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# Rigel Announces Top-line Results from FOCUS Phase 3 Clinical Trial of Fostamatinib in High Risk Hospitalized COVID-19 Patients

SOUTH SAN FRANCISCO, Calif., Nov. 1, 2022 /PRNewswire/ -- Rigel Pharmaceuticals, Inc. (Nasdaq: RIGL), today announced top-line efficacy and safety results from the FOCUS Phase 3 clinical trial of fostamatinib in hospitalized COVID-19 patients without respiratory failure who have certain high-risk prognostic factors. The trial approached but did not meet statistical significance (p=0.0603) in the primary efficacy endpoint of the number of days on oxygen through Day 29. All prespecified secondary endpoints in the study numerically favored fostamatinib over placebo, including mortality, time to sustained recovery, change in ordinal scale assessment, and number of days in the ICU.

"While the COVID-19 pandemic has abated, we believe that fostamatinib may have an important role in the treatment of patients with COVID-19 based upon these top-line data. We are encouraged by the results of our Phase 3 clinical trial in that regard. We are evaluating the opportunity and next steps in collaboration with our partner, the U.S. Department of Defense," said Raul Rodriguez, president and chief executive officer of Rigel. "I would also like to express my appreciation to the Rigel team, our partners, clinicians and especially the patients for their participation in this study."

This multi-center, double-blind, placebo-controlled Phase 3 study, supported by the U.S. Department of Defense, enrolled 280 patients that were randomly assigned to either fostamatinib plus standard of care (SOC) (N=141) or matched placebo plus SOC (N=139). Treatment was administered orally twice daily for 14 days with a follow-up period to Day 60. The primary endpoint of this study was the number of days patients spent on supplemental oxygen through Day 29. Secondary endpoints were designed to assess mortality risk, patient improvement from severe disease, duration of hospitalization, and number of days in the ICU, as well as safety. There were no meaningful imbalances between treatment groups at baseline.

Key findings from the Phase 3 clinical data readout include:

- The mean number of days on oxygen through Day 29 in the fostamatinib treatment arm was 6.9 days compared to 9.0 days in the placebo arm (p=0.0603).

- By Day 29, in the overall population, there were 4 deaths in the fostamatinib group compared to 8 in the placebo group. Fostamatinib numerically reduced patient all-cause mortality by 50% (p=0.4521).
- The mean change from baseline in clinical status score to Day 15 using the 8-point ordinal scale was -2.4 for fostamatinib and -1.9 for placebo (p=0.0428).
- The median number of days to first sustained hospital discharge by Day 29 was 6 days for fostamatinib and 7 days for placebo (p=0.2371)
- The proportion of patients alive and oxygen free on Day 29 was 85.1% for fostamatinib and 73.4% for placebo (p=0.0653).
- The number of days in the ICU was 2.2 for fostamatinib and 3.3 for placebo (p=0.1883).
- The safety profile for fostamatinib was consistent with prior clinical experience and no new safety issues were discovered. The safety profile between fostamatinib and placebo was generally comparable.

The Other Transaction Authority (OTA) agreement for this study was executed by the Defense Department's Joint Program Executive Office for Chemical, Biological, Radiological and Nuclear Defense (JPEO-CBRND), in collaboration with the U.S. Army Contracting Command – Aberdeen Proving Ground, using Coronavirus Aid, Relief, and Economic Security (CARES) Act funding.

Fostamatinib is also being evaluated in an ongoing study of patients who are experiencing more severe COVID-19-related complications. The Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV-4) study, initiated and funded by the National Heart Lung and Blood Institute (NHLBI), part of the National Institutes of Health, is a multi-site, randomized, placebo-controlled trial targeting the host response to COVID-19 in more severe hospitalized patients. Each active arm will include approximately 300 patients. Eligible participants will include patients hospitalized for COVID-19 with laboratory-confirmed SARS-CoV-2 infection on oxygen therapy. The primary outcome is oxygen-free days through day 28. Secondary outcomes include hospital mortality, use of mechanical ventilation, and World Health Organization scale scores. More details on the study can be found on clinicaltrials.gov: NCT04924660.

**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 small molecule drugs that significantly improve the lives of patients with hematologic disorders, cancer, and rare immune diseases. Founded in 1996, Rigel is based in South San Francisco, California. For more information on Rigel, the Company's marketed product and pipeline of potential products, visit www.rigel.com.


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**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 the opportunity and next steps in collaboration with Rigel's partner, the U.S. Department of Defense and the timing, enrollment 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, 2022, 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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