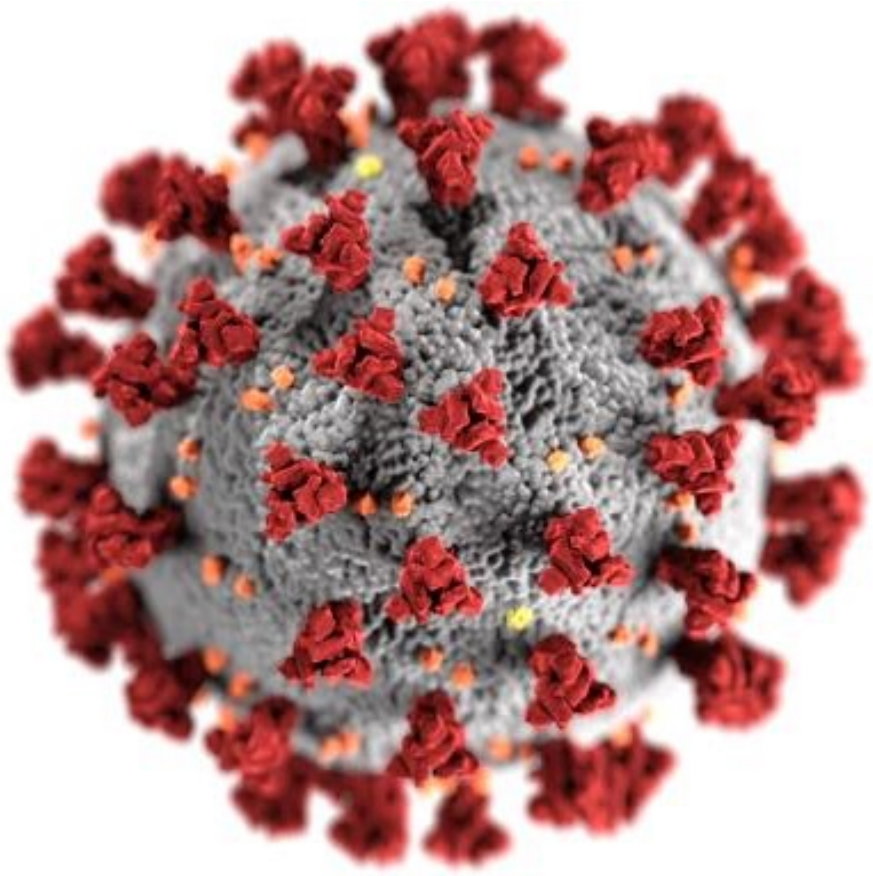
Administration of TAVALISSE® (fostamatinib disodium hexahydrate) in Treatment of Hospitalized Patients With COVID-19

September 14, 2021

ICD-10 Coordination & Maintenance Committee Meeting

rigel

Emergency Use Authorization (EUA) Under Review for TAVALISSE in Hospitalized Patients With COVID-19



COVID-19 is caused by Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2), which primarily infects the upper and lower respiratory tract and can lead to acute respiratory distress syndrome (ARDS) and other organ dysfunction[1]

The unique mechanism of action (SYK inhibition) of fostamatinib has therapeutic potential in COVID-19[2] and is supported by sound scientific rationale and external research[3]

The request for TAVALISSE EUA is currently under review by FDA, supported by the NIH/NHLBI, in collaboration with Inova, sponsored Phase 2 clinical trial

Other studies ongoing:

