Atea Pharmaceuticals Announces Publication of Data Supporting Bemnifosbuvir's (AT-527) Novel Mechanism of Action Against SARS-CoV-2 in Nature Communications

February 2, 2022

Data show bemnifosbuvir's unique mechanism of action increases barrier for emergence of resistance, making it an ideal candidate for treatment of COVID-19 and for combination therapy

BOSTON, Feb. 02, 2022 (GLOBE NEWSWIRE) -- Atea Pharmaceuticals, Inc. (Nasdaq: AVIR) ("Atea"), a clinical-stage biopharmaceutical company, today announced that new data highlighting bemnifosbuvir (AT-527) were published in the peer-reviewed journal, Nature Communications, in an article titled, "A dual mechanism of action of AT-527 against SARS-CoV-2 polymerase." The published data demonstrate that bemnifosbuvir's unique mechanism of action, with dual targets consisting of chain termination (RdRp) and nucleotidyltransferase (NiRAN) inhibition, has the potential to create a high barrier to resistance with broad antiviral activity across SARS-CoV-2 variants of concern. Bemnifosbuvir is an orally administered, non-mutagenic, direct-acting antiviral agent derived from Atea's purine nucleotide prodrug platform. In Phase 2 clinical trials, bemnifosbuvir has demonstrated rapid and sustained antiviral activity in high-risk patients with COVID-19 and has been shown to be generally safe and well tolerated.

Bemnifosbuvir targets SARS-CoV-2 RNA polymerase (nsp12), a highly conserved gene that is unlikely to change as the virus mutates and new variants emerge. This gene is responsible for both replication and transcription of SARS-CoV-2. The inhibition of RNA polymerase has been shown *in vitro* to effectively block production of coronavirus. In addition, *in vitro* data confirm that bemnifosbuvir is active against all variants of concern or interest that have been tested.

"These published data provide the first evidence that the NiRAN domain of the RNA polymerase is a key druggable site and highlight the underlying mechanism by which bemnifosbuvir inhibits the NiRAN function to block replication of SARS-CoV-2. These findings are of considerable interest for research and development as they highlight how AT-527 may block viral replication in this highly contagious virus," said Bruno Canard, Ph.D., lead investigator of the study at Architecture et Fonction des Macromolécules Biologiques, CNRS and Aix-Marseille University.

"With its unique dual mechanisms, demonstrated safety and broad antiviral activity across SARS-CoV-2 variants of concern, we strongly believe in bemnifosbuvir's potential to play an important role in the treatment of COVID-19," said Jean-Pierre Sommadossi, Ph.D., Founder and Chief Executive Officer of Atea Pharmaceuticals. "The nucleos(t)ide class has been the cornerstone of effective oral antiviral combination treatments for many severe viral diseases and bemnifosbuvir's profile is well suited to serve as a preferred backbone therapy of combination treatment for COVID-19 and other viral diseases. The data published today provide us with further confidence that we can meet the evolving needs of patients with COVID-19."

The SARS-CoV-2 nsp12 RNA polymerase has two functional domains, the well-established C-terminal RNA-dependent RNA polymerase (RdRp) and the previously uncharacterized N-terminal nidovirus RdRp associated NiRAN. To further detail the mechanism of action of bemnifosbuvir, researchers obtained a 2.9 Å cryo-EM structure of nsp12 with its cofactors nsp7 and nsp8, an RNA template, and AT-9010, the active triphosphate metabolite of bemnifosbuvir.

These new data demonstrate that the SARS-CoV-2 nsp12-nsp7-$(nsp8)_2$ minimal replication transcription complex can promote two reactions essential to virus growth: grafting nucleotides onto viral proteins nsp8 and nsp9 by means of the NiRAN domain and *de novo* synthesis of dinucleotide primers by RdRp in a NiRAN-independent fashion.

Both pathways are inhibited by AT-9010, the triphosphate metabolite of bemnifosbuvir, thus supporting bemnifosbuvir's unique dual mechanism of action for the treatment of COVID-19.

About the Bemnifosbuvir COVID-19 Clinical Development Program

Derived from Atea's nucleos(t)ide prodrug platform, bemnifosbuvir (AT-527) is an oral direct-acting antiviral which is being studied to determine its potential to protect against COVID-19 transmission and progression. Its unique mechanism of action, with dual targets including chain termination (RdRp) and NiRAN inhibition, has the potential to create a high barrier to resistance with broad antiviral coverage to different variants of SARS-CoV-2. Bemnifosbuvir is currently in Phase 2 development and has demonstrated rapid and sustained antiviral activity in high-risk patients with COVID-19 and has been shown to be generally safe and well tolerated. Atea has completed a comprehensive nonclinical program to characterize the safety profile of bemnifosbuvir. Results observed from these nonclinical studies demonstrated that bemnifosbuvir was non-mutagenic, had no effects on fertility or reproduction and was non-teratogenic.

About Atea Pharmaceuticals

Atea Pharmaceuticals is a clinical stage biopharmaceutical company focused on discovering, developing and commercializing oral therapies to address the unmet medical needs of patients with life-threatening viral diseases. Leveraging the Company's deep understanding of antiviral drug development, nucleos(t)ide chemistry, biology, biochemistry and virology, Atea has built a proprietary nucleotide prodrug platform to develop novel product candidates to treat single stranded ribonucleic acid, or ssRNA, viruses, which are a prevalent cause of severe viral diseases. Currently, Atea is focused on the development of orally-available, potent, and selective nucleotide prodrugs for difficult-to-treat, life-threatening viral infections, including severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus that causes COVID-19, hepatitis C virus (HCV), dengue virus and respiratory syncytial virus (RSV). For more information, please visit www.ateapharma.com.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. All statements contained in this press release that do not relate to matters of historical fact should be considered forward-looking statements, including without limitation statements regarding our expectations surrounding the potential of bemnifosbuvir as treatment for COVID-19, the advantages potentially conferred by bemnifosbuvir's dual mechanism and expectations regarding our clinical trials. These statements are neither promises nor guarantees, but involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements, including, but not limited to, the following: uncertainty around and costs associated with the development of bemnifosbuvir as a potential treatment for COVID-19; dependence on management, directors and other key personnel; the impact of the COVID-19 pandemic on our business; and risks related to the regulatory approval process. These and other important factors discussed under the caption "Risk Factors" in our most recent Quarterly Report on Form 10-Q, and our other filings with the SEC could cause actual results to differ materially from those indicated by the forward-looking statements made in this press release. Any such forward-looking statements represent management's estimates as of the date of this press release. While we may elect to update such forward-looking statements at some point in the future, we disclaim any obligation to do so, even if subsequent events cause our views to change.

Contacts

Jonae Barnes
SVP, Investor Relations and Corporate Communications
617-818-2985
Barnes.jonae@ateapharma.com

Will O'Connor
Stern Investor Relations
212-362-1200
will.oconnor@sternir.com