

Kyowa Kirin Announces FDA Approval of Poteligeo® (mogamulizumab-kpkc) for the Treatment of Mycosis Fungoides and Sézary Syndrome

- *Poteligeo has been approved for the treatment of the two most common types of Cutaneous T-cell lymphoma (CTCL) in previously treated patients based on data showing improved progression-free survival (PFS) and overall response rate (ORR) when compared to vorinostat.*
- *FDA approval was based on MAVORIC, the largest randomized study conducted in patients with mycosis fungoides (MF) and Sézary syndrome (SS), subtypes of CTCL, and the first pivotal trial in CTCL to use PFS as a primary endpoint.*
- *Poteligeo is the first biologic agent targeting CCR4 to be available for patients in the U.S.*

Tokyo, Japan, 8th August, 2018 – Kyowa Hakko Kirin Co., Ltd., (Kyowa Kirin) announces today that the U.S. Food and Drug Administration (FDA) has granted approval for Poteligeo® (mogamulizumab-kpkc) for the treatment of adult patients with relapsed or refractory mycosis fungoides (MF) or Sézary syndrome (SS) after at least one prior systemic therapy. FDA granted Priority Review and Breakthrough Therapy Designation in late 2017.

Poteligeo is a humanized monoclonal antibody (mAb) directed against CC chemokine receptor 4 (CCR4), which is frequently expressed on leukemic cells of certain blood cancers including CTCL. Using the proprietary POTELLIGENT® technology, the amount of fucose in the sugar chain structure of Poteligeo is reduced, which enhances the antibody dependent cellular cytotoxicity (ADCC).

“I believe the approval is very good news for patients who have been suffering from mycosis fungoides (MF) or Sézary syndrome (SS) in the US,” said Mitsuo Satoh Ph.D., Executive Officer, Vice President Head of R&D Division of Kyowa Hakko Kirin. “Since this antibody was discovered through our cutting-edge R&D activity, it is also another important achievement for Kyowa Hakko Kirin in leaping forward to become a global specialty pharmaceutical company.”

“Mycosis fungoides (MF) and Sézary syndrome (SS) can be disfiguring, and debilitating. MAVORIC, the largest study of systemic therapy ever conducted in MF and SS, showed that mogamulizumab prolonged progression-free survival compared to vorinostat in patients with relapsed or refractory MF or SS,” said Jeffrey S. Humphrey, MD, President of Kyowa Kirin Pharmaceutical Development, Inc.. “We look forward to the publication of MAVORIC’s primary results and to ongoing scientific exchange within the medical and academic communities.”

Because CTCL manifests itself in skin lesions, it is often mistaken for other non-critical skin conditions, which can delay conclusive diagnosis and treatment options. MF and SS are the two most common subtypes of CTCL. MF is the most common subtype, accounting for 50-70% of cases. It is a slow progressing form of lymphoma that can involve the skin, blood, lymph nodes and organs, and may be associated with severe infections. SS accounts for approximately 3% of CTCL cases and is a more aggressive, leukemic form of CTCL.

The FDA approval of Poteligeo is supported by the MAVORIC (Mogamulizumab anti-CCR4 Antibody Versus ComparatOR In CTCL) study, which is the largest randomized trial in MF and SS and the first pivotal trial in CTCL to use PFS as a primary endpoint. MAVORIC was 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 a total of 372 patients to mogamulizumab or vorinostat. The results showed that mogamulizumab demonstrated significantly superior PFS at a median of 7.6 months [95% CI: 5.6, 10.2] compared to 3.1 months with vorinostat [95% CI: 2.8, 4.0], [hazard ratio 0.53: 95% CI: 0.41, 0.69; p<0.001]. The confirmed overall response rate for mogamulizumab and vorinostat was 28% and 5%, respectively (p<0.001).

FDA granted Poteligeo Breakthrough Therapy Designation for the treatment of MF and SS in adult patients, and evaluated Poteligeo with Priority Review, which is reserved for drugs that treat a serious condition and, if approved, would provide a significant improvement in treatment safety or effectiveness.

Kyowa Kirin International PLC, a Kyowa Hakko Kirin Group company, will be responsible for commercializing Poteligeo in the U.S. and this is planned to commence in the fourth quarter of 2018. A Marketing Authorization application for mogamulizumab is currently under review by the European Medicines Agency.

The Kyowa Hakko 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.

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 the pivotal trial 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/medwatch.

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 realize 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 commercialization 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.

About POTELIGEO

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

In August 2017, the FDA granted POTELIGEO Breakthrough Therapy Designation status for the treatment of MF and SS in adult patients who have received at least one prior systemic therapy. In November 2017, the FDA accepted the BLA for filing and granted POTELIGEO Priority Review. POTELIGEO received FDA approval in August 2018.

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.

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Contact Kyowa Hakko Kirin Co. Ltd.
Media
Hiroki Nakamura
+81-3-5205-7205
Email: media@kyowa-kirin.co.jp

Callum Spreng
Spreng Thomson Ltd. (For Kyowa Kirin International PLC)
+44 (0)141 548 5191
Mobile: +44 (0)7803 970103
Email: Callum@sprengthomson.com

Yvette Venable
Kyowa Kirin International PLC
+1 908-375-2358
Or +44 7388 222 769
Email: Yvette.Venable@kyowakirin.com