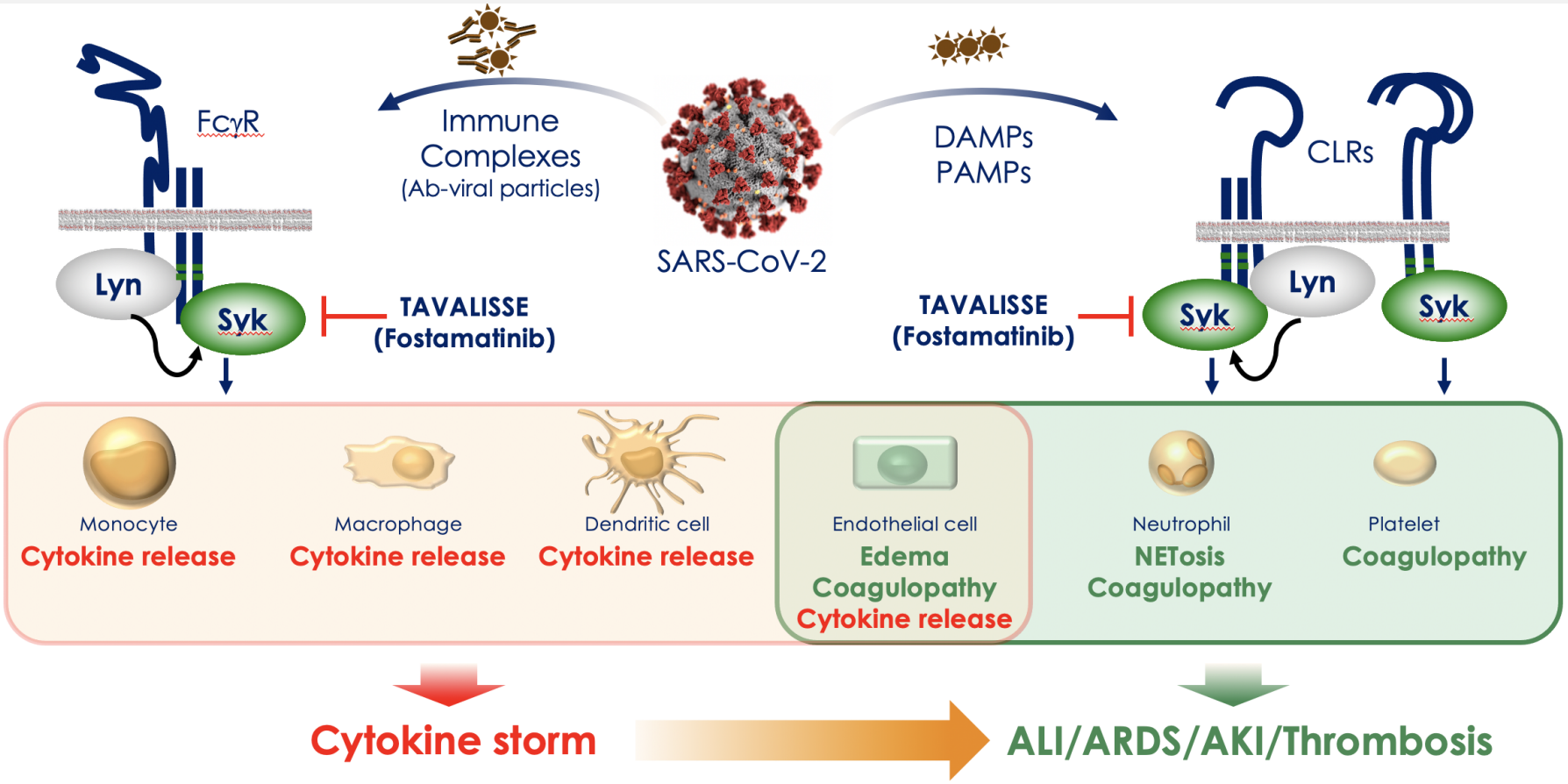
- Imperial College London sponsored Phase 2 clinical trial
- Rigel-led Phase 3 clinical trial

Need for therapeutics expected to persist even with vaccines

[1]Berlin, D.A., et al. Severe Cofid 19. N Engl J Med. 2020. [2]Investigational compound in this indication, under review by FDA for EUA. [3]Rigel internal data.

Sound Scientific Rationale to Explore SYK-Inhibition

SYK known to mediate aspects of COVID-19[1] pathogenesis[2,3]



[1]Investigational compound in this indication and has not been submitted for FDA review [2]Fu Y. et al. Understanding SARS CoV 2 Mediated Inflammatory Responses: From Mechanisms to Potential Therapeutic Tools. Virologica Sinica. March 3, 2020 [3]Nadeem A. et al. Inhibition of spleen tyrosine kinase signaling protects against acute lung injury through blockade of NADPH oxidase and IL 17A in neutrophils and γδ T cells respectively in mice. International Immunopharmacology 68 (2019) 39 47.

