Atea Pharmaceuticals Announces Publication of Preclinical Data Highlighting Potent Activity of AT-527 Against SARS-CoV-2

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Data underscore key mechanistic features enabling AT-527 to inhibit SARS-CoV-2 viral replication and support current late-stage clinical development program

BOSTON, Feb. 08, 2021 (GLOBE NEWSWIRE) -- Atea Pharmaceuticals, Inc. (Nasdaq: AVIR) ("Atea"), a clinical-stage biopharmaceutical company, today announced the publication of new data highlighting the highly potent *in vitro* antiviral activity of AT-527 against SARS-CoV-2. AT-527 is an orally administered, direct-acting antiviral developmental agent derived from Atea's purine nucleotide prodrug platform. The new findings are available in a manuscript published online in *Antimicrobial Agents and Chemotherapy*.

"To be effective, a direct-acting antiviral needs to be administered orally, and early, in the course of viral infection in order to inhibit viral replication and thereby reduce disease progression. These new data underscore AT-527's potential to treat COVID-19 and to have an impact on global health," said Jean-Pierre Sommadossi, Ph.D., Founder and Chief Executive Officer of Atea Pharmaceuticals. "The results demonstrated in several *in vitro* assays that AT-527 has highly potent antiviral activity against several human coronaviruses, including SARS-CoV-2, the causative agent of COVID-19. AT-527 was activated in cultured normal human nasal and bronchial epithelial cells, which are the primary targets of SARS-CoV-2 infection. Since the respiratory tract is the initial site of the SARS-CoV-2 infection, activation of AT-527 with its substantial half-life suggests sustained inhibition of viral replication of SARS-CoV-2 in these tissues."

Antiviral therapeutics are expected to have the greatest effect if given in early stages of the COVID-19 infection when SARS-CoV-2 is rapidly replicating in the respiratory epithelium and viral load levels are high. The goal of a direct-acting antiviral is to prevent disease progression by minimizing, or eliminating, viral replication and thereby reducing the severity of the disease, preventing or shortening hospitalization, and also potentially preventing transmission of the virus to others. This makes it ideal for potential use in both pre- and post-exposure prophylactic settings and complementary to vaccines.

In several *in vitro* assays, AT-511, which is the freebase of AT-527, demonstrated highly potent activity in inhibiting the replication of SARS-CoV-2, the virus responsible for the COVID-19 pandemic. The results show that AT-511 is extensively activated in the key human primary cells, nasal and bronchial epithelial cells. Importantly, the half-life observed in these primary human cells of the upper and lower respiratory tract was approximately 40 hours, which is a key pharmacokinetic /pharmacodynamic (PK/PD) characteristic that allows accumulation of the active triphosphate metabolite of the drug candidate in these key tissues, thus resulting in the potent inhibition of SARS-CoV-2 viral replication by AT-527.

A simulation using human PK data combined with non-human primate tissue levels was also detailed in the manuscript. The data indicate that within two hours of dosing, AT-9010 (triphosphate active metabolite of AT-527) achieved concentrations that should inhibit SARS-CoV-2 replication and that these effective levels should be maintained throughout therapy. Based on these data, a twice-daily oral regimen of AT-527 at 550 mg is currently being studied in clinical trials.

In addition, the authors discussed RNA polymerase (nsp12) of SARS-CoV-2 and other coronaviruses, focusing on two functional domains, including RdRp and nidovirus RdRp-associated nucleotidyltransferase (NiRAN). Recent data indicate that AT-9010 (triphosphate active metabolite of AT-527) is a potent inhibitor of NiRAN, a function essential for viral replication. These findings will be published in an upcoming manuscript.

Data Highlights

In cultured normal human airway epithelial cells, the concentration of AT-511 required to inhibit replication of SARS-CoV-2 by 90% (EC_{90}) was 0.47 µM, very similar to its EC_{90} against HCoV-229E, HCoV-OC43 and SARS-CoV in Huh-7 cells. Little to no cytotoxicity was observed for AT-511 at concentrations up to 100 µM. Substantial levels of the active triphosphate metabolite AT-9010 were formed in normal human bronchial and nasal epithelial cells incubated with 10 µM AT-511 (698 ± 15 and 236 ± 14 µM, respectively), with a half-life of at least 38 hours. Results from steady-state pharmacokinetic and tissue distribution studies of non-human primates administered oral doses of AT-527, as well as pharmacokinetic data from subjects given daily oral doses of AT-527, predict that twice daily oral doses of 550 mg AT-527 will produce AT-9010 trough concentrations in human lung that exceed the EC_{90} observed for the prodrug against SARS-CoV-2 replication. This suggests that AT-527 may be an effective treatment option for COVID-19.

About AT-527

AT-527 is an orally administered, direct-acting developmental antiviral agent derived from Atea's nucleotide prodrug platform. AT-527 is currently under evaluation as a treatment for patients with COVID-19. In collaboration with Roche, AT-527 is currently being evaluated in a global Phase 2 study for hospitalized patients with moderate COVID-19 and a Phase 2 virology study in an outpatient setting. A pivotal Phase 3 trial is planned in the outpatient setting.

About Atea Pharmaceuticals

Atea Pharmaceuticals is a clinical stage biopharmaceutical company focused on discovering, developing and commercializing therapies to address the unmet medical needs of patients with life-threatening viral diseases. Leveraging the Company's deep understanding of antiviral drug development,

nucleoside biology, and medicinal chemistry, 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, dengue virus, hepatitis C virus (HCV) and respiratory syncytial virus (RSV). For more information, please visit www.ateapharma.com.

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