January 10, 2022

Rigel Pharmaceuticals Provides Business Update

- TAVALISSE preliminary 2021 net product sales of approximately $63.0 million

- Topline data from Phase 3 clinical trial in warm autoimmune hemolytic anemia (wAIHA) expected in mid-2022

- R289, a potent and selective IRAK1/4 inhibitor, to start open-label Phase 2 study in low-risk myeloid dysplastic syndrome (MDS) in Q1 2022

- R552, a potent and selective RIPK1 inhibitor, will advance into Phase 2 development in psoriasis in 1H 2022 with partner Lilly

SOUTH SAN FRANCISCO, Calif., Jan. 10, 2022 /PRNewswire/ -- Rigel Pharmaceuticals, Inc. (Nasdaq: RIGL) today provided a business update including preliminary 2021 full-year total revenue, the status of the Phase 3 study in COVID-19, and upcoming catalysts in 2022.

"Despite the challenges the global pandemic continued to present in 2021, our team responded with creative solutions to navigate the evolving landscape and now look forward to several catalysts that have the potential to be transformative for the company in 2022," said Raul Rodriguez, Rigel's president and chief executive officer. "We've made strategic investments designed to accelerate TAVALISSE ITP sales in the U.S., prepare for pivotal readouts in two Phase 3 studies that have the potential to expand the market for fostamatinib into new indications such as wAIHA and COVID-19, and advance our clinical-stage IRAK1/4 and RIPK1 programs into Phase 2 development."

Commercial and Preliminary Financial Update

In the fourth quarter of 2021, a total of 1,814 bottles of TAVALISSE® (fostamatinib disodium hexahydrate) were sold in the U.S., of which 1,785 were shipped directly to patients and clinics, representing the highest daily bottles shipped to patients and clinics in a quarter since launch. For the full year ended December 31, 2021, 6,787 bottles of TAVALISSE were shipped directly to patients and clinics, representing an increase of 8% compared to 2020. While Rigel is still in the process of determining final results for the fourth quarter of 2021,

Rigel expects to report net product sales of $17.6 million compared to $17.7 million for the same period of 2020.

Contract revenues for the quarter ended December 31, 2021, are expected to be approximately $2.8 million, consisting of $1.8 million in revenue from collaborative partners and $1.0 million in government contract revenue from the U.S. Department of Defense (DOD).

For the fourth quarter of 2021, Rigel expects to report total revenue of approximately $20.4 million.

The company expects to report cash, cash equivalents, and short-term investments as of December 31, 2021, of approximately $124.9 million compared to $57.3 million as of December 31, 2020.

The above information is preliminary, has not been audited, and is subject to change upon the audit of the company's financial statements for the year ended December 31, 2021.

Portfolio Update

Phase 3 Trial in wAIHA

Enrollment of Rigel's FORWARD study, a Phase 3 pivotal trial of TAVALISSE in patients with wAIHA, is complete. Rigel expects to report topline data from the 24-week study in mid-2022 and proceed with regulatory filings if the data is positive. If approved, TAVALISSE has the potential to be the first-to-market therapy for patients with wAIHA in 2023.

COVID-19 Program

Rigel's Phase 3 clinical trial evaluating fostamatinib in high-risk patients hospitalized with COVID-19 has enrolled 231 of the targeted 308 patients to date. In December, Rigel expanded the inclusion criteria to include patients with more severe disease (NIAID Ordinal Scale 6) to more accurately reflect the clinically predominant patient population hospitalized with COVID-19 and help speed enrollment. In collaboration with the United States Food and Drug Administration (FDA) and DOD, Rigel has also updated the primary endpoint for the study from progression to severe disease within 29 days, to the number of days on oxygen through day 29.

"As a study endpoint, reducing the number of days a patient spends on supplemental oxygen has proven to be clinically meaningful, is a good measure for recovery, and has been widely used in other large NIH sponsored trials in the recent past," said Wolfgang Dummer, M.D., Ph.D., Rigel's chief medical officer. "The findings of the NIH/NHLBI phase 2 study provided evidence of broad, consistent and clinically meaningful improvement in mortality, time to sustained recovery, and the number of days on oxygen, for patients treated with fostamatinib in addition to standard of care. We look forward to confirming these findings in a larger patient population in our Phase 3 study."

This endpoint allows for closer comparison of the results with earlier results from the NIH/NHLBI Phase 2 trial with fostamatinib and various other NIH-sponsored trials, such as ACTIV-4, which uses a similar outcome measure as a primary endpoint. Rigel expects to complete enrollment and report topline data in mid-2022.

In addition to Rigel's Phase 3 study, fostamatinib is also being evaluated as a treatment for

COVID-19 in two ongoing studies, the NIH/NHLBI-funded Phase 3 ACTIV-4 Host Tissue trial and a Phase 2 open-label clinical trial conducted by Imperial College London.