NIH Research in COVID-19 Plasma Patients[1]

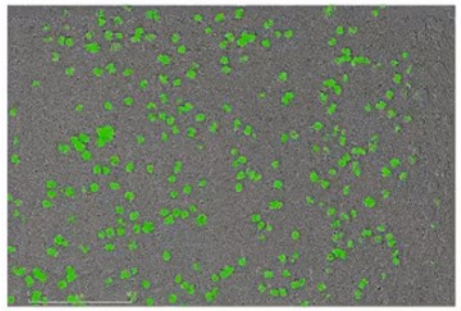
Fostamatinib shown to inhibit NETosis, a unique form of cell death that is associated with mortality in COVID-19; differentiates fostamatinib from other immunomodulators in COVID Trials

Fostamatinib Inhibits Neutrophils Extracellular Traps Induced by COVID-19 Patient Plasma: A Potential Therapeutic

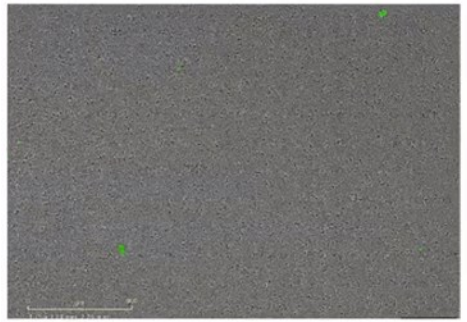
Strich, et al., Journal of Infectious Disease, 2020

NIH National Institutes of Health

Neutrophils Extracellular Traps (NETs) released by NETosis after 6 hours (identified by green fluorescence)



+ Plasma from COVID-19 positive patient



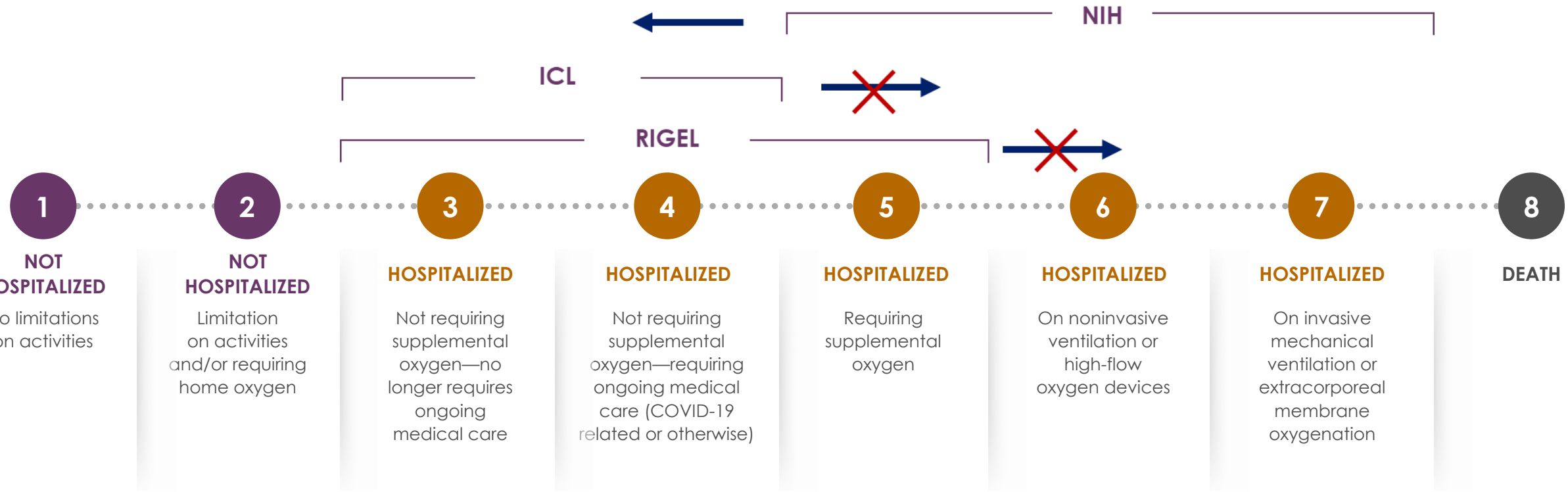
Fostamatinib (R406) + Plasma from COVID-19 positive patient

[1]Strich, J. et al. Fostamatinib Inhibits Neutrophils Extracellular Traps Induced by COVID 19 Patient Plasma: A potential Therapeutic. Journal of Infectious Disease December 24, 2020.

rigel

COVID-19 Trials Address Broad Patient Population

8-POINT ORDINAL SCALE[1]



[1]World Health Organization (WHO) R&D Blueprint: Novel Coronavirus. COVID 19 Therapeutic Trial Synopsis. February 18, 2020.

