisfaction by identifying patient populations with high potential for efficacy and safety. In addition, MTPC is working to develop “around the pill solutions” to address specific patient concerns based on therapeutic medicine, including prevention of diseases, pre-symptomatic disease care, prevention of aggravation and prognosis. For more information, go to https://www.mt-pharma.co.jp/e/

< About the introduction of the conditional/time-limited authorization system >

This refers to the early approval system for "regenerative medicine products," including gene therapy, introduced by the revised Pharmaceutical Affairs Law (Pharmaceutical and Medical Devices Law), which came into effect in November 2014.

At the time of the enforcement, there were high expectations for the practical application of regenerative medicine such as iPS cells as an innovative medical treatment. On the other hand, since regenerative medicine products use human cells, their quality is uneven, and it is sometimes difficult to predict their efficacy. In order to ensure their safety and promote their practical application quickly, this system will allow early approval of regenerative medicine products with presumed efficacy and approved safety under certain conditions and deadlines.

After obtaining conditional and time-limited approval, drug use-results surveys, post-marketing database surveys, and post-marketing clinical studies will be planned and conducted, and in principle, within a period not exceeding seven years, efficacy and safety will be verified, followed by another application for approval within the deadline to obtain a condition release (formal approval).

Contact:

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