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Rigel Announces Publication of Data from Phase 2 Clinical Study of Fostamatinib for the Treatment of Warm Antibody Autoimmune Hemolytic Anemia in the American Journal of Hematology

-- Results demonstrate clinically meaningful hemoglobin responses anda safety and tolerability profile consistent with existing fostamatinib safety database

-- Topline Phase 3 data expected in mid-2022 from Rigel's FORWARD study of fostamatinib in patients with wAIHA

SOUTH SAN FRANCISCO, Calif., March 8, 2022 /PRNewswire/ -- Rigel Pharmaceuticals, Inc. (Nasdaq: RIGL) today announced the publication of data in the *American Journal of Hematology* from the open label, multicenter, Phase 2 clinical study of fostamatinib in adults with warm antibody autoimmune hemolytic anemia (wAIHA) who had failed at least one prior treatment. The published data demonstrate that fostamatinib, an oral spleen tyrosine kinase (SYK) inhibitor, rapidly and durably increased hemoglobin (Hgb) levels, with clinically meaningful Hgb responses observed in nearly half of the patients, and a safety and tolerability profile consistent with the existing fostamatinib safety database of patients across multiple disease programs studied. The publication, entitled "Fostamatinib for the treatment of warm antibody autoimmune hemolytic anemia: Phase 2, multicenter, open-label study", is available on the journal website, https://onlinelibrary.wiley.com/doi/10.1002/ajh.26508.

"The results observed in our Phase 2 study in warm autoimmune hemolytic anemia reinforce the potential of fostamatinib to help patients with this rare, serious blood disorder for whom no disease-targeted therapies are currently approved," said Raul Rodriguez, Rigel's president and chief executive officer. "If approved, fostamatinib has the potential to be the first-to-market therapy for patients with wAIHA in 2023 and would be fostamatinib's second approved indication."

The Phase 2 study evaluated the response to fostamatinib at 150 mg BID (twice daily) in adult patients with wAIHA and active hemolysis with Hgb of less than 10 g/dL who had failed at least one prior treatment. The primary endpoint was Hgb greater than 10 g/dL with an increase of ≥2 g/dL from baseline by Week 24 without rescue therapy or red blood cell transfusion. The study demonstrated that 46% (11/24) of patients achieved the primary endpoint, with 1 late responder at week 30 (total of 12 responders [50%]). Increases in median Hgb were detected at Week 2 and sustained over time. The most common adverse events (AEs) were diarrhea (42%), fatigue (42%), hypertension (27%), dizziness (27%), and insomnia (23%). AEs were manageable and consistent with the fostamatinib safety database of over 3,900 patients across multiple diseases (rheumatoid arthritis, B-cell lymphoma, COVID-19, and immune thrombocytopenia (ITP)). No new safety signals were detected.

About the FORWARD Phase 3 Study

Fostamatinib is currently being evaluated in a Phase 3 randomized, double-blind, placebo-controlled clinical study in 90 patients with wAIHA who have failed at least one prior treatment. The study will evaluate the efficacy of fostamatinib versus placebo in achieving a durable hemoglobin response, defined as a hemoglobin level ≥ 10 g/dL, with an increase from baseline and durability measure in hemoglobin level of ≥ 2 g/dL, with the response not being attributed to rescue therapy, on 3 consecutive available visits during the 24-week treatment period. Secondary endpoints include other measures of hemoglobin response, use of rescue medication and safety.

The FDA has granted fostamatinib Orphan Drug and Fast Track designations for the treatment of patients with wAIHA.

Fostamatinib is commercially available in the U.S. under the brand name TAVALISSE® (fostamatinib disodium hexahydrate) tablets, which is the first and only FDA-approved SYK inhibitor indicated for the treatment of thrombocytopenia in adult patients with chronic ITP who have had an insufficient response to a previous treatment.

About AIHA

Autoimmune hemolytic anemia (AIHA) is a rare, serious blood disorder in which the immune system produces antibodies that lead to the destruction of the body's own red blood cells. Warm antibody AIHA (wAIHA), which is the most common form of AIHA, is characterized by the presence of antibodies that react with the red blood cell surface at body temperature. wAIHA affects approximately 36,000 adult patients in the U.S.[1] and can be a severe, debilitating disease. To date, there are no disease-targeted therapies approved for wAIHA, despite the unmet medical need that exists for these patients.

About TAVALISSE

Indication

TAVALISSE® (fostamatinib disodium hexahydrate) tablets are 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.TAVALISSEUSPI.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 and TAVLESSE are registered trademarks of Rigel Pharmaceuticals, Inc.

About Rigel

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. 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 is also commercially available in Europe, the United Kingdom (TAVLESSE) and Canada (TAVALISSE) for the treatment of chronic immune thrombocytopenia in adult patients.

Fostamatinib is currently being studied in a Phase 3 clinical trial (NCT03764618) for the treatment of warm autoimmune hemolytic anemia (wAIHA)[2]; a Phase 3 clinical trial (NCT04629703) for the treatment of hospitalized high-risk patients with COVID-19[2]; an NIH/NHLBI-sponsored Phase 3 clinical trial (ACTIV-4 Host Tissue Trial, NCT04924660) for the treatment of COVID-19 in hospitalized patients, and a Phase 2 clinical trial (NCT04581954) for the treatment of COVID-19 being conducted by Imperial College London.

Rigel's other clinical programs include its interleukin receptor-associated kinase (IRAK) inhibitor program, and a receptor-interacting serine/threonine-protein kinase (RIPK) inhibitor program in clinical development with partner Eli Lilly and Company. In addition, Rigel has product candidates in development with partners BerGenBio ASA and Daiichi Sankyo.

For further information, visit www.rigel.com or follow us on Twitter or LinkedIn.

1. Prevalence: A. Zanella, et al, *haematologica* 2014; 99(10); % Warm AIHA: T. Kalfa; Hematology Am Soc Hematol Educ Program. 2016 Dec 2; 2016(1): 690–697

2. 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, the benefits of fostamatinib in treating wAIHA; the timing and results of the Phase 3 clinical trial of fostamatinib in wAIHA patients; and Rigel's plans to seek regulatory approval for use of fostamatinib in treating wAIHA. 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", "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; 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 Annual Report on Form 10-K for the year ended December 31, 2021 and subsequent filings. 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, except as required by law.

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