News release

Kyowa Kirin Announces Application for Partial Change of Approved Indication of LUMICEF® for Systemic Sclerosis in Japan

Tokyo, Japan, December 15, 2021 --Kyowa Kirin Co., Ltd. (Kyowa Kirin, TSE:4151, President and CEO: Masashi Miyamoto) announced that the company has filed an application to the Japanese Ministry of Health, Labour and Welfare for partial change of approved indication of LUMICEF® [KHK4827, generic name: brodalumab (genetical recombination)] for systemic sclerosis in Japan on December 15th.

This application is based on the results in a Phase 3 study conducted in Japan in patients with systemic sclerosis who have moderate to severe skin sclerosis. The primary endpoint of this study was the change from baseline in mRSS at Week 24. Significant decreases in mRSS were observed in brodalumab-treated arm relative to the placebo arm, which indicated its improvement effect for skin sclerosis. There was no emerging safety issue.

LUMICEF® has been designated as an Orphan Drug by the Ministry of Health, Labour and Welfare for the expected indication of systemic sclerosis on December 10th, 2019 and is subject to Priority Review.

“Systemic sclerosis is a chronic disease included in the connective tissue diseases which could cause skin thickening and fibrosis of organs such as lung and gastrointestinal tract, and then could lead to dysfunction of internal organs,” said Prof. Shinichi Sato at Department of Dermatology, The University of Tokyo, Graduate School of Medicine, Tokyo, Japan. “Since systemic sclerosis is one of the poor prognosis diseases in connective tissue diseases, it is important to start treatment early to prevent a progression of skin sclerosis and internal organ fibrosis as much as possible, in addition, to improve the advanced lesion. However, highly effective therapeutic options for systemic sclerosis are extremely limited.”

Yoshifumi Torii, Ph.D, Executive Officer, Vice President, Head of R&D Division of Kyowa Kirin said, “We are profoundly pleased that we could file an application for partial change of approved indication of LUMICEF® for systemic sclerosis. A safe, highly effective treatment that can be used for a long time has been desired for the treatment of systemic sclerosis. We highly hope that LUMICEF® would be a drug that can meet unmet medical needs of the patients with systemic

sclerosis."

The Kyowa Kirin Group companies strive to contribute to the health and well-being of people around the world by creating new value through the pursuit of advances in life sciences and technologies.

About LUMICEF®

LUMICEF is a fully human anti-interleukin-17 (IL-17) receptor A antibody that inhibits biological activity of inflammatory cytokines such as IL-17A, IL-17A/F, IL-17F, IL-17C by binding to IL-17A receptor selectively. It was approved in Japan in July 2016 for the treatment of psoriasis (psoriasis vulgaris, psoriatic arthritis, pustular psoriasis, and psoriatic erythroderma) that respond inadequately to existing therapies. In November 2020, this drug was also approved for the additional indications of ankylosing spondylitis and non-radiographic axial spondyloarthritis.

About systemic sclerosis

Systemic sclerosis is a chronic disease characterized by sclerosis of skin and internal organs. The progression of the disease and the course of symptoms vary from patient to patient, and its pathogenesis is considered to be related to immune abnormalities, fibrosis, and vascular disorders, but the cause of this disease has not been identified. The number of patients in Japan is estimated to be more than 20,000, and it is positioned as a designated intractable disease (designated intractable disease 51).

About the Phase 3 clinical trial and the summary of the results

This is a Japanese Phase 3 clinical trial consisting of a placebo-controlled double-blind study and an open-label continuous administration study both in patients with systemic sclerosis who have moderate to severe skin sclerosis (mRSS: 10~30). The study was conducted for 100 Japanese patients with systemic sclerosis at 7 sites in Japan, mainly at the University of Tokyo (Coordinating Investigator: Ayumi Yoshizaki, Lecturer, Department of Dermatology, University of Tokyo, Graduate School of Medicine, Tokyo, Japan). The primary endpoint, the change from baseline in mRSS at Week 24, was -16.8 in the brodalumab group (95% CI: -18.7, -14.8) and 4.4 in the placebo group (95% CI: 2.5, 6.4). The difference in change in mRSS between the brodalumab arm and placebo arm was -21.2 (95% CI: -23.9, -18.5), indicating a statistically significant decrease in mRSS ($p<0.0001$). In addition, the safety profile in patients with systemic sclerosis was similar to other previously approved indications.

About mRSS (Modified Rodnan total skin thickness score)

This score is a semi-quantitative method of assessing skin stiffness by palpation, dividing the body into 17 areas and scoring the degree of skin stiffness in each area on a 4-point scale (0-3), with the sum of the scores used as the skin score. mRSS is considered to be the most useful index for evaluating the effect of treatment on skin sclerosis because it reflects pathological fibrotic changes in the skin and is consistent with disease activity.