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Rigel Announces Investigator-Sponsored Trial of Fostamatinib in Patients with COVID-19 Pneumonia

High content screen identifies fostamatinib as a candidate for repurposing for Acute Lung Injury

SOUTH SAN FRANCISCO, Calif., July 14, 2020 /PRNewswire/ -- Rigel Pharmaceuticals, Inc. (Nasdaq: RIGL) today announced the initiation of an investigator-sponsored trial (IST) being conducted by Imperial College London to evaluate the efficacy of fostamatinib, its oral spleen tyrosine kinase (SYK) inhibitor, for the treatment of COVID-19 pneumonia. 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).

SYK is a key mediator of immunoreceptor signaling in a host of inflammatory cells. Studies of severe acute respiratory syndrome (SARS) and other acute viral respiratory infections suggest that the pathogenesis relies on a series of SYK-dependent events involving activation of C-type lectin receptors (CLR) and immunoglobulin Fcg receptors (FcgR) in multiple cell types. Such SYK-mediated processes result in excessive cytokine and chemokine release, neutrophil activation associated with extensive NETosis (a highly inflammatory and thrombogenic type of cell death), and endothelial cell stimulation leading to vascular endothelium leakage and edema in the lungs. Together, these events can contribute to acute respiratory distress syndrome (ARDS), micro-thrombosis and associated systemic complications. [1,2]

The hallmark of severe COVID-19 is hypoxemia and a radiological pattern of acute lung injury (ALI) that shares features with ARDS. By inhibiting SYK, fostamatinib may specifically inhibit the infiltration and activation of monocytes and neutrophils in the lungs that are prominent in COVID-19.[1,2]

"The COVID-19 global pandemic continues to extract a significant human and economic toll and there remains a serious and immediate need for safe and effective therapies," said Raul Rodriguez, Rigel's president and CEO. "Severe COVID-19 pneumonia can lead to acute respiratory distress syndrome, or ARDS, which can often be fatal. Given encouraging data from pre-clinical models of fostamatinib, we believe there is potential for SYK inhibition to

help treat the severity of the disease for these patients and to prevent ARDS.

"We are pleased to be able to support the exciting work being done by our colleagues at Imperial College London. Their efforts will be valuable as we explore fostamatinib in COVID-19 and pursue our plans for a Rigel-led study."

The Imperial College London IST will be a two-stage open label, controlled clinical trial with patients randomized (1:1:1) to fostamatinib, ruxolitinib, or standard of care. Treatment will be administered twice daily for 14 days and patients will receive a follow-up assessment at day 14 and day 28 after the first dose. The primary objective will be to determine the efficacy of fostamatinib and the efficacy of ruxolitinib compared to standard of care to reduce the proportion of hospitalized patients progressing from mild or moderate to severe COVID-19 pneumonia. Rigel will provide support for this trial along with Novartis.

In addition, researchers at The Broad Institute of the Massachusetts Institute of Technology (MIT) and Harvard led a recent screen to identify FDA-approved compounds that reduce mucin-1 (MUC1) protein abundance. MUC1 is a biomarker used to predict the development of ALI and ARDS and correlates with poor clinical outcomes. Of the 3,713 compounds that were screened, fostamatinib was the only compound identified which both decreased expression of MUC1 and is FDA approved, and so allows for rapid repurposing for patients with COVID-19 lung injury. Fostamatinib demonstrated preferential depletion of MUC1 from epithelial cells without affecting cell viability. The research was focused on drug repurposing for the much lower risk of toxicity and the ability of FDA-approved treatments to be delivered on a shortened timescale, which is critical for patients afflicted with lung disease resulting from COVID-19.[3]

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).

Rigel's clinical programs include a Phase 3 study of fostamatinib in warm autoimmune hemolytic anemia (AIHA); a completed Phase 1 study of R835[4], a proprietary molecule from its interleukin receptor associated kinase (IRAK) inhibitor program; and an ongoing Phase 1 study of R552[4], a proprietary molecule from its receptor-interacting protein kinase (RIP) inhibitor program. In addition, Rigel has product candidates in clinical development with partners Aclaris Therapeutics, AstraZeneca, BerGenBio ASA, and Daiichi Sankyo.

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

[1]*Braselmann S. et al. R406, an orally available spleen tyrosine kinase inhibitor blocks fc receptor signaling and reduces immune complex-mediated inflammation. J Pharmacol Exp*

Ther. 2006 Dec;319(3):998-1008. Epub 2006 Aug 31

[2]*Fu Y. et al. Understanding SARS-CoV-2-Mediated Inflammatory Responses: From Mechanisms to Potential Therapeutic Tools. Virologica Sinica. March 3, 2020*

[3]Alimova M. et al. A High Content Screen for Mucin-1-Reducing Compounds Identifies Fostamatinib as a Candidate for Rapid Repurposing for Acute Lung Injury during the COVID-19 pandemic. bioRxiv June 30, 2020. doi: https://doi.org/10.1101/2020.06.30.180380.

[4]*This product candidate is investigational and has not been established safe or effective by the U.S. Food and Drug Administration (FDA) or any regulatory authority.*

Forward Looking Statements

This release contains forward-looking statements relating to, among other things, Rigel's plans to support Imperial College London's IST, the potential clinical benefit of fostamatinib in COVID-19 patients and the prevention of ARDS; and Rigel's plans to pursue exploration of fostamatinib in COVID-19 patients and a Rigel led 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," "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 TAVALISSE in the U.S. and TAVLESSE in 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 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 its Quarterly Report on Form 10-Q for the quarter ended March 31, 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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