News release

Kyowa Kirin Announces Lancet Publication of Phase 2b Study Results for Rocatinlimab (KHK4083/AMG 451) in Adult Patients with Moderate-to-Severe Atopic Dermatitis

- **The study met its primary objective of demonstrating statistically greater improvement in change from baseline in Eczema Area and Severity Index (EASI) score at week 16 versus placebo across all rocatinlimab doses evaluated**
- **Patients receiving rocatinlimab showed numerically greater improvements in additional secondary efficacy endpoints versus placebo**
- **There was a durable off-treatment response after rocatinlimab discontinuation**
- **Rocatinlimab generally showed acceptable adverse event profile and the most common adverse events during the double-blind period in patients receiving rocatinlimab were pyrexia, chills, headache, aphthous ulcer, and nausea**

TOKYO, December 13, 2022 — Kyowa Kirin Co., Ltd. (TSE:4151) today announced publication in *the Lancet* of results of a Phase 2b study of rocatinlimab (KHK4083/AMG 451), an investigational, potential first-in-class anti-OX40 human monoclonal antibody for the treatment of moderate-to-severe atopic dermatitis developed in collaboration with Amgen.

The Phase 2b multicenter, randomized, double-blind, placebo-controlled trial investigated the efficacy and safety of rocatinlimab in adults with moderate-to-severe atopic dermatitis who were not adequately controlled with topical agents (NCT03703102). The study was conducted at 65 sites in the United States, Canada, Japan, and Germany and enrolled 274 adult patients over 18 years of age. The patients were randomized 1:1:1:1:1 to receive double-blind subcutaneous rocatinlimab 150 mg every 4 weeks (Q4W), 600 mg Q4W, 300 mg every 2 weeks (Q2W), or 600 mg Q2W, or placebo from baseline (week 0) through week 18 (last injection at week 16). At week 18, patients entered an 18-week active-treatment extension through week 36 (last injection at week 34) in a blinded fashion, during which patients initially randomized to rocatinlimab continued to receive the same dose and patients initially randomized to placebo received rocatinlimab 600 mg Q2W. The double-blind period and active-treatment extension were followed by a 20-week off-treatment follow-up (weeks 36–56).

The study met the primary efficacy endpoint, showing statistically greater improvements in change from baseline in Eczema Area and Severity Index (EASI) score at week 16 with all rocatinlimab dose groups compared with placebo (150 mg Q4W = -48%; 600 mg Q4W = -50%; 300 mg Q2W = -61%; 600 mg Q2W = -57%; placebo = -15%; all P vs placebo <0.001).
All treatment groups of patients treated with rocatinlimab achieved greater numerical improvement compared to placebo cohort at week 16 for most of the secondary endpoints, including achieving at least a 75% reduction from baseline in EASI score (EASI-75; rocatinlimab:44%, 40%, 54%, and 39%, respectively; placebo: 11%), EASI-50 (rocatinlimab: 58% to 69%; placebo: 30%), EASI-90 (12% to 37%; placebo: 4%), an validated Investigator's Global Assessment for Atopic Dermatitis (vIGA-ADTM) 0/1 endpoint (score of 0 (clear) or 1 (almost clear) with at least two-point reduction from baseline) was achieved by 19%, 15%, 31%, and 19% of the subjects in the respective rocatinlimab dose groups (placebo: 2%).
Additionally, numerically greater improvements in itch and quality of life were observed at week 16 with rocatinlimab versus placebo.

Patients receiving rocatinlimab continued to show improvement in efficacy after week 16 up to week 36, which was maintained in most patients after discontinuation of rocatinlimab at week 36 through end of study at week 56.

The most frequent adverse events (≥5% and greater than placebo) in the rocatinlimab groups during the double-blind period were pyrexia, chills, headache, aphthous ulcer, and nausea. The events of pyrexia and chills were mild to moderate in intensity, occurred primarily after the first dose administration of rocatinlimab, and did not result in treatment discontinuations. There were no serious injection reactions, nor an adverse event considered as a hypersensitivity or anaphylactic reaction. The incidence of serious adverse events was 4% in the rocatinlimab group and 2% in the placebo group.

"I am pleased that the results of our Phase 2b study have been published in the Lancet," said Yoshifumi Torii, Ph.D., Executive Officer, Vice President, Head of R&D Division of Kyowa Kirin. "These results suggest inhibition and reduction of the OX40-expressing cells may provide an important new approach to treating moderate-to-severe atopic dermatitis, with the potential to help patients maintain responses."

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 the rocatinlimab (KHK4083/AMG 451) Phase 2b Study

The Phase 2b, multicenter, randomized, double-blind, placebo-controlled trial (NCT03703102) investigated the efficacy and safety of rocatinlimab in adults with moderate-to-severe atopic dermatitis who were not adequately controlled with topical agents. The study enrolled 274 patients in the U.S., Japan, Canada and Germany across four dose-ranging active treatment groups, which received subcutaneous (rocatinlimab 600 mg Q2W, 600 mg Q4W, 300 mg Q2W, or 150 mg Q4W), and a comparator placebo arm.

The primary endpoint was percentage change from baseline in EASI score at week 16. Additional endpoints include achievement of ≥ 75%, 50% and 90% reduction (improvement) from baseline in EASI score, IGA score of 0 (clear) or 1 (almost clear) with ≥ 2 points reduction from baseline, and ≥ 4 points reduction from baseline in the pruritus numeric rating scale (NRS) score. Patients in the study were followed up to week 56.

The publication is available on the Lancet website: https://doi.org/10.1016/S0140-6736(22)02037-2

Dr. Emma Guttman-Yassky is the leading investigator of the study and a paid consultant for the rocatinlimab development by Kyowa Kirin.

About rocatinlimab

Rocatinlimab (KHK4083/AMG 451) is an anti-OX40 human monoclonal antibody that inhibits and reduces the number of OX40-expressing pathogenic T cells, responsible for driving systemic and local inflammatory responses.

It has been reported that effector T cells expressing OX40 are present in the lesions of patients with atopic dermatitis and are critical in the disease pathophysiology.

The initial antibody was discovered in collaboration between Kyowa Kirin US Research and La Jolla Institute for Immunology.

Amgen and Kyowa Kirin Collaboration

On June 1, 2021, Kyowa Kirin and Amgen entered into an agreement to jointly develop and commercialize rocatinlimab. Under the terms of the agreement, Amgen will lead the development, manufacturing, and commercialization for KHK4083/AMG 451 for all markets globally, except Japan, where Kyowa Kirin will retain all rights. If approved, the companies will

co-promote the asset in the United States and Kyowa Kirin has opt-in rights to co-promote in certain other markets including Europe and Asia.

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 a more than 70-year heritage, we apply cutting-edge science including 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/.