October 11, 2023

Rigel Announces Presentation at the Upcoming IDWeek 2023

-- Provides Update on ACTIV-4 Host Tissue Trial --

SOUTH SAN FRANCISCO, Calif., Oct. 11, 2023 /PRNewswire/ -- Rigel Pharmaceuticals, Inc. (Nasdaq: RIGL) today announced an upcoming oral presentation highlighting data from the FOCUS Phase 3 clinical trial of fostamatinib in hospitalized COVID-19 patients without respiratory failure who have certain high-risk prognostic factors at IDWeek 2023 being held October 11-15, 2023, in Boston, MA and provided an update on the ACTIV-4 Host Tissue trial of fostamatinib in hospitalized patients with COVID-19.

"From the outset of the COVID-19 pandemic, we were hopeful of making an impact. However, our focus remains on our hematology-oncology commercial and clinical portfolio," said Raul Rodriguez, Rigel's president and CEO. "As we have previously reported, we do not plan to submit an Emergency Use Authorization or a supplemental New Drug Application given the end of the federal COVID-19 Public Health Emergency in May 2023, and based on feedback from the FDA, US Department of Defense and other advisors regarding the program's regulatory requirements, costs, timeline and potential for success."

Details of the oral presentation at IDWeek 2023 are as follows:

Abstract #: 88
Title: Fostamatinib for the Treatment of Hospitalized Patients With COVID-19 Who Required Oxygen Supplementation: Results of a Phase 3 Trial
Presenter: Dr. Deepa Gotur, MD, FCCP, FCCM, Associate Professor Clinical Medicine, Weill Cornell Medical College and Houston Methodist Hospital, Houston, TX
Session Name: Clinical Trials
Date: Thursday, October 12, 2023
Presentation Time: 11:15 – 11:30AM ET
Location: 102 AB, Boston Convention and Exhibition Center

- This presentation reports severe COVID-19 is linked to hyperactivation of the host immune response involving signaling through multiple spleen tyrosine kinase (SYK) pathways. Fostamatinib is an orally administered potent and selective inhibitor of SYK that has been approved in the US, Canada, Japan, and Europe for the treatment of chronic immune thrombocytopenia (ITP).
- The FOCUS Phase 3 clinical trial was a double-blind, randomized, placebo-controlled

trial of fostamatinib in adults hospitalized for COVID-19 who required oxygen supplementation (NCT04629703). Patients were randomly assigned 1:1 to receive fostamatinib (150 mg BID administered orally) or placebo for 14 days. All patients additionally received standard of care at their hospital. The primary endpoint was days on oxygen (days 1-29).

- A total of 280 patients underwent randomization (with 141 assigned to fostamatinib and 139 to placebo). The primary endpoint was met; those who received fostamatinib had lower mean days on oxygen than those who received placebo (4.8 vs. 7.6 days, p=*0.0136*).
- Fostamatinib showed significance or trend towards significance in all secondary endpoints of reducing mortality and morbidity compared to placebo. The mean change in the 8-point ordinal score from baseline to the average of Day 5 to 15 was significantly improved in patients who received fostamatinib vs. placebo (p=*0.0092*). Furthermore, 6 patients were enrolled with baseline ordinal score of 6 (3 in each group). All patients in the fostamatinib group survived, and all in the placebo group died by Day 30. A significantly higher proportion of patients who received fostamatinib were discharged from the hospital by Day 15 compared to placebo (p=*0.0029*). Significantly more patients were alive and oxygen-free by Day 29 and Day 60 with fostamatinib treatment in comparison to placebo (p=*0.0213* and p=*0.0271,* respectively). Treatment-emergent adverse events were consistent with previous studies and were similar between the 2 groups.
- The addition of fostamatinib to standard of care treatment resulted in significantly fewer days on oxygen, an improved 8-point ordinal scale score, and significantly more patients alive and oxygen-free by Day 60 compared to placebo in patients with COVID-19 requiring hospitalization and supplemental oxygen.

ACTIV-4 Host Tissue (NECTAR) Trial Update

On September 26, 2023, the Data and Safety Monitoring Board (DSMB) recommended that the fostamatinib study arm of the ACTIV-4 Host Tissue (NECTAR) platform cease enrollment. Based on their review of a conditional power analysis, the DSMB determined that there was an extremely low likelihood of fostamatinib providing benefits related to the primary outcome (Oxygen Free Days) or other secondary outcomes in patients hospitalized and on oxygen therapy for COVID-19. No safety concerns were identified.

The National Heart, Lung, and Blood Institute (NHLBI), part of the National Institutes of Health, concurs with the DSMB's recommendations and has asked the trial investigators to cease enrollment, complete follow-up for participants already enrolled, and complete study closeout. The full study data will be analyzed and disseminated as previously planned.

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.[1] 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.[2]

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.[3,4,5,6] Furthermore, SYK inhibition in neutrophils and platelets may lead to decreased thrombo-inflammation, alleviating organ dysfunction in critically ill patients with COVID-19.

About Rigel
Rigel Pharmaceuticals, Inc. (Nasdaq: RIGL) is a biotechnology company dedicated to discovering, developing and providing novel therapies that significantly improve the lives of patients with hematologic disorders and cancer. Founded in 1996, Rigel is based in South San Francisco, California. For more information on Rigel, the Company's marketed products and pipeline of potential products, visit www.rigel.com.

1. Berlin DA, Gulick RM, and Martinez FJ. *Severe Covid-19*. N Engl J Med 2020. DOI: https://doi.org/10.1056/NEJMcp2009575
2. 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
3. Hoepel W et al. *High titers and low fucosylation of early human anti–SARS-CoV-2 IgG promote inflammation by alveolar macrophages*. Science Translational Medicine 02 Jun 2021. DOI: https://www.doi.org/10.1126/scitranslmed.abf8654
4. Sung P-S and Hsieh S-L. *CLEC2 and CLEC5A: Pathogenic Host Factors in Acute Viral Infections*. Frontiers in Immunology December 6, 2019. DOI: https://doi.org/10.3389/fimmu.2019.02867
5. Bye AP et al. *Aberrant glycosylation of anti-SARS-CoV-2 IgG is a pro-thrombotic stimulus for platelets*. BioRxiv March 26, 2021. DOI: https://doi.org/10.1101/2021.03.26.437014
6. Strich J et al. *Fostamatinib Inhibits Neutrophils Extracellular Traps Induced by COVID-19 Patient Plasma: A Potential Therapeutic*. Journal of Infectious Disease March 15, 2021. DOI: https://doi.org/10.1093/infdis/jiaa789

Forward-Looking Statements
This release contains forward-looking statements relating to, among other things, our expectations related to the role of fostamatinib in the treatment of patients with COVID-19 and in future pandemics, including next steps in collaboration with Rigel's partner, the U.S. Department of Defense, and the timing and results of the ACTIV-4 study. 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. 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 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 June 30, 2023, and subsequent filings. 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 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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