New Data Showcasing Favorable Profile of Bemnifosbuvir for Treatment of COVID-19 and Hepatitis C Presented at 2023 International Conference on Antiviral Research

March 14, 2023

Low risk for drug-drug interactions with bemnifosbuvir based upon results from in vitro metabolism and transporter studies

Bemnifosbuvir retains activity against all SARS-CoV-2 variants of concern evaluated as well as other human coronaviruses such as HCoV-229E, HCoV-OC43, and SARS-CoV-1

Favorable absorption, distribution, metabolism, and excretion profile demonstrated for bemnifosbuvir

Synergistic antiviral effect observed for the combination of bemnifosbuvir and ruzasvir against HCV in vitro

BOSTON, March 14, 2023 (GLOBE NEWSWIRE) -- Atea Pharmaceuticals, Inc. (Nasdaq: AVIR) ("Atea"), a clinical-stage biopharmaceutical company engaged in the discovery and development of oral direct acting therapeutics for serious viral diseases, today announced the presentation of new Phase 1, *in vitro and in vivo* data that demonstrate key profile attributes of Atea's lead drug candidate, bemnifosbuvir, for the treatment of COVID-19 and hepatitis C (HCV). Additionally, new data for AT-752 for dengue and a nucleotide analogue are being presented. These results are being presented at the 36th International Conference on Antiviral Research (ICAR 2023) taking place March 13-17, 2023 in Lyon, France.

Key highlights of the presentations include results from a Phase 1 human absorption, distribution, metabolism, and excretion (ADME) study for bemnifosbuvir demonstrating a favorable ADME profile supportive of the dosing regimen used in SUNRISE-3, a global, multicenter Phase 3 registrational trial for the treatment of COVID-19. *In vitro* metabolism and transporter interaction studies showed bemnifosbuvir has a low risk for interactions with medicines commonly prescribed to patients at risk for COVID-19 progression and for those with HCV infection. *In vitro* studies also demonstrated advantages of bemnifosbuvir's mechanism of action, which targets conserved regions of the viruses that cause COVID-19 and HCV infection. These advantages include a higher barrier to resistance and maintenance of antiviral activity in the presence of COVID-19 variants. Additionally, the combination of bemnifosbuvir and ruzasvir for the treatment of HCV demonstrated potent *in vitro* synergistic antiviral activity and *in vivo* preclinical safety without adverse interactions.

"As COVID-19 becomes endemic, it is essential to have new oral antiviral medicines that are safe, well tolerated and address the current limitations of existing treatments," said Bruno Canard, Ph.D., lead investigator of the *in vitro* studies of bemnifosbuvir conducted at Architecture et Fonction des Macromolécules Biologiques, CNRS and Aix-Marseille University. "The data presented at ICAR demonstrate bemnifosbuvir's unique metabolic activation pathway and how it inhibits enzymes essential to the viral replication of COVID-19 and HCV and its potential to play an important role in the treatment of these serious viral diseases."

Bemnifosbuvir is an investigational, oral, direct-acting antiviral being evaluated in the Phase 3 SUNRISE-3 trial for the treatment of COVID-19 in non-hospitalized patients at high risk for disease progression, and in Phase 2 development for the treatment of HCV in combination with ruzasvir, an oral NS5A inhibitor.

"As we continue to advance late-stage development of bemnifosbuvir, these data demonstrate that our lead compound has the potential to improve the current standard of care and address key unmet needs and limitations for patients with COVID-19 and HCV," said Jean-Pierre Sommadossi, PhD, Chief Executive Officer and Founder of Atea Pharmaceuticals. "These data support a favorable safety and drug interaction profile of bemnifosbuvir to treat these conditions and to provide vulnerable patients with another therapeutic option."

COVID-19

Oral Presentation Number: 019
Date/Time: Wednesday, March 15 from 10:35 am-10:45 am CET
Title: Bemnifosbuvir (BEM, AT-527) a Potent Inhibitor of SARS-CoV-2 Variants of Concern (VOC), and a Promising Oral Antiviral with a High Resistance Barrier for Treatment of COVID-19 and other Coronaviruses Infections

In vitro results demonstrate that bemnifosbuvir is a potent inhibitor of all tested SARS-CoV-2 variants of concern as well as other human coronaviruses such as HCoV-229E, HCoV-OC43, and SARS-CoV-1. Results from an *in vitro* resistance study conducted with the surrogate virus HCoV-229E in Huh7 cells suggest that bemnifosbuvir may have a high barrier to drug resistance during treatment of COVID-19 and other coronavirus infections.

