

October 11, 2018



Rigel Receives EMA Validation of the Marketing Authorization Application for Fostamatinib Disodium Hexahydrate in Chronic Immune Thrombocytopenia (ITP) in Adult Patients

First SYK inhibitor for the treatment of adult chronic ITP

SOUTH SAN FRANCISCO, Calif., Oct. 11, 2018 /PRNewswire/ -- Rigel Pharmaceuticals, Inc. (Nasdaq: RIGL) today announced that the European Medicines Agency (EMA) has validated the Marketing Authorization Application (MAA) for fostamatinib in adult chronic immune thrombocytopenia. The validation was received on October 4, 2018 and initiated the MAA review process. The company anticipates a decision from the Committee on Human Medicinal Products by the fourth quarter of 2019. Currently, fostamatinib is commercially available in the U.S. under the brand name TAVALISSE™ (fostamatinib disodium hexahydrate), which is the first and only SYK inhibitor indicated for the treatment of thrombocytopenia in adult patients with chronic ITP who have had an insufficient response to a previous treatment.

"The EMA's validation of our MAA is an important milestone in the execution of our global commercial strategy for fostamatinib for the treatment of adult chronic ITP," said Raul Rodriguez, president and CEO of Rigel. "Europe is the second largest ITP market, and we are working diligently to secure a European commercial collaboration in 2019. We are committed to making fostamatinib available to physicians worldwide for patients affected with chronic ITP."

The MAA review follows the U.S. Food and Drug Administration (FDA) approval and commercial launch in the U.S. of TAVALISSE.

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

(TPOs) 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 are indicated in the U.S. 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 (eg, rosuvastatin) and P-Glycoprotein (P-gp) substrate drugs (eg, 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 U.S. 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 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), an 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 current clinical programs include Phase 2 studies of fostamatinib in autoimmune hemolytic anemia and IgA nephropathy. In addition, Rigel has product candidates in development with partners BerGenBio AS, Daiichi Sankyo, and Aclaris Therapeutics.

Forward Looking Statements

This release contains forward-looking statements relating to, among other things, the timing of the EMA's MAA review process and when Rigel expects a decision. 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 "may," "anticipates," "working to," 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 of fostamatinib; risks that the EMA or other regulatory authorities may make adverse decisions regarding fostamatinib; risks associated with being able to partner fostamatinib in Europe; risks that fostamatinib clinical trials may not be predictive of real-world results or of results in subsequent clinical trials; risks that fostamatinib 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 period ended June 30, 2018. 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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