September 23, 2019

Rigel's fostamatinib Enters Phase 3 Clinical Trial in Japan with Kissei Pharmaceuticals for the Treatment of Chronic Immune Thrombocytopenia

SOUTH SAN FRANCISCO, Calif., Sept. 23, 2019 /PRNewswire/ -- Rigel Pharmaceuticals, Inc. (Nasdaq: RIGL) today announced that its collaboration partner, Kissei Pharmaceuticals Co., Ltd. ("Kissei"), has initiated a Phase 3 trial in Japan of fostamatinib disodium hexahydrate in adult patients with chronic immune thrombocytopenia (ITP). The efficacy and safety of orally administered fostamatinib will be assessed by comparing it with placebo in a randomized, double-blind study. Fostamatinib is commercially available in the U.S. under the brand name TAVALISSE® for the treatment of adult patients with chronic ITP who have had an insufficient response to a previous treatment.

Kissei is a Japan-based pharmaceutical company addressing patients' unmet medical needs through its research, development and commercialization efforts, as well as through collaborations with partners. Earlier this year, Kissei submitted a Phase 3 trial design to Japan's Pharmaceuticals and Medical Devices Agency (PMDA) and it was recently accepted by the agency. The results of this trial will be used to support a new drug application (NDA) that Kissei plans to file in Japan in late 2021 or early 2022. Japan has the third highest prevalence of chronic ITP in the world behind the U.S. and EU. Currently a marketing authorization application for fostamatinib in chronic ITP in adult patients is being reviewed by the European Medicines Agency for potential approval in Europe.

In October 2018, Rigel and Kissei entered into an agreement for the development and commercialization of fostamatinib in all current and potential indications in Japan, China, Taiwan and the Republic of Korea. Under the terms of the agreement, Rigel received an upfront cash payment of $33 million, with the potential for an additional $147 million in development and commercial milestone payments and will receive product transfer price payments in the mid to upper twenty percent range based on tiered net sales.

About ITP

In patients with ITP, the immune system attacks and destroys the body's own blood platelets, which play an active role in blood clotting and healing. Common symptoms of ITP are excessive bruising and bleeding. People suffering with chronic ITP may live with an increased risk of severe bleeding events that can result in serious medical complications or

even death. Current therapies for ITP include steroids, blood platelet production boosters (TPO receptor agonists) and splenectomy. However, not all patients are adequately treated with existing therapies. As a result, there remains a significant medical need for additional treatment options for patients with ITP.

About TAVALISSE

Indication

TAVALISSE® (fostamatinib disodium hexahydrate) tablets is indicated for the treatment of thrombocytopenia in adult patients with chronic immune thrombocytopenia (ITP) who have had an insufficient response to a previous treatment.

Important Safety Information

Warnings and Precautions

- Hypertension can occur with TAVALISSE treatment. Patients with pre-existing hypertension may be more susceptible to the hypertensive effects. Monitor blood pressure every 2 weeks until stable, then monthly, and adjust or initiate antihypertensive therapy for blood pressure control maintenance during therapy. If increased blood pressure persists, TAVALISSE interruption, reduction, or discontinuation may be required.
- Elevated liver function tests (LFTs), mainly ALT and AST, can occur with TAVALISSE. Monitor LFTs monthly during treatment. If ALT or AST increase to >3 x upper limit of normal, manage hepatotoxicity using TAVALISSE interruption, reduction, or discontinuation.
- Diarrhea occurred in 31% of patients and severe diarrhea occurred in 1% of patients treated with TAVALISSE. Monitor patients for the development of diarrhea and manage using supportive care measures early after the onset of symptoms. If diarrhea becomes severe (≥Grade 3), interrupt, reduce dose or discontinue TAVALISSE.
- Neutropenia occurred in 6% of patients treated with TAVALISSE; febrile neutropenia occurred in 1% of patients. Monitor the ANC monthly and for infection during treatment. Manage toxicity with TAVALISSE interruption, reduction, or discontinuation.
- TAVALISSE can cause fetal harm when administered to pregnant women. Advise pregnant women the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment and for at least 1 month after the last dose. Verify pregnancy status prior to initiating TAVALISSE. It is unknown if TAVALISSE or its metabolite is present in human milk. Because of the potential for serious adverse reactions in a breastfed child, advise a lactating woman not to breastfeed during TAVALISSE treatment and for at least 1 month after the last dose.