There Is No ICD-10-PCS Procedure Code To Identify Administration of TAVALISSE In the Inpatient Setting

Dosing of TAVALISSE (fostamatinib disodium hexahydrate) for hospitalized COVID-19 patients:

- Twice daily oral dose of 150 mg for 14 days
- Study protocol allowed dose reduction to 100 mg, if necessary, because of adverse events

Administration of TAVALISSE will be documented in the patient's medication record

Fostamatinib will be available to hospitals immediately upon EUA approval as it has received full FDA approval and is commercially available under the brand name, TAVALISSE, for a non-COVID, chronic, outpatient indication: treatment of thrombocytopenia in adult patients with chronic immune thrombocytopenia (ITP) who have had an insufficient response to a previous treatment.

Current commercially available stock keeping units (SKUs) are:

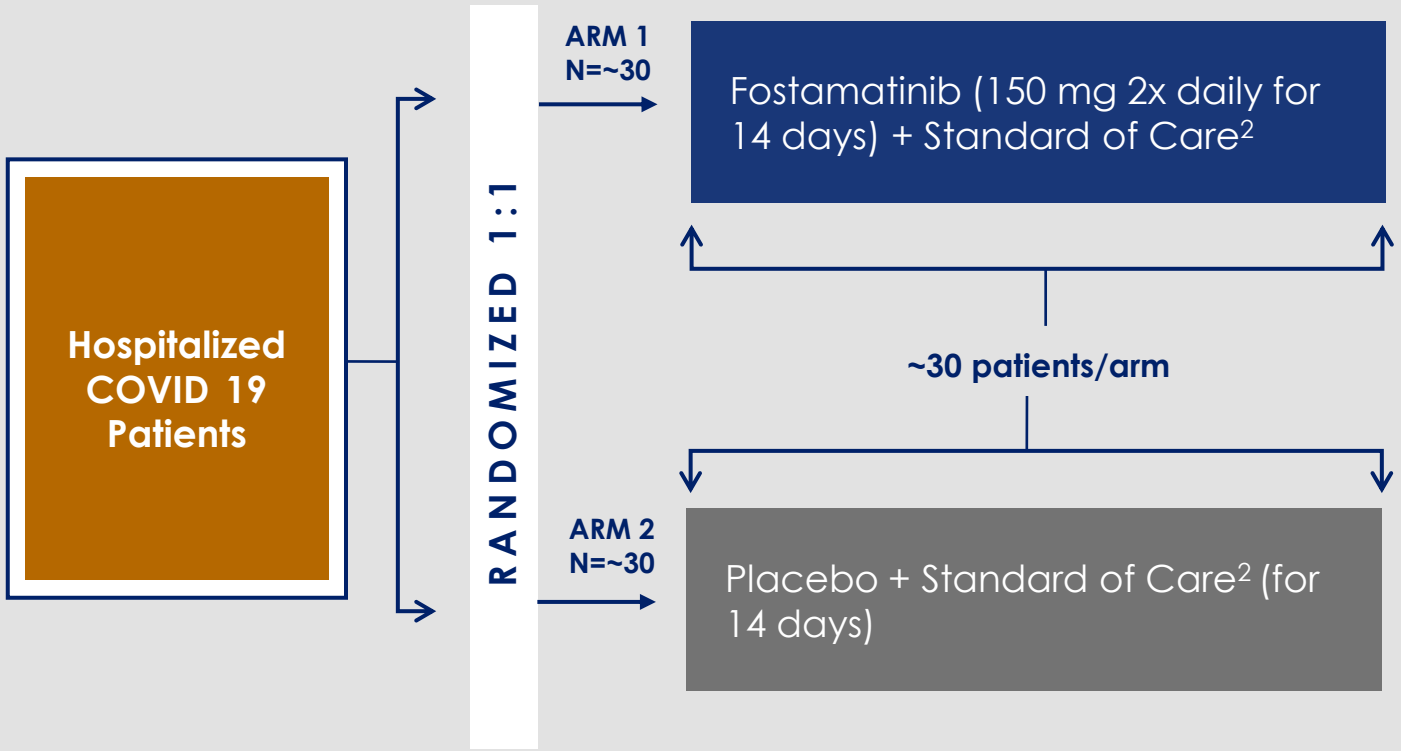
- NDC 71332-001-01, 100 mg tablets: Available in bottle of 60 with 2 desiccant canisters
- NDC 71332-002-01,150 mg tablets: Available in bottle of 60 with 2 desiccant canisters

