Kyowa Kirin Presents data at EORTC-Cutaneous Lymphoma Task Force meeting showing significantly improved Quality of Life for patients with mycosis fungoides (MF) and Sézary Syndrome (SS) on Mogamulizumab

First oral presentation of Quality of Life data from the phase III trial (MAVORIC), the largest randomised trial in MF and SS – the two most common types of Cutaneous T Cell Lymphoma[1]

Tokyo, Japan, September 28, 2018 – Kyowa Hakko Kirin Co., Ltd., (Kyowa Kirin) announces that Quality of Life (QoL) data from the pivotal MAVORIC trial will be the subject of an oral presentation,[2] at the European Organization for Research and Treatment of Cancer (EORTC) Cutaneous Lymphoma Task Force (CLTF) meeting, September 27-29, St. Gallen, Switzerland. A case report of a long-term responder in the MAVORIC[3] trial will also be reported as a poster.[4]

Presentation titles at the 2018 EORTC CLTF Mtg:

- Quality of Life in Cutaneous T Cell Lymphoma Patients Treated with the Anti-CCR4 Monoclonal Antibody Mogamulizumab Versus Vorinostat: Results from MAVORIC [Abstract 105; Fri 28th Sept, 11am-12.30pm]
- Long-term complete remission induced by mogamulizumab in a severe Sezary patient, together with five different possible autoimmune manifestations [Abstract #059; Case study poster (external)]

QoL was a secondary end-point of the phase 3 MAVORIC (mogamulizumab versus vorinostat in previously treated cutaneous T-cell lymphoma) trial and significant improvements were seen with mogamulizumab versus vorinostat as early as cycle three and continued throughout. Using QoL measurements including Skindex-29, Functional Assessment of Cancer Therapy-General (FACT-G) and EuroQol-5D-3L (EQ-5D-3L), clinically meaningful improvements in patient-reported skin-related symptoms and preservation of physical well-being were observed. ≥ 61% of mogamulizumab patients reported clinically-meaningful improvements in skin-related symptoms from Cycles 3 through to 11 and significantly more vorinostat patients reported clinically-meaningful declines in physical well-being in Cycles 1 through to 11. There was also delay in patient reported deterioration in the Skindex-29 Summary and Emotions subscores in patients given mogamulizumab.

Dr Pierluigi Porcu, Sidney Kimmel Cancer Center at Jefferson Health, Thomas Jefferson University, USA elaborates further on the data: “Cutaneous T cell lymphomas are highly visible cancers, that can significantly impact patients' QoL. The effects of the disease can be extremely debilitating, which in turn can affect the patient both mentally and emotionally. We are extremely excited about these findings as it demonstrates the potential benefits of mogamulizumab beyond efficacy and, in particular, for outcomes that are especially important to people affected by CTCL. It is reassuring to see quick improvements and benefits across Symptom, Emotional, and Functional domains. Importantly, patients with the highest symptom burden and functional impairment derived the most QoL benefit from mogamulizumab.”

Mogamulizumab met its primary endpoint in the MAVORIC trial, which is the first pivotal trial in CTCL to use progression-free survival (PFS) as a primary endpoint. The results demonstrated a

significant improvement in PFS and overall response rate (ORR) for mogamulizumab compared to vorinostat in patients with previously treated MF and SS.[3] Results of the study were published in Lancet Oncology in August 2018.

On Friday 21st September 2018, the Committee for Medicinal Products for Human Use (CHMP), the European Medicines Agency's (EMA) scientific committee, adopted a Positive Opinion recommending approval of the marketing authorisation of mogamulizumab for the treatment of adult patients with MF or SS who have received at least one prior systemic therapy.

KKI Chief Executive, Tom Stratford, said "There has been limited innovation in the last fifteen years for patients with MF and SS and quality of life is a big factor in these diseases. The Kyowa Hakko Kirin Group companies strive to contribute to the health and wellbeing of people around the world through advances in life sciences and technologies and mogamulizumab addresses a universal unmet need in this patient population. The recent positive CHMP opinion brings us one step closer to bringing this much needed treatment to patients with MF and SS."

If mogamulizumab is approved, Kyowa Kirin International PLC, a Kyowa Hakko Kirin Group company, will be responsible for commercialising mogamulizumab in Europe.

About Mogamulizumab

Mogamulizumab is a humanised monoclonal antibody (mAb) directed against CC chemokine receptor 4 (CCR4), which is frequently expressed on leukemic cells of certain haematologic malignancies including CTCL (cutaneous T-cell lymphoma). Mogamulizumab was produced using Kyowa Hakko Kirin's proprietary POTELLIGENT® platform, which is associated with enhanced antibody-dependent cellular cytotoxicity (ADCC).

