News release

Kyowa Kirin Announces Positive Phase 2 Results for KHK4083 in Patients with Moderate to Severe Atopic Dermatitis

- *Atopic dermatitis is a chronic, pruritic, inflammatory dermatosis that is believed to affect an estimated number of 26M patients in North America, EU, and Japan*[1]
- *KHK4083, an anti-OX40 fully human monoclonal antibody discovered by Kyowa Kirin, shows a combination of antibody dependent cellular cytotoxicity (ADCC) and antagonist activity against OX40*
- *Kyowa Kirin plans to present the detailed results of the Phase 2 study through future academic conferences or publications*

TOKYO, Japan, February 18, 2021 -Kyowa Kirin Co., Ltd. (TSE: 4151, President and CEO: Masashi Miyamoto, "Kyowa Kirin"), a global specialty pharmaceutical company that strives to create new value through the pursuit of advances in life sciences and technologies, announces today that the Phase 2 study of investigational agent KHK4083 in patients with atopic dermatitis has met the primary endpoint.

KHK4083 is a potential first-in-class, anti-OX40 fully human monoclonal antibody for the treatment of autoimmune diseases, including atopic dermatitis. KHK4083 was first discovered by Kyowa Kirin, and is produced with the Company's patented POTELLIGENT® defucosylation technology to enhance its antibody dependent cellular cytotoxicity (ADCC) activity[2]. The combination of ADCC and antagonist activity against OX40 may suppress inflammatory responses found to be the cause of atopic dermatitis[3-6].

The Phase 2 study was a multicenter, randomized, double-blind and placebo-controlled clinical study conducted in Japan, the United States, Canada, and Germany to investigate the efficacy and safety of KHK4083. Globally, 274 patients with moderate to severe atopic dermatitis, who were not adequately controlled with topical agents, were enrolled in the study.

In this study, all KHK4083 cohorts achieved superiority to placebo cohort for the primary endpoint of "percent change from baseline in Eczema Area and Severity Index (EASI) [7] at 16 weeks" with statistical significance. In addition, there was significant difference in "the percentage of patients achieving an EASI-75 (EASI score of 75% or greater improvement from baseline) at 16 weeks" and "the percentage of patients achieving the Investigator's Global Assessment (IGA) of 0 or 1 with an improvement of 2 points or more at 16 weeks" in all

KHK4083 cohorts compared to the placebo cohort. Further improvement in efficacy of KHK4083 was observed after week 16. Common treatment-emergent adverse events for KHK4083 cohorts were pyrexia, nasopharyngitis, worsening of atopic dermatitis and chills during the first 16 weeks. There was no death observed in the study.

"The results of the KHK4083 Phase 2 study show that OX40 is a relevant target for atopic dermatitis and may provide a new treatment paradigm," said the lead investigator of this study, Dr. Emma Guttman-Yassky, MD./PhD., System Chair for the Department of Dermatology and Waldman Professor of Dermatology and Immunology, Icahn School of Medicine at Mount Sinai and Director of the Center for Excellence in Eczema, and the Laboratory of Inflammatory Skin Diseases at Mount Sinai. "In addition to the primary endpoint, this study also showed progressive improvement in efficacy by continuous KHK4083 administration beyond 16 weeks and the potential for long-term sustained therapeutic effect after the completion of KHK4083 treatment."

"We are very pleased with the results of this study assessing efficacy and safety of KHK4083 in chronic, recurrent, moderate to severe atopic dermatitis," said Yoshifumi Torii, Ph.D., Executive Officer, Vice President, Head of Global R&D Division of Kyowa Kirin. "We look forward to sharing the results of the full analysis in the near future. I would like to express my deep gratitude to the medical professionals and patients for their participation in the study. We will continue KHK4083 development with the hope it can help patients in need."

The full results of the study are planned to be presented through future academic conferences and publications.

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 Atopic Dermatitis

Atopic dermatitis is a disease in which the main lesion is an itchy eczema that repeatedly flares up and flares down, and many patients have a predisposition to atopic dermatitis (family and previous history, predisposition to produce IgE antibodies). It is an eczematous disease with a characteristic symmetrical distribution, and the site of predilection differs according to age. Characteristic eczematous lesions that develop in infancy or early childhood, remit in childhood, or recur without remission, and persist into adulthood, are seen chronically.

About OX40

OX40 is a co-stimulatory molecule that is one of the tumor necrosis factor receptor (TNFR) family

member and plays an important role in maintaining T cell proliferation and survival by inhibiting apoptosis and in the formation of memory T cells. OX40 is expressed on the surface of effector T cells (CD4 positive) activated by antigens. It has been reported that effector T cells expressing OX40 are present in the lesions of atopic dermatitis[3-6].

About Eczema Area and Severity Index（EASI）

EASI is an internationally used classification of atopic dermatitis severity and is recommended for use by Harmonising Outcome Measures for Eczema, an international group for standardizing clinical trial outcomes in atopic dermatitis[7].

About Kyowa Kirin

Kyowa Kirin strives to create and deliver novel medicines with life-changing value. As a Japan-based Global Specialty Pharmaceutical Company with over 70-year heritage, we apply cutting-edge science including an expertise in antibody research and engineering, to address the needs of patients and society across multiple therapeutic areas including Nephrology, Oncology, Immunology/Allergy and Neurology. Across our four regions – Japan, Asia Pacific, North America and EMEA/International – we focus on our purpose, to make people smile, and are united by our shared values of commitment to life, teamwork/Wa, innovation, and integrity. You can learn more about the business of Kyowa Kirin at: https://www.kyowakirin.com.

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