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Positive Topline Data Shows Fostamatinib Meets Primary Endpoint of Safety in Phase 2 Clinical Trial in Hospitalized Patients with COVID-19

Broad and consistent improvement in clinical outcomes including serious adverse events, mortality, ordinal scale assessment and number of days in the ICU

Rigel plans to share these results with health authorities, including the US FDA

Conference call and webcast today at 8:00 am ET/5:00 am PT

SOUTH SAN FRANCISCO, Calif., April 13, 2021 /PRNewswire/ -- Rigel Pharmaceuticals, Inc. (Nasdaq: RIGL), today announced positive topline results from a multi-center, Phase 2 clinical trial to evaluate the safety of fostamatinib, its oral spleen tyrosine kinase (SYK) inhibitor, for the treatment of hospitalized patients with COVID-19.

The trial, being conducted in collaboration with the National Heart, Lung, and Blood Institute (NHLBI), part of the National Institutes of Health (NIH), and Inova Health System, met its primary endpoint of safety. Fostamatinib reduced the incidence of Serious Adverse Events (SAEs) by half. By day 29, there were three SAEs in the fostamatinib plus standard of care (SOC) group of thirty patients compared to six SAEs in the placebo plus SOC group of twenty-nine patients (p=0.23). Of these, there was a reduction for the disease related SAE of hypoxia in the fostamatinib group compared to placebo (1 vs 3, respectively; p=0.29).

"Despite the growing arsenal of vaccines gaining emergency use authorization, COVID-19 continues to spread and patients remain in need of effective therapies. We are extremely pleased with the outcome of this trial, which provides early indications of the potential positive impact of fostamatinib for patients with COVID-19," said Raul Rodriguez, president and CEO of Rigel. "These results are an important addition to the extensive accumulation of data evaluating fostamatinib in COVID-19, which also include the ongoing Phase 2 study with Imperial College London and our own Phase 3 clinical trial being conducted in the U.S.

and Latin America."

"Fostamatinib was shown to be well tolerated in hospitalized patients with COVID-19 on oxygen. Taken altogether, the results of this trial suggest fostamatinib may be a useful addition to improve the outcome of severe and critically ill COVID-19 patients who are at the highest risk of death despite treatment with the best conventional therapies under the current standard of care (including remdesivir and steroids)," said Wolfgang Dummer, M.D., Ph.D., Rigel's Chief Medical Officer. "Consistent with the observed clinical outcomes, we are encouraged to see that in patients receiving fostamatinib there was a more rapid decline in a number of inflammatory biomarkers, that have previously been shown to be associated with the course of COVID-19 disease, compared to those receiving placebo."

Key findings from the Phase 2 clinical data readout include:

- *At Day 29, in the overall population there were zero deaths in the fostamatinib group of thirty patients compared to three deaths in the placebo group of twenty-nine patients (p=0.07). In more severe patients, those with an ordinal scale assessment of 6 or 7, the difference was zero of nineteen patients compared to three of seventeen patients (p=0.049), respectively.*
- *There were four intubated patients in the trial on mechanical ventilation (ordinal scale 7) with two patients randomized to each treatment group. Both patients in the fostamatinib group improved within 7 days and came off the ventilator, while both patients in the placebo group deceased.*
- *Fostamatinib was superior to placebo in accelerating improvement in clinical status by day 15 (mean change -3.6 compared to -2.6, p=0.035) and by day 29 (mean change -4.2 compared to -3.3, p=0.12) using ordinal scale assessments.*
- *The median number of days in the ICU was reduced by 4 days, from 7 days in the placebo group to 3 days in the fostamatinib group (p=0.07).*
- *Despite general SOC use of both steroids and remdesivir in all 59 patients, there was a consistently greater reduction in NETosis and other inflammatory biomarkers (CRP, Ferritin, D-Dimer, Fibrinogen) in the fostamatinib group as compared to the placebo group.*

Investigators will conduct full and detailed analyses in the coming weeks.

Based on these data, Rigel plans to discuss the potential for emergency use authorization (EUA) with the U.S. Food and Drug Administration (FDA) of fostamatinib as a treatment for hospitalized patients with COVID-19. Fostamatinib, marketed in the U.S. as TAVALISSE® (fostamatinib disodium hexahydrate) tablets, is approved in the U.S., Europe, and Canada as a treatment for adult chronic immune thrombocytopenia (ITP).

Phase 2 Clinical Trial Design

This is a double-blind, placebo-controlled Phase 2 clinical trial sponsored by the NHLBI, part of the NIH, in collaboration with Inova Health System. Fifty-nine hospitalized patients with COVID-19 who were 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) were randomly assigned to one of two cohorts: fostamatinib plus SOC or matched placebo plus SOC (1:1). Treatment was administered orally twice daily for 14 days, with a follow-up period through day 60. Notably, all patients received dexamethasone as well as remdesivir.

For more information on Rigel's comprehensive clinical program in COVID-19, go to: https://www.rigel.com/pipeline/proprietary-programs/covid-19

Conference Call and Webcast with Slides Today at 8:00 am Eastern Time

Rigel will hold a live conference call and webcast today to discuss the Phase 2 trial results at 8:00 am Eastern Time (5:00 am Pacific Time).

Participants can access the live conference call by dialing (877) 407-3088 (domestic) or (201) 389-0927 (international). The conference call and accompanying slides will also be webcast live and can be accessed from the Investor Relations section of the company's website at www.rigel.com. The webcast will be archived and available for replay after the call via the Rigel website.

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 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 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 is currently being studied in a Phase 3 trial for the treatment of warm autoimmune hemolytic anemia (wAIHA)[6]; an NIH/NHLBI-sponsored Phase 2 trial for the treatment of hospitalized COVID-19[6] 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 has launched a Phase 3 clinical trial of fostamatinib for the treatment of hospitalized COVID-19 patients.

Rigel's other clinical programs include its interleukin receptor-associated kinase (IRAK) inhibitor program, and a receptor-interacting serine/threonine-protein kinase (RIP1) inhibitor program in clinical development with partner Eli Lilly and Company. In addition, Rigel has product candidates in development with partners AstraZeneca, BerGenBio ASA, and Daiichi Sankyo.

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

1. Berlin DA, Gulick RM, Martinez FJ. Severe Covid-19. N Engl J Med 2020
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, the ability to improve the outcome of all COVID-19 patients by the use of fostamatinib; the continuing need for effective therapies for COVID-19 patients; Rigel's plans for the further investigation of fostamatinib in COVID-19 patients; as well as Rigel's plans to seek emergency use authorization for fostamatinib for the treatment of COVID-19. 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. 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 that the FDA, EMA or other regulatory authorities may make adverse decisions regarding fostamatinib; risks that clinical trials may not be predictive of real-world results or of results in subsequent clinical trials; risks that fostamatinib 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, 2020 and subsequent filings. 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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