About Mycosis Fungoides (MF) and Sézary Syndrome (SS)

MF and SS are the two most common subtypes of CTCL[1], a rare type of non-Hodgkin's lymphoma, which is characterised by localisation of malignant T lymphocytes to the skin, and depending on the stage, the disease may involve skin, blood, lymph nodes, and viscera.

About MAVORIC

MAVORIC is a Phase 3 open-label, multi-center, randomised study of mogamulizumab versus vorinostat in patients with MF and SS who have failed at least one prior systemic treatment. The study was conducted in the U.S., Europe, Japan and Australia, and randomized 372 patients to receive either mogamulizumab or vorinostat.

Additional Data from Analyses

Mogamulizumab resulted in symptomatic and functional improvement with differences in Skindex-29 Symptoms (Cycle 3 (C3), C5, and C7; $p<0.05$) and Functional (C3 and C5; $p<0.05$) scales.

The proportion of patients who improved by at least the meaningful change threshold (MCT) from baseline was significantly greater for mogamulizumab vs vorinostat on Skindex-29 Symptoms at C3 (61.1% vs 45.3%), C5 (64.5% vs 42.4%), C7 (67.1% vs 47.5%), and C11 (84.1% vs 50.0%) and Skindex-29 Functioning domain at C5 (54.3% vs 28.8%). Significant difference in the FACT-G Physical Well-Being scale (C1, C3, and C5; $p<0.05$) were observed in favour of mogamulizumab and a greater proportion of patients declined by at least the MCT in favour of mogamulizumab vs vorinostat at C1 (19.3% vs 34.7%), C3 (17.4% vs 42.9%), C5 (13.1% vs 43.3%), and C7 (15.9% vs 37.5%). The median time to worsening of symptoms on Skindex-29 was 27.4 m for mogamulizumab vs 6.6 m for vorinostat.

Mogamulizumab Regulatory Status

The Positive Opinion from the Committee for Medicinal Products for Human Use (CHMP), the European Medicines Agency's (EMA) scientific committee, recommending approval of the marketing authorisation of mogamulizumab for the treatment of adult patients with MF or SS who have received at least one prior systemic therapy has been referred to the European Commission (EC), which is expected to render its final decision by the end of 2018. The EC typically adheres to the recommendation of the CHMP but is not obligated to do so.

On the 8th August 2018, the U.S. Food and Drug Administration (FDA) granted approval for mogamulizumab for the treatment of adult patients with relapsed or refractory MF or SS after at least one prior systemic therapy. Mogamulizumab was granted Priority Review and Breakthrough Therapy Designation by the FDA in late 2017.

In Japan, mogamulizumab has received approval for: relapsed or refractory CCR4-positive ATL in March 2012; relapsed or refractory CCR4-positive PTCL and relapsed or refractory CCR4-positive CTCL in March 2014; chemotherapy-native CCR4-positive ATL in December 2014; and, relapsed or refractory CTCL (CCR4-positive removed) in August 2018.

About Kyowa Kirin

Kyowa Hakko Kirin Co., Ltd. is a research-based life sciences company, with special strengths in biotechnologies. In the core therapeutic areas of oncology, nephrology and immunology/allergy, Kyowa Hakko Kirin leverages leading-edge biotechnologies centered on antibody technologies, to continually discover innovative new drugs and to develop and market those drugs world-wide. In this way, the company is working to realise its vision of becoming a Japan-based global specialty pharmaceutical company that contributes to the health and wellbeing of people around the world.

Kyowa Kirin International PLC is a wholly owned subsidiary of Kyowa Hakko Kirin and is a rapidly growing specialty pharmaceutical company engaged in the development and commercialisation of prescription medicines for the treatment of unmet therapeutic needs in Europe and the United States. Kyowa Kirin International is headquartered in Scotland.

You can learn more about the business at: www.kyowa-kirin.com.

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[1] Leukemia & Lymphoma Society. Cutaneous T-Cell Lymphoma Facts. http://www.lls.org/sites/default/files/file_assets/FS5_Cutaneous%20T-Cell%20Lymphoma_2014_Final.pdf. Accessed May 2, 2018

[2] Pierluigi Porcu et al. Quality of Life in Cutaneous T Cell Lymphoma Subjects Treated with the Anti-CCR4 Monoclonal Antibody Mogamulizumab Versus Vorinostat: Results from MAVORIC. Data presented at ASCO and EHA, and oral presentation at EORTC, 2018

[3] Youn H Kim et al. Mogamulizumab versus vorinostat in previously treated cutaneous T-cell lymphoma (MAVORIC): an international, open-label, randomised, controlled phase 3 trial. Lancet Oncology 2018. Sep;19(9):1192-1204

[4] Long-term complete remission induced by mogamulizumab in a severe Sezary patient, together with five different possible autoimmune manifestations [Abstract #059; Case study poster (external)]