November 17, 2020

# Rigel Finalizes the Study Design of its Ongoing Phase 3 Clinical Trial of Fostamatinib in Warm Autoimmune Hemolytic Anemia

## FDA agrees to the proposed primary efficacy endpoint and additional secondary endpoints

SOUTH SAN FRANCISCO, Calif., Nov. 17, 2020 /PRNewswire/ -- Rigel Pharmaceuticals, Inc. (Nasdaq: RIGL) today announced that it has reached agreement with the U.S. Food and Drug Administration (FDA) on the final design of its FORWARD study, a pivotal Phase 3 clinical trial of fostamatinib disodium hexahydrate (fostamatinib) in warm autoimmune hemolytic anemia (AIHA). The FDA agreed to Rigel's proposed durable response measure for the primary efficacy endpoint as well as the inclusion of additional secondary endpoints.

The Phase 3 clinical trial is a randomized, double-blind, placebo-controlled study of approximately 90 patients with primary or secondary warm AIHA who have failed at least one prior treatment. The primary efficacy endpoint for the trial is a durable response defined as a hemoglobin level ≥ 10 g/dl with an increase from baseline of ≥ 2 g/dl on three consecutive available visits during the 24-week treatment period, with the response not being attributed to rescue therapy. This endpoint allows for missed visits due to the COVID-19 pandemic without impacting a durable outcome. As of November 5, the trial had enrolled 57 of the 90 patients targeted for enrollment and currently has over 90 clinical trial sites established across 22 countries.

"Our conversations with the FDA have enabled us to finalize the primary efficacy endpoint for the only ongoing Phase 3 trial in warm AIHA, a condition for which there is no approved therapy," said Raul Rodriguez, Rigel's president and CEO. "We are over 60% of our enrollment target despite the headwinds drug development is facing due to COVID-19. We believe this progress is a result of the geographic diversity of our clinical sites, the ability of fostamatinib to be given orally, and the FDA's clinical trial guidance during the pandemic."

Fostamatinib is commercially available in the U.S. under the brand name TAVALISSE® (fostamatinib disodium hexahydrate) tablets, which is the first and only spleen tyrosine kinase (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 FDA has granted TAVALISSE Orphan Drug designation for the treatment of patients with warm AIHA.

## About AIHA

Autoimmune hemolytic anemia (AIHA) is a rare, serious blood disorder in which the immune system produces antibodies that result in the destruction of the body's own red blood cells. AIHA affects approximately 45,000 adult patients in the U.S. and can be a severe, debilitating disease. Warm AIHA (wAIHA), the most common form of AIHA, is characterized by the presence of antibodies that react with the red blood cell surface at body temperature. To date, there are no disease-targeted therapies approved for AIHA, despite the unmet medical need that exists for these patients.

## 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 (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 Prescribing Information.**

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

TAVALISSE and TAVLESSE are registered trademarks 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. 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 is marketed in Europe under the name TAVLESSE® (fostamatinib).

Fostamatinib[1] is currently being studied in a Phase 3 trial for the treatment of warm autoimmune hemolytic anemia (AIHA); a NIH/NHLBI-Sponsored Phase 2 trial for the treatment of hospitalized COVID-19 patients, in collaboration with Inova Health System; and a Phase 2 trial for the treatment of COVID-19 being conducted by Imperial College London. Additionally, we plan to launch a Phase 3 clinical trial of fostamatinib for the treatment of hospitalized COVID-19 patients in the fourth quarter of 2020.

Rigel's other clinical programs include an ongoing 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 AstraZeneca, BerGenBio ASA, and Daiichi Sankyo.

*[1]The product for this use or indication is investigational and has not been proven safe or effective by any regulatory authority.*

**Forward Looking Statements**

*This release contains forward-looking statements relating to, among other things, Rigel's ability to complete enrollment in its phase 3 clinical trial as a treatment for AIHA and the trial design for such indication. 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 fostamatinib in the U.S. and 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 and, if approved, commercialize fostamatinib or any other of Rigel's product candidates; the progress of our and our collaborators' product development programs, including clinical testing, and the timing of results thereof; our expectations with respect to regulatory submissions and approvals; our research and development expenses; protection of our intellectual property; 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 September 30, 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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