January 11, 2021

# Rigel Pharmaceuticals Provides Business Update

## TAVALISSE® preliminary 2020 net product sales of approximately $61.7 million, a year-over-year increase of 41%

## U.S. FDA awards Fast Track designation to TAVALISSE® for warm autoimmune hemolytic anemia

## Topline data from NIH Phase 2 clinical trial in COVID-19 expected in April '21

SOUTH SAN FRANCISCO, Calif., Jan. 11, 2021 /PRNewswire/ -- Rigel Pharmaceuticals, Inc. (Nasdaq: RIGL) today provided a business update, including preliminary total revenue, TAVALISSE® (fostamatinib disodium hexahydrate) bottles sold for the quarter, Fast Track designation granted for warm autoimmune hemolytic anemia (wAIHA), and the company's expanding COVID-19 program. The company's president and CEO, Raul Rodriguez, will provide a more detailed company overview during his presentation taking place on Thursday, January 14, 2020 at 10:00 am ET at the 39th Annual J.P. Morgan Virtual Healthcare Conference.

"Rigel's accomplishments during the extraordinary global events of 2020 position the company well as we enter the new year," said Raul Rodriguez, Rigel's president and CEO. "Annual sales of TAVALISSE grew by 41% compared to 2019, and its use as an earlier line treatment option for ITP is resonating with both patients and physicians. We are continuing to enroll our Phase 3 trial in wAIHA and we have received Fast Track designation from the FDA which is intended to expedite the review of a potential regulatory filing.

"The availability of vaccines is a critical step in managing the COVID-19 pandemic, but we expect there will continue to be a significant need for therapeutics. Our Phase 3 trial in COVID-19 has launched and topline data from the National Institutes of Health Phase 2 trial is expected in April, which will provide a near-term look at the potential of fostamatinib in this disease."

**Commercial and Preliminary Financial Update**

In the fourth quarter of 2020, a total of 1,899 bottles of TAVALISSE were sold in the U.S., of

which 1,725 were shipped directly to patients and clinics. While Rigel is still in the process of determining final results for the fourth quarter of 2020, the company expects to report net product sales of approximately $17.7 million, compared to $13.8 million in the same period of 2019, an increase of 28%.

Contract revenues from collaborations for the quarter ended December 31, 2020, are expected to be approximately $697,000, which consists of $500,000 from Grifols related to an option for commercialization in additional territories and $197,000 in revenues earned from the performance of certain research and development services from Rigel's collaboration agreement with Grifols.

For the fourth quarter 2020, Rigel expects to report total revenue of approximately $18.4 million.

The company expects to report cash, cash equivalents and short-term investments as of December 31, 2020 of approximately $57.3 million, compared to $98.0 million as of December 31, 2019.

The above information is preliminary, has not been audited and is subject to change upon completion of the audit of the company's financial statements as of and for the year ended December 31, 2020.

**Portfolio Update**

**Phase 3 Trial in wAIHA**

The U.S. Food and Drug Administration (FDA) has granted Fast Track designation to TAVALISSE for the treatment of wAIHA based on the significant medical need that exists and the product's potential in the treatment of these patients. Fast Track designation is designed to enable an expedited review process for any potential regulatory filings. Currently, the study has enrolled 64 of 90, or 71%, of the patients planned for enrollment.

**COVID-19 Program**

The Phase 2 clinical trial sponsored by NIH/NHLBI, in collaboration with Inova Health System, to evaluate the safety of fostamatinib for the treatment of COVID-19 has enrolled 44 of the 60 patients planned for enrollment. In this trial, patients are being randomized to fostamatinib plus standard of care (SOC) or matched placebo plus SOC (1:1), administered orally twice daily for 14 days. There will be a follow-up period to day 60. The primary endpoint of this study is cumulative incidence of serious adverse events (SAE) through day 29, with multiple secondary endpoints designed to assess the early efficacy and clinically relevant endpoints of disease course as well as in vitro biological correlatives evaluating the effects of the drug on pathways involved in the pathophysiology of COVID-19, including NETosis. Rigel anticipates topline data to be reported in April of this year.

In addition, Rigel has launched its Phase 3 clinical trial to evaluate the safety and efficacy of fostamatinib in hospitalized COVID-19 patients without respiratory failure that have certain high-risk prognostic factors. The multi-center, double-blind, placebo-controlled, adaptive design study is expected to enroll over 300 evaluable patients that will be randomly assigned to either fostamatinib plus SOC or matched placebo plus SOC (1:1). Treatment will be administered orally twice daily for 14 days with a follow-up period to day 60. The primary endpoint of this study is the proportion of subjects who progress to severe/critical disease within 29 days.

