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# New clinical developments in the search of therapies to protect host tissue against COVID-19

*Notwithstanding the significant achievements of the current vaccines, the need for therapeutics against the infection are not diminished as evidenced by the emergence of variants, the uncertainty regarding duration of efficacy of the vaccines, and the real prospect of the virus becoming endemic.* ***Cresswell*** *proposes that attention be paid to two therapeutic programs in development of prospective consequence:*

- A nationwide three-arm clinical trial announced by **Vanderbilt University Medical Center (VUMC)** researchers, supported by the National Institutes of Health (NIH), which explores the safety and effectiveness of **Constant Therapeutics' TXA127**, an agonist hypothesized to restore RAAS balance and protect patients hospitalized with COVID-19 at high risk of poor outcomes.

  The ACTIV-4 Host Tissue trial will first explore the efficacy of drugs that target the Renin Angiotensin Aldosterone System (RAAS) and the immune system, both of which become dysregulated during COVID-19 and cause widespread damage in patients infected with the SARS-CoV-2 virus. ***To read the complete release from VUMC, click here***

- Upcoming data anticipated prior to year-end, 2021, from **Appili Therapeutics**'s Phase 3 PRESECO (PREventing SEvere COVID-19) trial, that evaluates Avigan®/Reeqonus™ (favipiravir) as a potential oral therapy for patients with mild-to-moderate COVID-19. ***To read more information about Appili, click here***

**Cresswell Advisors Inc.**

*Assistance and direction to development-stage companies in the life sciences and for earlier-stage companies in multiple fields.*
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**MANAGEMENT'S DISCUSSION AND ANALYSIS**

*For the Interim Period Ended June 30, 2021*

Dear Appili Shareholders,

Thanks to the efforts of our team and partners, we are rapidly approaching our first Phase 3 trial readout, evaluating the oral antiviral Avigan®/Reeqonus™ (favipiravir) for the treatment of mild-to-moderate COVID-19. As we approach this critical juncture, I wanted to take a minute to highlight a few recent trends that underscore the importance of Appili's mission and the value of the programs we are advancing in our pipeline.

The need for safe and effective oral antivirals has never been clearer. While the U.S. and now Europe initiated strong vaccination programs in the first half of 2021 to bring down infections, cases have come surging back and COVID-19 is increasingly establishing itself as a seasonal endemic disease. To contain outbreaks and stay ahead of variants, more effective countermeasures, and in particular oral antivirals, are needed. We are starting to see governments recognize this need, as the U.S. recently announced a $3 billion USD investment in antiviral development and public health figures increasingly highlight the need for oral agents. I believe this is only the beginning of an important reprioritization of antivirals and pandemic preparedness tools.

Even as the world is focused on COVID-19, new infectious disease threats are emerging. As recently as last month, the CDC reported on clusters of untreatable *Candida auris*, a highly resistant fungus and emerging public health threat that is establishing itself in health care settings in the U.S. and abroad.

These recent developments have validated our commitment at Appili Therapeutics to novel anti-infective development, and I am excited to share an update on our recent progress.

Over the last quarter, we achieved key milestones on our PRESECO Phase 3 trial, in particular:

- We are now only a few months away from a potentially transformational top-line readout that may position us to deliver the first FDA approved and globally available oral COVID-19 antiviral.
- This May, we completed our interim analysis and received a unanimous recommendation from the independent Data and Safety Monitoring Board (DSMB) to continue without modification Appili's ongoing Phase 3 PRESECO trial, an important milestone keeping us on track to deliver results later this year.
- Shortly after the interim read-out in June, we announced the expansion of PRESECO to several clinical research sites in Mexico and Brazil. Especially as cases of the Delta variant continue to rise, we recognize the importance of having global, diverse populations at different stages of the pandemic be a part of our trial.

In addition to these exciting developments with the PRESECO trial, I'm pleased to report that we have secured a $3.5 million funding agreement from The Lind Partners with funding expected on or before August 20. 2021. We are grateful for this support and recognition of the value anti-infectives can bring. These funds will enable us to continue driving PRESECO forward, while also advancing and expanding our pipeline.

We continue to execute across our portfolio and are rapidly approaching key milestones for our broader anti-infective pipeline, especially ATI-2307, our novel, broad-spectrum clinical-stage antifungal with the potential to address severe and hard to treat invasive fungal infections. Working with leading antifungal trialists and investigators, we are making significant progress on the necessary preparatory work, including generating a robust preclinical data package, to enable Phase 2 study start in 2022.

I look forward to the rest of what fiscal 2022 will bring. The future is exciting for Appili and I want to thank you for your continued support of our mission and the valuable work we're doing to improve and save the lives of patients worldwide.

**Armand Balboni**
Chief Executive Officer, Appili Therapeutics