December 23, 2022
KISSEI PHARMACEUTICAL CO., LTD.

Marketing Authorization Approval in Japan for TAVALISSE® Tab. 100mg and 150mg, an Oral Spleen Tyrosine Kinase Inhibitor

Kissei Pharmaceutical Co., Ltd. (Head Office: Matsumoto, Nagano, Japan; Chairman and CEO: Mutsuo Kanzawa; "Kissei") announced that the Ministry of Health, Labour and Welfare (MHLW) has granted manufacturing and marketing approval to Kissei for the oral spleen tyrosine kinase (SYK) inhibitor, TAVALISSE® Tab. 100mg and 150mg (generic name: fostamatinib disodium hexahydrate, development code: R788), for chronic idiopathic thrombocytopenic purpura (chronic ITP).

TAVALISSE® is an oral SYK inhibitor discovered by Rigel Pharmaceuticals, Inc. (Head Office: USA, President and CEO: Raul Rodriguez; "Rigel"). It suppresses platelet destruction by macrophages thereby preventing platelet depletion and potentially improving the bleeding symptoms caused by chronic ITP. TAVALISSE®' has a different mechanism of action than existing treatments. Therefore, it represents a new treatment option for patients with chronic ITP who have had an insufficient response to or were unable to tolerate conventional treatments such as steroids.

The approval is based on the the results of the Phase 3 clinical trials of TAVALISSE in ITP patients in Japan and outside of Japan. The results of the Japanese Phase 3 clinical trial (Study R788-1301) were published in the British Journal of Haematology in December 2022 (https://doi.org/10.1111/bjh.18582).

In October 2018, Kissei acquired the development and commercialization rights for this agent in Japan, China, South Korea and Taiwan from Rigel.

It has been approved in the United States since 2018, under the brand name of TAVALISSE® (fostamatinib disodium hexahydrate) tablets and indicated for the treatment of adult patients with chronic ITP who have had an insufficient response to a previous treatment. Product approvals have followed in Europe and Canada. It has been granted orphan drug designation in the United States, Japan and South Korea.

Kissei has engaged in the research and development of new drugs focusing on rare diseases and diseases for which there is no sufficient treatments. We strive to contribute to the treatments for patients suffering from serious illness.

The projected financial results for the fiscal year ending March 2023, which incorporates this progress, were disclosed at the time of the announcement of the financial results in November 2022.

《 Reference 》

Product Summary of TAVALISSE®

Brand Name	TAVALISSE® Tab. 100mg,150mg
General Name	Fostamatinib disodium hexahydrate
Indications	Chronic Idiopathic Thrombocytopenic Purpura
Dosage and Administration	The usual oral dosage for adults patients is 100mg of fostamatinib twice daily. The dosage should be increased to 150 mg twice daily if the platelet count does not increase to the target after 4 weeks or longer with initial dosage,and there are no safety concerns,. The dosage may be adjusted based on the platelet count and symptoms, up to 150 mg twice a day.
Formulation	Film coated tablets
Manufactured and Distributed by	Kissei Pharmaceutical Co., Ltd.
Date of Marketing Approval in Japan	December 23, 2022

About Idiopathic Thrombocytopenic Purpura (ITP)

ITP is a disease which causes serious bleeding events and bruising due to a decrease in platelet counts below 100,000/μL, despite the absence of other obvious illnesses and medications that cause thrombocytopenia. In Japan, idiopathic thrombocytopenic purpura is listed as a designated intractable disease name and used widely, while immune thrombocytopenia is the internationally accepted name for the disease.

The clinical symptoms of ITP include subcutaneous bleeding (petechiae or purpura) as well as bleeding from the gums or nose, and gastrointestinal, reproductive or urinary tracts, as well as intracranial bleeding.

ITP is designated as an "intractable disease" by the Minister of Health, Labour and Welfare. The number of patients with ITP is estimated to be approximately 19,000* and 2.16 per 100,000** people are newly diagnosed with ITP every year in Japan. The cause of ITP has still not been definitively elucidated. It is believed that one of the possible causes is the decreased platelet count as a result of the production of autoantibodies against platelets, leading to the destruction of opsonized platelets by

macrophages in the spleen. ITP is currently treated with corticosteroids or thrombopoietin (TPO) receptor agonists as well as surgical removal of the spleen.

*: Estimated based on the number of patients having certificates issued for specific disease treatment (designated intractable disease)
**: Int J Hematol, 2011, 93: 329-35

About Rigel Pharmaceuticals (Nasdaq: RIGL)

Rigel Pharmaceuticals, Inc., is a biotechnology company dedicated to discovering, developing and providing novel small molecule drugs that significantly improve the lives of patients with hematologic disorders, cancer and rare immune diseases. Founded in 1996, Rigel is based in South San Francisco, California, U.S.A. For more details, please visit www.rigel.com.