

News release

Kyowa Kirin Announces Final Safety Data of POTELIGEO[®] (mogamulizumab-kpkc) from MAVORIC Trial

PRINCETON, NJ, January 31, 2020--- Kyowa Kirin, Inc., (Kyowa Kirin, TSE: 4151) announces the final safety data from the MAVORIC (Mogamulizumab anti-CCR4 Antibody Versus ComparatOR In CTCL) trial of POTELIGEO[®] (mogamulizumab-kpkc), which will be presented today at the 12th Annual T-Cell Lymphoma Forum (TCLF) in La Jolla, California.

MAVORIC is the first pivotal trial in cutaneous T-cell lymphoma (CTCL) to use progression free survival (PFS) as a primary endpoint. It is also the largest randomized study to compare systemic therapies in subtypes of CTCL.¹ Secondary endpoints included a proportion of patients achieving an overall response rate (ORR), duration of response and safety.¹ Primary results were based on a data cutoff of December 31, 2016, which served as the basis of the U.S. Food and Drug Administration (FDA) and European Medicines Agency (EMA) approvals of mogamulizumab for the treatment of the most common subtypes of CTCL as well as a partial change of the product label in Japan.¹ The analysis being presented at TCLF reports final safety results of MAVORIC as of the safety data available on January 3, 2019, based on patients who continued participating in the trial post-approval.²

For the final safety analysis, median duration of follow-up was 34.5 months (range, 0.13-70.0).² Median treatment exposure was 170 days (range, 1-1813) for mogamulizumab and 84 days (4-1230) for vorinostat, which represent the same median values but broader ranges compared to the primary analysis (primary analysis, 170 days [1-1379] for mogamulizumab and 84 days [4-1058] for vorinostat).²

This final safety analysis from the MAVORIC study in patients with previously treated mycosis fungoides (MF) and Sézary syndrome (SS) demonstrated that mogamulizumab did not identify any new safety signals. The type and frequency of adverse events (AEs) in either the mogamulizumab or vorinostat treatment groups were consistent with those reported in the primary analysis.² Treatment-emergent adverse events (TEAEs), regardless of causality, were reported at similar rates in the two treatment groups and included constipation, peripheral edema, headache, and anemia.² TEAEs that occurred at higher frequency in the mogamulizumab vs. vorinostat arm included infusion-related reaction (33.2% vs 0.5%) and drug eruption (25.0% vs 1.1%).² The majority of these events were grade 1 or 2, and the types and frequencies of AEs attributable to mogamulizumab included infusion-related reaction (33.2% [61/184]), drug eruption (23.9%

[44/184]), and fatigue (18.5% [34/184]).² AEs attributed to vorinostat included diarrhea (55.4% [103/186]), nausea (38.2% [71/186]), and fatigue (33.3% [62/186]).²

In the trial, patients on vorinostat for at least two cycles who demonstrated confirmed disease progression or experienced intolerable toxicity (grade ≥ 3 adverse events [AEs], excluding inadequately treated nausea, vomiting, and diarrhea; and alopecia), despite dose reduction and appropriate management of side effects, could cross over to treatment with mogamulizumab. This analysis confirmed earlier findings showing that the type and incidence of TEAEs among patients receiving mogamulizumab after crossover were similar to those observed for patients initially randomized to mogamulizumab.²

“We are pleased that this final safety analysis from the MAVORIC study in patients with previously treated MF and SS demonstrates the additional two years of mogamulizumab safety follow up and treatment exposure did not identify any unexpected safety findings,” said Jeffrey S. Humphrey, MD, Chief Development Officer of Kyowa Kirin, Inc.

POTELIGEO[®] (mogamulizumab-kpkc) is approved in the U.S. for the treatment of adult patients with relapsed or refractory MF or SS after at least one prior systemic therapy.³ MF and SS are the most common subtypes of CTCL.⁴

Please see Poteligeo Indication and Important Safety Information below.

INDICATION

POTELIGEO[®] (mogamulizumab-kpkc) injection, for intravenous infusion is indicated for the treatment of adult patients with relapsed or refractory mycosis fungoides (MF) or Sézary syndrome (SS) after at least one prior systemic therapy.