Drug Interactions

- Concomitant use of TAVALISSE with strong CYP3A4 inhibitors increases exposure to the major active metabolite of TAVALISSE (R406), which may increase the risk of adverse reactions. Monitor for toxicities that may require a reduction in TAVALISSE dose.
- It is not recommended to use TAVALISSE with strong CYP3A4 inducers, as concomitant use reduces exposure to R406.
- Concomitant use of TAVALISSE may increase concentrations of some CYP3A4 substrate drugs and may require a dose reduction of the CYP3A4 substrate drug.
- Concomitant use of TAVALISSE may increase concentrations of BCRP substrate

drugs (e.g., rosuvastatin) and P-Glycoprotein (P-gp) substrate drugs (e.g., digoxin), which may require a dose reduction of the BCRP and P-gp substrate drug.

Adverse Reactions

- Serious adverse drug reactions in the ITP double-blind studies were febrile neutropenia, diarrhea, pneumonia, and hypertensive crisis, which occurred in 1% of TAVALISSE patients. In addition, severe adverse reactions occurred including dyspnea and hypertension (both 2%), neutropenia, arthralgia, chest pain, diarrhea, dizziness, nephrolithiasis, pain in extremity, toothache, syncope, and hypoxia (all 1%).
- Common adverse reactions (≥5% and more common than placebo) from FIT-1 and FIT-2 included: diarrhea, hypertension, nausea, dizziness, ALT and AST increased, respiratory infection, rash, abdominal pain, fatigue, chest pain, and neutropenia.

Please see www.TAVALISSE.com for full Prescribing Information.

**To report side effects of prescription drugs to the FDA,
visit www.fda.gov/medwatch or call 1-800-FDA-1088 (800-332-1088).**

TAVALISSE is a registered trademark of Rigel Pharmaceuticals, Inc.

About Rigel (www.rigel.com)
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 immune and hematologic disorders, cancer and rare diseases. Rigel's pioneering research focuses on signaling pathways that are critical to disease mechanisms. The company's first FDA approved product is TAVALISSE® (fostamatinib disodium hexahydrate) tablets, the only oral spleen tyrosine kinase (SYK) inhibitor, for the treatment of adult patients with chronic immune thrombocytopenia who have had an insufficient response to a previous treatment. Rigel's clinical programs include a Phase 3 study of TAVALISSE in warm autoimmune hemolytic anemia (AIHA) and a Phase 1 study of R835, a proprietary molecule from its interleukin receptor associated kinase (IRAK) program. In addition, Rigel has product candidates in clinical development with partners BerGenBio ASA, Daiichi Sankyo, Aclaris Therapeutics, and AstraZeneca.

Forward Looking Statements
This release contains forward-looking statements relating to, among other things, the payments that will be received by Rigel under the Collaboration and License Agreement; the potential opportunity for fostamatinib to obtain approval in the EU; the management and advancement of Rigel's clinical programs; and the design, timing and results of Rigel's clinical trials. Any statements contained in this press release that are not statements of historical fact may be deemed to be forward-looking statements. Words such as "planned," "will," "may," "expect," "anticipate," and similar expressions are intended to identify these forward-looking statements. These forward-looking statements are based on Rigel's current expectations and inherently involve significant risks and uncertainties. Actual results and the timing of events could differ materially from those anticipated in such forward looking statements as a result of these risks and uncertainties, which include, without limitation, risks and uncertainties associated with the commercialization and marketing of TAVALISSE; risks that the FDA, EMA or other regulatory authorities may make adverse decisions regarding fostamatinib; risks that TAVALISSE clinical trials may not be predictive of real-world results

or of results in subsequent clinical trials; risks that TAVALISSE may have unintended side effects, adverse reactions or incidents of misuses; the availability of resources to develop Rigel's product candidates; market competition; as well as other risks detailed from time to time in Rigel's reports filed with the Securities and Exchange Commission, including its Quarterly Report on Form 10-Q for the quarter ended June 30, 2019. Rigel does not undertake any obligation to update forward-looking statements and expressly disclaims any obligation or undertaking to release publicly any updates or revisions to any forward-looking statements contained herein.

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