In December, the Journal of Infectious Diseases (JID) published research from NIH which demonstrated that R406, the active metabolite of fostamatinib, was able to inhibit NETosis ex vivo in donor plasma from patients with COVID-19. NETosis is a unique type of cell death resulting in the release of neutrophil extracellular traps (NETs). NETs contribute to thromboinflammation and have been associated with mortality in COVID-19. These data provide insights for how fostamatinib may mitigate neutrophil-associated mechanisms contributing to COVID-19 immunopathogenesis.[1]

**Clinical Development Pipeline**
Rigel's IRAK1/4 program includes R835, an orally available, potent and selective inhibitor and the only molecule in clinical development that inhibits both IRAK1 and IRAK4. The company plans to pursue this program's potential in hematology/oncology and rare diseases, where it believes there are areas of significant unmet medical need.

Rigel has an extensive RIPK1 inhibitor program. This program includes R552, an oral systemic RIPK1 inhibitor which has completed a Phase 1 study, as well as RIPK1 inhibitor candidates that cross the blood-brain barrier (CNS-penetrants). RIPK1 inhibitors have broad potential in numerous large indications. In order to fully develop these assets, Rigel intends to enter into a collaboration for this program.

**39th Annual J.P. Morgan Webcast Presentation Details**
Rigel's presentation will be webcast and is scheduled to take place Thursday, January 14 at 10:00 am ET. To access the live and subsequently archived webcast, go to the Investor Relations section of the company's website at www.rigel.com. Please connect to the website several minutes prior to the start of the live webcast to ensure adequate time for any software download that may be necessary.

**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 include fatigue, 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. In addition to fostamatinib, current therapies for ITP include 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 AIHA**
Autoimmune hemolytic anemia (AIHA) is a rare, serious blood disorder in which the immune system produces antibodies that recognize and mediate 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 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 inflammatory cytokine release by monocytes and macrophages, production of neutrophil extracellular traps (NETs) by neutrophils, and platelet aggregation.[4,5,6] Furthermore, SYK inhibition in neutrophils and platelets may lead to decreased thromboinflammation, 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 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).**

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**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 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) and Canada (TAVALISSE) for the treatment of chronic immune thrombocytopenia in adult patients.

Fostamatinib[7] is currently being studied in a Phase 3 trial for the treatment of warm autoimmune hemolytic anemia (wAIHA); an 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, Rigel launched a Phase 3 clinical trial of fostamatinib for the treatment of hospitalized COVID-19 patients.

Rigel's other clinical programs include an ongoing Phase 1 study of R835[7], a proprietary

molecule from its interleukin receptor-associated kinase (IRAK) inhibitor program, and a recently completed Phase 1 study of R552[7], a proprietary molecule from its receptor-interacting serine/threonine-protein kinase (RIPK) inhibitor program. In addition, Rigel has product candidates in clinical development with partners AstraZeneca, BerGenBio ASA, and Daiichi Sankyo.

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2. Berlin DA, Gulick RM, Martinez FJ. Severe Covid-19. N Engl J Med 2020
3. Becker RC. COVID-19 Update: COVID-19 associated coagulopathy. Journal of Thrombosis and Thrombolysis May 15, 2020. DOI: https://doi.org/10.1007/s11239-020-02134-3
4. Hoepel W. et al. Anti-SARS-CoV-2 IgG from severely ill COVID-19 patients promotes macrophage hyper-inflammatory responses. bioRxiv July 13, 2020. DOI: https://doi.org/10.1101/2020.07.13.190140
5. Sung P-S and Hsieh S-L (2019) CLEC2 and CLEC5A: Pathogenic Host Factors in Acute Viral Infections. Front. Immunol. 10:2867. DOI: https://doi.org/10.3389/fimmu.2019.02867
6. Behnen M. Immobilized Immune Complexes Induce Neutrophil Extracellular Trap Release by Human Neutrophil Granulocytes via Fcγ RIIIB and Mac-1. The Journal of Immunology July 2014. DOI: https://doi.org/10.4049/jimmunol.1400478
7. *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 commercial success of TAVALISSE in the U.S.; Rigel's ability to achieve development and commercial milestones; Rigel's expected operating results for the quarter ending and as of December 31, 2020, including net sales and cash, cash equivalents and short-term investments; expectations related to the market opportunity for fostamatinib as a COVID-19 therapeutic; Rigel's ability to enter into a collaboration for its RIPK1 inhibitor program; and the safety, tolerability, design, timing and results of Rigel's products, product candidates and clinical trials. 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," intends," "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 Rigel may not be able to enter into a definitive agreement regarding its RIPK1 program on terms favorable or acceptable to Rigel, or at all; 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, 2019 and Quarterly Report on Form 10-Q for

the quarter ended September 30, 2020. In addition, the COVID-19 pandemic may result in further delays in Rigel's studies, trials and sales, or impact Rigel's ability to obtain supply of TAVALISSE. 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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