Important Safety Information

Warnings and Precautions:

- **Dermatologic toxicity:** Monitor patients for rash throughout the course of treatment. For patients who experienced dermatologic toxicity in Trial 1, the median time to onset was 15 weeks, with 25% of cases occurring after 31 weeks. Interrupt POTELIGEO for moderate or severe rash (Grades 2 or 3). Permanently discontinue POTELIGEO for life-threatening (Grade 4) rash or for any Stevens-Johnson syndrome (SJS) or toxic epidermal necrolysis (TEN).
- **Infusion reactions:** Most infusion reactions occur during or shortly after the first infusion. Infusion reactions can also occur with subsequent infusions. Monitor patients closely for signs and symptoms of infusion reactions and interrupt the infusion for any grade reaction

and treat promptly. Permanently discontinue POTELIGEO for any life-threatening (Grade 4) infusion reaction.

- **Infections:** Monitor patients for signs and symptoms of infection and treat promptly.
- **Autoimmune complications:** Interrupt or permanently discontinue POTELIGEO as appropriate for suspected immune-mediated adverse reactions. Consider the benefit/risk of POTELIGEO in patients with a history of autoimmune disease.
- **Complications of allogeneic HSCT after POTELIGEO:** Increased risks of transplant complications have been reported in patients who received allogeneic HSCT after POTELIGEO. Follow patients closely for early evidence of transplant-related complications.

Adverse Reactions:

- The most common adverse reactions (reported in $\geq 10\%$ of patients) with POTELIGEO in the clinical trial were rash, including drug eruption (35%), infusion reaction (33%), fatigue (31%), diarrhea (28%), drug eruption (24%), upper respiratory tract infection (22%), musculoskeletal pain (22%), skin infection (19%), pyrexia (17%), edema (16%), nausea (16%), headache (14%), thrombocytopenia (14%), constipation (13%), anemia (12%), mucositis (12%), cough (11%), and hypertension (10%).

You are encouraged to report suspected adverse reactions to Kyowa Kirin, Inc. at 1-844-768-3544 or FDA at 1-800-FDA-1088 or www.fda.gov/safety/medwatch/.

About Kyowa Kirin

Kyowa Kirin commits to innovative drug discovery driven by state-of-the-art technologies. The company focuses on discovering and creating new value through advances in four therapeutic areas: nephrology, oncology, immunology/allergy and neurology. Under the Kyowa Kirin brand, employees from 36 group companies across North America, EMEA and Asia/Oceania unite to champion the interests of patients and their caregivers in areas of unmet medical need. You can learn more about the business of Kyowa Kirin at <https://www.kyowakirin.com/>.

About POTELIGEO

POTELIGEO is a humanised monoclonal antibody (mAb) directed against CC chemokine receptor 4 (CCR4), which is frequently expressed on leukaemic cells of certain haematologic malignancies including CTCL (cutaneous T-cell lymphoma). POTELIGEO was produced using Kyowa Kirin's proprietary POTELLIGENT® platform, which is associated with enhanced antibody-dependent cellular cytotoxicity (ADCC).⁵

About mycosis fungoides (MF) and Sézary Syndrome (SS)

MF and SS are the two most common subtypes of CTCL, a rare type of non-Hodgkin's lymphoma,

which is characterized by localization of malignant T lymphocytes to the skin, and depending on the stage, the disease may involve skin, blood, lymph nodes, and viscera.⁴

About MAVORIC

MAVORIC is a Phase 3 open-label, multi-center, randomized 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.¹

References

¹ Kim Y, Bagot M, Pinter-Brown, L 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. 1192-1204.

² Kim Y, Bagot M, Zinzani PL, et al. Safety of Mogamulizumab in Mycosis Fungoides and Sézary Syndrome: Final Results from the Phase 3 MAVORIC Study. Data presented at: T-Cell Lymphoma Forum 2020: January 30-February 1, 2020; La Jolla, California.

³ FDA approves treatment for two rare types of non-Hodgkin lymphoma. U.S. Food and Drug Administration. August 8, 2018. <https://www.fda.gov/news-events/press-announcements/fda-approves-treatment-two-rare-types-non-hodgkin-lymphoma>. Accessed January 2020.

⁴ Leukemia & Lymphoma Society. Cutaneous T-Cell Lymphoma. https://www.lls.org/sites/default/files/file_assets/PS96_CTCL_Booklet_Final.pdf. Accessed January 2020.

⁵ National Cancer Institute. Mogamulizumab. <https://www.cancer.gov/publications/dictionaries/cancer-drug/def/mogamulizumab>. Accessed January 2020.