Bemnifosbuvir

Oral Presentation Number: 047
Date/Time: Thursday, March 16 from 5:20-5:30 pm CET
Title: Five Cellular Enzymes in the Activation Pathway of Bemnifosbuvir, a Drug Candidate Against SARS-CoV-2 Infections

Results from this *in vitro* study showed that bemnifosbuvir required a minimal set of 5 cellular enzymes (Cat/CES1, HINT1, ADALP1, GUK1, and NDPK) to be metabolized to its active triphosphate form, AT-9010, with an obligate order of reactions, as demonstrated by functional and structural data at each step. *In vitro,* AT-9010 inhibits enzymes essential to viral replication such as the SARS-CoV-2 bi-functional nsp12 RNA polymerase/nucleotidyltransferase, the dengue virus bi-functional NS5 RNA polymerase/RNA methyltransferase, and the HCV NS5B RNA

polymerase.

Poster Number: 537
Date/Time: Tuesday, March 14 from 5:00-7:00 pm CET and Wednesday, March 15 from 12:15-2:15 pm CET
Title: Low Risk of Drug-Drug Interactions (DDIs) for Bemnifosbuvir (BEM) Based Upon *In Vitro* Metabolism and Transporter Interaction Studies

Results from these *in vitro* studies suggest that bemnifosbuvir has a low risk of drug-drug interactions when co-administered with drugs that are substrates of CYP450 enzymes, UGT1A1 or ABC/SLC transporters. The enzymes that support metabolic activation of bemnifosbuvir are of high capacity and are not likely to be inhibited by commonly prescribed drugs. The observations from these *in vitro* studies have been subsequently validated with Phase 1 clinical drug-drug interaction studies.

Poster Number: 549
Date/Time: Tuesday, March 14 from 5:00-7:00 pm CET and Wednesday, March 15 from 12:15-2:15 pm CET
Title: Pharmacokinetics and Metabolism of [^{14}C]-Bemnifosbuvir in Healthy Male Participants

Results from a Phase 1, open-label, single-dose, mass balance study demonstrated that bemnifosbuvir 550 mg was well absorbed and nearly completely recovered in urine and feces. The data showed bemnifosbuvir and its metabolites did not accumulate in red blood cells, with similar exposure in plasma and whole blood, and that bemnifosbuvir underwent rapid and extensive metabolic activation to the intracellular active triphosphate metabolite and thereafter entered general circulation mostly as nucleoside metabolites. AT-273, the nucleoside metabolite considered a surrogate of the intracellular phosphates, exhibited a long half-life in plasma, supporting once- and twice-daily dosing.

Hepatitis C

Poster Number: 411
Date/Time: Tuesday, March 14 from 5:00-7:00 pm CET and Wednesday, March 15 from 12:15 pm-2:15 pm CET
Title: The Combination of Bemnifosbuvir (BEM) and Ruzasvir (RZR), the HCV NS5B and NS5A Inhibitors, Demonstrates Potent *In Vitro* Synergistic Antiviral Activity and *In Vivo* Preclinical Safety Without Adverse Interactions

In vitro, the combination of bemnifosbuvir and ruzasvir demonstrated greater inhibition of HCV replication compared to the sum of inhibition of each agent alone in HCV replicon cells, suggesting a synergistic antiviral effect when bemnifosbuvir and ruzasvir are administered together.

In a 13-week toxicity study in rats in which bemnifosbuvir and ruzasvir were administered alone or in combination at 500 mg/kg once daily, treatments were well tolerated, and no adverse events were observed. Results demonstrated that systemic exposures of bemnifosbuvir, its metabolites, and ruzasvir were similar when administered independently or in combination, suggesting no significant drug-drug interactions between bemnifosbuvir and ruzasvir.

This synergistic activity and no significant drug-drug interactions, together with the previously demonstrated potent, pan-genotypic, antiviral activity of each agent alone, suggest the combination of bemnifosbuvir and ruzasvir has the potential to offer a differentiated, short duration, pan-genotypic, protease inhibitor-sparing regimen for patients with HCV, with or without cirrhosis.

Dengue

Oral Presentation Number: 046
Date/Time: Thursday, March 16 from 4:50-5:00 pm CET

Title: AT-752 Targets Multiple Sites and Activities on the Dengue Virus Replication Enzyme NS5

Results from this *in vitro* study demonstrated the mechanism of action of AT-752. AT-9010, the active triphosphate metabolite of AT-752, inhibited the essential DENV NS5 enzyme. AT-9010 targets two NS5-associated enzyme activities, the RNA 2'-O-MTase and the RNA-dependent RNA polymerase (RdRp) at its RNA elongation step. RNA synthesis inhibition occurred for all 4 DENV serotypes. These results illustrate at atomic resolution (1.97 Å) how RNA cap methylation was prevented by AT-9010.

