October 9, 2020

Rigel Announces First Patients Enrolled in NIH/NHLBI-Sponsored Trial of Fostamatinib in Hospitalized COVID-19 Patients in Collaboration with Inova

Trial being conducted at NIH Clinical Center in Bethesda, Maryland and Inova Fairfax Hospital in Virginia

SOUTH SAN FRANCISCO, Calif., Oct. 9, 2020 /PRNewswire/ -- Rigel Pharmaceuticals, Inc. (Nasdaq: RIGL) today announced enrollment of the first patients in a multicenter, Phase 2 trial to evaluate the safety of fostamatinib, Rigel's oral spleen tyrosine kinase (SYK) inhibitor, for the treatment of hospitalized COVID-19 patients. The study is sponsored by the National Heart, Lung, and Blood Institute (NHLBI), part of the National Institutes of Health (NIH), in collaboration with Inova® Health System. Fostamatinib, marketed in the U.S. as TAVALISSE® (fostamatinib disodium hexahydrate) tablets, is approved in the U.S. and Europe as a treatment for adult chronic immune thrombocytopenia (ITP).

"As mortality continues to rise, it is evident that new therapeutics selectively targeting immune response are desperately needed to treat patients infected with SARS-CoV-2," stated Dr. Richard Childs, M.D., clinical director of the NHLBI. "This is a rigorously-designed clinical trial, which should provide insight into the potential safety and efficacy of fostamatinib in the treatment of severely ill patients suffering from COVID-19."

The clinical trial is being conducted at the NIH Clinical Center in Bethesda, Maryland, the nation's largest hospital devoted entirely to clinical research, and Inova Fairfax Hospital.

"We are very excited to be a part of this clinical trial with the NIH/NHLBI and Rigel. This study fits seamlessly within our portfolio of research options that we have within the Inova Health System to offer our COVID-19 population," said Dr. Steven Nathan M.D., medical director, Advanced Lung Disease & Lung Transplant Program, at Inova. "Research into novel compounds is a key component in finding therapeutic options for COVID-19 patients, and with the first patients enrolled, we are one step closer to understanding the potential of fostamatinib and SYK inhibition in this disease."

This is a randomized, double-blind, placebo-controlled trial to evaluate the safety of

fostamatinib for the treatment of hospitalized COVID-19 patients. The study will randomly assign fostamatinib or matched placebo (1:1) to approximately 60 evaluable patients who are a 5 to 7 on the 8-point ordinal scale (requiring supplemental oxygen via nasal canula or non-invasive ventilation, requiring mechanical ventilation or extracorporeal membrane oxygenation). Treatment will be administered orally twice daily for 14 days. There will be a follow-up period to day 60. The primary objective of this study is to evaluate the safety of fostamatinib compared to placebo for the treatment of hospitalized COVID-19 patients. The secondary objective will be to assess the early efficacy and clinically relevant measures of disease progression.

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 inflammatory cytokine release by monocytes and macrophages, production of neutrophil extracellular traps (NETs) by neutrophils, and platelet aggregation.[3,4,5] Furthermore, SYK inhibition in neutrophils and platelets may lead to decreased thromboinflammation, alleviating organ dysfunction in critically ill patients with COVID-19.

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 immune and hematologic disorders, cancer and rare 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 has been approved by the European Commission for the treatment of chronic immune thrombocytopenia in adult patients who are refractory to other treatments and is marketed in Europe under the name TAVLESSE® (fostamatinib).

Fostamatinib[6] is currently being studied in a Phase 3 trial for the treatment of warm autoimmune hemolytic anemia (AIHA); a 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 pneumonia being conducted by Imperial College London.

Rigel's other clinical programs include a completed Phase 1 study of R835[6], a proprietary molecule from its interleukin receptor associated kinase (IRAK) inhibitor program, and an ongoing Phase 1 study of R552[6], a proprietary molecule from its receptor-interacting protein

kinase (RIP) inhibitor program. In addition, Rigel has product candidates in clinical development with partners AstraZeneca, BerGenBio ASA, and Daiichi Sankyo.

Please see www.TAVALISSE.com for the full Prescribing Information.

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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. 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
4. 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
5. 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
6. *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, Rigel's plans to support the NIH Phase 2 trial, the trial design, the potential clinical benefit of fostamatinib for the treatment of hospitalized COVID-19 patients and the role of SYK inhibition in potentially improving outcomes of critically ill COVID-19 patients, including by alleviating thromboinflammation. 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," "aim," "believe," "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 fostamatinib in the U.S. and Europe; risks that the FDA, European Medicines Agency (EMA) or other regulatory authorities may make adverse decisions regarding fostamatinib or any of Rigel's product candidates; risks that clinical trials may not be predictive of real-world results or of results in subsequent clinical trials; the availability of resources to develop and, if approved, commercialize fostamatinib or any other of Rigel's product candidates; the progress of our and our collaborators' product development programs, including clinical testing, and the timing of results thereof; our expectations with respect to regulatory submissions and approvals; our research and development expenses; protection of our intellectual property, 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 June 30, 2020. In addition, the ongoing COVID-19 pandemic may result in further delays in Rigel's studies and trials, or impact Rigel's sales and ability to obtain supply of fostamatinib. 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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