July 9, 2020

Rigel Announces Availability of TAVLESSE® (Fostamatinib Disodium Hexahydrate) in Europe

TAVLESSE initial launch in Germany and the U.K. by Grifols S.A.

SOUTH SAN FRANCISCO, Calif., July 9, 2020 /PRNewswire/ -- Rigel Pharmaceuticals, Inc. (Nasdaq: RIGL) today announced that Grifols S.A., its collaborative partner in Europe, has launched TAVLESSE® in Germany and the United Kingdom. It was approved by the European Commission in January 2020 for the treatment of chronic immune thrombocytopenia (ITP) in adult patients who are refractory to other treatments. TAVLESSE, which is marketed in the U.S. under the brand name TAVALISSE®, is an oral spleen tyrosine kinase (SYK) inhibitor that targets the underlying autoimmune cause of ITP by impeding platelet destruction.

"The launch of TAVLESSE in Germany and the United Kingdom is an important step in making our product available to ITP patients across Europe," said Raul Rodriguez, Rigel's president and CEO. "Europe represents approximately half of the estimated $900 million ITP market outside of the U.S., and Grifols's experience with treatments for hematological disorders make them the ideal collaborative partner for our product."

Spain-based Grifols S.A. (MCE: GRF, MCE: GRF.P, NASDAQ: GRFS) is a global healthcare company and a leading producer of plasma-derived medicines for the treatment of rare and chronic diseases, including intravenous immunoglobulin (IVIG) which is used in the treatment of ITP.

About ITP

In patients with ITP (immune thrombocytopenia), 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 IVIG, steroids, blood platelet production boosters (TPO-RAs) and splenectomy. However, not all patients respond to existing therapies. As a result, there remains a significant medical need for additional treatment options for patients with ITP.

About TAVLESSE

Indication

TAVLESSE® (Fostamatinib Disodium Hexahydrate) is indicated for the treatment of chronic immune thrombocytopenia (ITP) in adult patients who are refractory to other treatments.

TAVLESSE Dosage

Fostamatinib dosing requirements must be individualized based on the patient's platelet counts. The lowest dose of fostamatinib to achieve and maintain a platelet count of at least 50,000/μL should be used. Dose adjustments are based upon the platelet count response and tolerability.

The recommended starting dose of fostamatinib is 100 mg twice daily. After initiating fostamatinib, the dose can be increased to 150 mg twice daily after 4 weeks based on platelet count and tolerability. A daily dose of 300 mg daily must not be exceeded. Management of some adverse reactions may require dose interruption, reduction, or discontinuation.

Discontinuation: Treatment with fostamatinib should be discontinued after 12 weeks of fostamatinib therapy if the platelet count does not increase to a level sufficient to avoid clinically important bleeding. For Monitoring and dose modifications please refer to SmPC.

Special populations: No dose adjustment is necessary in patients with renal impairment or the elderly. Fostamatinib should not be used in patients with severe hepatic impairment or children and adolescents less than 18 years of age because of adverse reactions on actively growing bones observed in nonclinical studies.

Administration: Fostamatinib is for oral use. The tablets should be taken twice daily, whole with or without food. In the event of gastric upset, tablets may be taken with food.

Contra-indications: Hypersensitivity to the active substance or to any of the excipients. Pregnancy (see SmPC)

Special warnings and precautions for use (for more information see the SmPC):
Information is based on ITP placebo-controlled population unless specified.

Excipients:
TAVLESSE 100 mg film-coated tablets contains 23 mg sodium per tablet, equivalent to 1.2% of the WHO recommended maximum daily intake of 2 g sodium for an adult.

TAVLESSE 150 mg film-coated tablets contains 34 mg sodium per tablet, equivalent to 1.7% of the WHO recommended maximum daily intake of 2 g sodium for an adult.

Hypertension
In the ITP placebo-controlled population, increased blood pressure, including the development of hypertension, was reported in patients treated with fostamatinib. Hypertensive crisis occurred in 1 (1%) patient. Patients with pre-existing hypertension may be more susceptible to the hypertensive effects of fostamatinib.

The patient's blood pressure should be monitored every two weeks until stable, then monthly, and adjust or initiate antihypertensive therapy to ensure maintenance of blood

pressure control during fostamatinib therapy. If increased blood pressure persists despite appropriate therapy, the physician should consider fostamatinib dose interruption, reduction or discontinuation.

Liver function test abnormalities and risk of hepatotoxicity
In the placebo-controlled studies, laboratory testing showed maximum ALT/AST levels more than 3 x the upper limit of normal (ULN) in 9% of patients receiving fostamatinib and no patients receiving placebo.

Sparse data suggest an increased risk of hyperbilirubinemia in patients with genetic polymorphisms of UGT1A1, e.g. Gilbert, the physician should monitor these patients frequently.

For all patients, transaminases recovered generally to baseline levels within 2 to 6 weeks of dose-modification. The physician should monitor liver function tests monthly during treatment. If ALT or AST increase more than 3 x ULN, the physician should manage hepatotoxicity by treatment interruption, reduction or discontinuation. Concomitant total bilirubin increases greater than 2 X ULN should lead to treatment discontinuation.

Complete blood counts (CBCs)
The physician should monitor CBCs, including platelet counts, monthly until a stable platelet count (of at least 50,000/μL) is achieved. Thereafter, the physician should continue to monitor CBCs, including neutrophils, regularly.