Nucleotide Analogue

Poster Number: 504
Date/Time: Tuesday, March 14 from 5:00-7:00 pm CET and Wednesday, March 15 from 12:15-2:15 pm CET
Title: A Non-Excisable Nucleotide Analogue Active against SARS-CoV-2
AT-1000 is a 2'-ribose modified nucleotide analog, related to bemnifosbuvir but bearing a sulfur atom at its α-phosphate (i.e., α-thio). Results from this *in vitro* study show that AT-1000 exhibited potent anti-SARS-CoV2 activity, similar to bemnifosbuvir in human airway epithelial cells. Unlike bemnifosbuvir, neither the Sp or Rp isomer binds or inhibits the NiRAN domain nucleotidylation activity. The α-thio modification therefore creates a novel compound, exhibiting an original mechanism of action. These results suggest that this single atom modification may provide a general approach to potentiate a wide array of nucleotide analogues against RNA viruses carrying natural resistance to nucleotide analogue antivirals, such as highly pathogenic coronaviruses.

About Bemnifosbuvir for COVID-19

Bemnifosbuvir, a nucleotide polymerase inhibitor, targets the SARS-CoV-2 RNA polymerase (nsp12), a highly conserved gene that is unlikely to change as the virus mutates and new variants continue to emerge. This gene is responsible for both replication and transcription of SARS-CoV-2. Bemnifosbuvir has a unique mechanism of action, with dual targets consisting of chain termination (RdRp) and nucleotityltransferase (NiRAN) inhibition, which has the potential to create a high barrier to resistance. *In vitro* data confirm that bemnifosbuvir is active with similar efficacy against all variants of concern and variants of interest that have been tested, including Omicron subvariants BA.4 and BA.5. Bemnifosbuvir is currently being evaluated in SUNRISE-3, a global multicenter Phase 3 registrational trial for the treatment of COVID-19.

About Bemnifosbuvir and Ruzasvir for Hepatitis C Virus
Bemnifosbuvir has been shown to be approximately 10-fold more active than sofosbuvir (SOF) *in vitro* against a panel of laboratory strains and clinical isolates of HCV genotypes 1–5. *In vitro* studies demonstrated bemnifosbuvir remained fully active against SOF resistance-associated strains (S282T),

with up to 58-fold more potency than SOF. The pharmacokinetic (PK) profile of bemnifosbuvir supports once-daily dosing for the treatment of HCV and bemnifosbuvir has been well tolerated at doses up to 550 mg for durations up to 8-12 weeks in healthy and HCV infected subjects.

Ruzasvir (RZR), an oral NS5A inhibitor, has demonstrated highly potent and pangenotypic antiviral activity in preclinical (picomolar range) and clinical studies. RZR has been administered to over 1,200 HCV-infected patients at daily doses of up to 180 mg for up to 24 weeks and has demonstrated a favorable safety profile. RZR's PK profile supports once-daily dosing.

The combination of bemnifosbuvir and ruzasvir for the treatment of HCV is in Phase 2 development.

About Atea Pharmaceuticals
Atea is a clinical stage biopharmaceutical company focused on discovering, developing and commercializing oral therapies to address the unmet medical needs of patients with serious viral infections. Leveraging the Company's deep understanding of antiviral drug development, nucleos(t)ide chemistry, biology, biochemistry and virology, Atea has built a proprietary nucleos(t)ide prodrug platform to develop novel product candidates to treat single stranded ribonucleic acid, or ssRNA, viruses, which are a prevalent cause of serious viral diseases. Atea plans to continue to build its pipeline of antiviral product candidates by augmenting its nucleos(t)ide platform with other classes of antivirals that may be used in combination with its nucleos(t)ide product candidates. Currently, Atea is focused on the development of orally-available antiviral agents for serious viral infections, including severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus that causes COVID-19, and hepatitis C virus (HCV). 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 our product candidates, including bemnifosbuvir combination product candidates, and expectations regarding our pipeline, including trial design and development timelines. 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 uncertainty around and costs associated with the clinical development of bemnifosbuvir as a potential treatment for COVID-19 and the combination of bemnifosbuvir and ruzasvir as a potential treatment for HCV. These and other important factors discussed under the caption "Risk Factors" in our Annual Report on Form 10-K for the year ended December 31, 2022 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