IRAK1/4 Program

Rigel expects to advance R289[9], a potent and selective IRAK1/4 inhibitor, into an open-label Phase 1b/2 clinical study in patients with low-risk myeloid dysplastic syndrome (MDS) in Q1 2022. R289 blocks inflammatory cytokine production in response to toll-like receptor (TLR) and interleukin-1 receptor family (IL-1R) signaling. TLRs and IL-1Rs play a critical role in the innate immune response, and dysregulation of these pathways can lead to various inflammatory conditions. Chronic stimulation of both these receptor systems is thought to cause the pro-inflammatory environment in the bone marrow responsible for persistent cytopenias in lower-risk MDS patients[1].

RIPK1 Program Partnered with Eli Lilly

R552[9], a potent and selective RIPK1 inhibitor, will advance into Phase 2 development in psoriasis in the 1H 2022 with partner Lilly. RIPK1 is implicated in a broad range of key inflammatory cellular processes and plays a key role in TNF signaling, especially in the induction of pro-inflammatory necroptosis. The program also includes RIPK1 compounds that cross the blood-brain barrier (CNS-penetrants) to address neurodegenerative diseases such as Alzheimer's disease and ALS. Rigel is completing early discovery work on a potential candidate that Lilly may advance into clinical development.

Progress on Global Expansion in ITP

In December 2021, partner Kissei reported positive topline results for a Phase 3 study in ITP in Japan and is preparing a new drug application (NDA) for submission to Japan's Pharmaceuticals and Medical Devices Agency (PMDA). In October 2018, Rigel entered into an exclusive license and supply agreement with Kissei to develop and commercialize fostamatinib in all current and potential indications in Japan, China, Taiwan and the Republic of Korea. Fostamatinib has Orphan Drug Designation in Japan and Korea.

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 AIHA

Autoimmune hemolytic anemia (AIHA) is a rare, serious blood disorder in which the immune system produces antibodies that destroy 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. To date, there are no disease-targeted therapies approved for AIHA, despite the unmet medical need that exists for these patients. Warm antibody 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.

About COVID-19 & SYK Inhibition

COVID-19 is the infectious disease caused by Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2). SARS-CoV-2 primarily infects the upper and lower respiratory tract and can lead to acute respiratory distress syndrome (ARDS). Additionally, some patients develop other organ dysfunction including myocardial injury, acute kidney injury, shock resulting in endothelial dysfunction and subsequently micro and macrovascular thrombosis.[2] Much of the underlying pathology of SARS-CoV-2 is thought to be secondary to a hyperinflammatory immune response associated with increased risk of thrombosis.[3]

SYK is involved in the intracellular signaling pathways of many different immune cells. Therefore, SYK inhibition may improve outcomes in patients with COVID-19 via inhibition of key Fc gamma receptor (FcγR) and c-type lectin receptor (CLR) mediated drivers of pathology such as pro-inflammatory cytokine release by monocytes and macrophages, production of neutrophil extracellular traps (NETs) by neutrophils, and platelet aggregation.[4,5,6,7] Furthermore, SYK inhibition in neutrophils and platelets may lead to decreased thrombo-inflammation, alleviating organ dysfunction in critically ill patients with COVID-19.

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 about 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

Rigel Pharmaceuticals, Inc., is a biotechnology company dedicated to developing, and commercializing 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 (TAVLESSE), the United Kingdom, 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)[8]; a Phase 3 clinical trial (NCT04629703) for the treatment of hospitalized high-risk patients with mild-to-moderate

COVID-19[8]; an NIH/NHLBI-funded Phase 3 ACTIV-4 Host Tissue Study NCT04924660) for the treatment of COVID-19 in hospitalized patients on oxygen therapy, 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 (RIPK1) 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.

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8. *The product for this use or indication is investigational and has not been proven safe or effective by any regulatory authority.*
9. *R289 and R552 are investigational compounds not approved by FDA.*

Forward Looking Statements

This press release contains forward-looking statements relating to, among other things, expected commercial and financial results for the fourth quarter and fiscal year ended December 31, 2021, reporting of topline data from its Phase 3 trial in wAIHA, its Phase 3 clinical trial evaluating fostamatinib on COVID-19, its Phase 2 development in psoriasis of R552 with partner Eli Lilly, and its partner Kissei's Phase 3 study in ITP-. Forward-looking statements can be identified by words such as "plan", "potential", "may", "expects", "will" and similar expressions in reference to future periods. Forward-looking statements are neither historical facts nor assurances of future performance. Instead, they are based on Rigel's current beliefs, expectations, and assumptions regarding the future of our business, future plans and strategies, projections, anticipated events and trends, the economy and other future conditions, and hence they inherently involve significant risks, uncertainties and changes in circumstances that are difficult to predict and many of which are outside of our

control. Therefore, you should not rely on any of these forward-looking statements. 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, PMDA or other regulatory authorities may make adverse decisions regarding fostamatinib; 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 quarter ended September 30, 2021. Any forward-looking statement made by us in this press release is based only on information currently available to us and speaks only as of the date on which it is made. Rigel does not undertake any obligation to update forward-looking statements, whether written or oral, that may be made from time to time, whether as a result of new information, future developments or otherwise, 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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