Diarrhea
Diarrhea is the most common adverse reaction with fostamatinib treatment, but severe diarrhea occurred in 1% of patients. Patients should be monitored for the development of diarrhea and managed by using supportive care measures (e.g., dietary changes, hydration and/or antidiarrheal medication) early after the onset of symptoms. If diarrhea becomes severe (Grade 3 or above), administration of fostamatinib should be interrupted, reduced, or discontinued.

Neutropenia
Neutropenia occurred in 7% of patients treated with fostamatinib; febrile neutropenia occurred in 1% of patients. Patients with neutropenia may be more susceptible to infections. The physician should monitor the absolute neutrophil count monthly. The physician should manage toxicity with fostamatinib interruption, reduction or discontinuation.

Infections
Infections, including pneumonia and respiratory tract infections, have been reported during clinical trials. The patient should be monitored for infection during treatment. The benefit risk of continuing therapy during an infection should be evaluated by the physician.

Bone remodeling
Since fostamatinib was shown in vitro to not only target SYK but also other tyrosine kinases that are involved in the bone metabolism (e.g., VEGFR, RET), any potential untargeted effects on bone remodeling or formation remain undetermined, especially in patients with osteoporosis, patients with fractures or young adults where epiphyseal fusion has not yet occurred. Closer monitoring in these patients is therefore recommended. The benefit risk of continuing therapy during the healing of a bone fracture should be thoroughly evaluated by

the physician.

(see SmPC for interactions with other medicinal products and other form of interactions)

Women of childbearing potential must use effective contraception during treatment and at least one month after the last dose.

Pregnancy: Based on findings from animal studies and its mechanism of action, fostamatinib can cause fetal harm when administered to a pregnant woman. Pregnant women should be advised about the potential risk to a fetus. Pregnancies occurring during clinical trials resulted in healthy newborns as well as stillbirths/spontaneous abortions and miscarriages. If a patient becomes pregnant while taking fostamatinib, therapy should be discontinued. Fostamatinib is contraindicated during pregnancy.

Breast-feeding: It is unknown whether fostamatinib/metabolites are excreted in human milk. Available pharmacodynamic/toxicological data in animals have shown excretion of fostamatinib metabolites in milk. A risk to the newborns/infants cannot be excluded. Breast-feeding should be discontinued during treatment with fostamatinib and for at least one month after the last dose.

Fertility: There are no data on the effect of fostamatinib on human fertility. Based on the finding of reduced pregnancy rates in animal studies, fostamatinib may affect female fertility. Studies in animals have shown no adverse effect on male fertility. Given there is no evidence for mutagenic or clastogenic potential, there is no concern for male-mediated birth defects.

Undesirable effects
In the ITP placebo-controlled studies, serious adverse drug reactions were febrile neutropenia, diarrhea, pneumonia, and hypertensive crisis, which each occurred in 1% of patients receiving fostamatinib. In addition, severe adverse reactions observed in patients receiving fostamatinib included dyspnea and hypertension (both 2%); and neutropenia, arthralgia, chest pain, diarrhea, dizziness, nephrolithiasis, pain in extremity, toothache, syncope and hypoxia (all 1%).

The most common reported adverse reactions associated with fostamatinib were: Upper respiratory tract infection, respiratory tract infection, bronchitis, lower respiratory tract infection, viral upper respiratory tract infection, Neutropenia, febrile neutropenia, Dizziness, Dysgeusia, Hypertension, Diarrhea, nausea, frequent bowel movement, upper abdominal pain, abdominal pain, rash, rash erythematous, rash macular, Chest pain, fatigue, influenza like illness, Alanine aminotransferase increased, aspartate aminotransferase increased, blood pressure (BP) increased, BP diastolic abnormal, BP diastolic increased, BP systolic increased, hepatic enzyme increased, liver function test abnormal, Neutrophil count decreased. For full details please refer to the SmPC.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V (refer to SmPC).

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. The product has been approved by the European Commission for the treatment of chronic immune thrombocytopenia in adult patients who are refractory to other treatments and will be marketed in Europe under the name TAVLESSE® (fostamatinib).

Rigel's clinical programs include a Phase 3 study of fostamatinib in warm autoimmune hemolytic anemia (AIHA); a completed Phase 1 study of R835[1], a proprietary molecule from its interleukin receptor associated kinase (IRAK) inhibitor program; and an ongoing Phase 1 study of R552[1], a proprietary molecule from its receptor-interacting protein kinase (RIP) inhibitor program. In addition, Rigel has product candidates in clinical development with partners Aclaris Therapeutics, AstraZeneca, BerGenBio ASA, and Daiichi Sankyo.

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

[1]*This product candidate is investigational and has not been established safe or effective by the U.S. Food and Drug Administration (FDA) or any regulatory authority.*

Forward Looking Statements

This release contains forward-looking statements relating to, among other things, Rigel's plans to make TAVLESSE available to ITP patients across Europe. *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 "potential," "may," "aim," "believe," "expects" 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 in the U.S. and TAVLESSE in Europe; risks that the FDA, European Medicines Agency (EMA) or other regulatory authorities may make adverse decisions regarding fostamatinib or any of Rigel's product candidates; risks that clinical trials may not be predictive of real-world results or of results in subsequent clinical trials; 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 Annual Report on Form 10-K for the year ended December 31, 2019 and its Quarterly Report on Form 10-Q for the quarter ended March 31, 2020. In addition, the ongoing COVID-19 pandemic may result in further delays in Rigel's studies and trials, or impact Rigel's sales and ability to obtain supply of fostamatinib. 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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