Rigel is also working on the manufacturer of SKUs specific to use of TAVALISSE under EUA:

- NDC 71332-001-05, 100 mg tablets: Available in bottle of 30 with 2 desiccant canisters
- NDC 71332-002-05, 150 mg tablets: Available in bottle of 30 with 2 desiccant canisters

Fostamatinib Phase 2 Clinical Trial Design[1]

Currently marketed as TAVALISSE (fostamatinib disodium hexahydrate)



Primary Endpoints:

- Cumulative incidence of serious adverse events (SAE) through day 29

Secondary Endpoints:

- Multiple secondary measures designed to assess the early efficacy and clinically relevant endpoints of disease course

[1]Conducted at NIH Clinical Center and Inova Fairfax Hospital. [2]Standard of care includes any treatments currently in use to treat the underlying disease, or comorbidities associated with COVID 19 (eg, remdesivir).

Fostamatinib Phase 2 Baseline Characteristics Summary
Currently marketed as TAVALISSE (fostamatinib disodium hexahydrate)

- Baseline characteristics were generally well balanced between treatment groups
- There was representation from multiple race and ethnic groups balanced between treatment groups
- There was representation of all included severity grades on the ordinal scale – 5, 6 & 7
  - There were 2 patients in each dose group who entered the trial on mechanical ventilation (ordinal scale 7)
- All 59 subjects received both remdesivir and dexamethasone as background Standard of Care (SOC) medication; approximately 40% of subjects in both groups also received convalescent plasma

Key Findings from Fostamatinib Phase 2[1]
Currently marketed as TAVALISSE (fostamatinib disodium hexahydrate)

- The incidence of SAEs was approximately half in the fostamatinib + standard of care (SOC) group compared to the placebo + SOC group.
- There were no deaths in the fostamatinib group compared to 3 deaths in the placebo group (p=0.07). There was improvement in patients on mechanical ventilation.
- Multiple clinical endpoints consistently favor the fostamatinib group including
  - Ordinal scale improvement (day 15, p=0.035; day 29, p=0.12)
  - Number of days in the ICU (reduced by 4 days)
- Benefits were achieved on top of remdesivir and dexamethasone for every patient (and convalescent plasma for some).
- The clinical findings are consistent with improvements in inflammatory biomarkers including NETosis, CRP, Ferritin, D-Dimer and others.

[1]Conducted at NIH Clinical Center and Inova Fairfax Hospital. [2]Standard of care includes any treatments currently in use to treat the underlying disease, or comorbidities associated with COVID 19 (eg, remdesivir).

Overall Phase 2 Summary – Use of Fostamatinib in Treatment of Hospitalized Patients With COVID-19

Currently marketed as TAVALISSE (fostamatinib disodium hexahydrate)

- Fostamatinib met the primary endpoint and was shown to be well tolerated
- Key safety, mortality and efficacy endpoints favored the fostamatinib group compared to placebo, with the greatest benefit in the sickest patients
- Benefits were achieved on top of remdesivir and dexamethasone for every patient (and convalescent plasma for some)
- The clinical findings are consistent with improvements in inflammatory biomarkers, such as NETosis, CRP, Ferritin, D-Dimer, and IL-6 in severe patients
- EUA is currently under review by FDA

Rigel's Ongoing Global Efforts to Combat COVID-19

- Fostamatinib has been selected for a NIH ACTIV-4 (Accelerating COVID-19 Therapeutic Interventions and Vaccines) Phase 3 trial in hospitalized patients with COVID-19
  - The ACTIV-4 Host Tissue trial is a large, multi-site trial funded by the National Heart, Lung, and Blood Institute (NHLBI) of the NIH and coordinated by Vanderbilt University Medical Center (VUMC)
  - The trial is evaluating treatments, including fostamatinib, that aim to protect and heal host tissues in hospitalized patients with COVID-19
  - The primary outcome is oxygen free days through day 28; secondary outcomes include hospital mortality, use of mechanical ventilation, and WHO scale scores
- Rigel is also conducting a Phase 3 clinical trial (NCT04629703) for the treatment of hospitalized high-risk patients with mild-to-moderate COVID 19
  - The primary endpoint is the proportion of subjects who progress to severe/critical disease within 29 days
- In addition, an investigator-sponsored trial is currently being conducted by Imperial College London