Applied Therapeutics Announces Positive Topline Results of Pivotal Phase 2 ACTION-Galactosemia Study of AT-007 in Galactosemia Patients

January 8, 2020

AT-007 demonstrated a robust and sustained reduction in galactitol vs placebo; significant plasma galactitol reduction of ~50% (p<0.01)

AT-007 was well-tolerated; no drug-related adverse events reported at any dose to date

Applied Therapeutics expects to file for regulatory approval of AT-007 in the second half of 2020

Company to host conference call and webcast today at 8:30 a.m. ET

NEW YORK, Jan. 08, 2020 (GLOBE NEWSWIRE) -- Applied Therapeutics Inc. (Nasdaq:APLT), a clinical-stage biopharmaceutical company developing a pipeline of novel drug candidates against validated molecular targets in indications of high unmet medical need, today announced positive topline results from the Pivotal Phase 2 portion of the ACTION-Galactosemia study of AT-007, a central nervous system (CNS) penetrant Aldose Reductase inhibitor, in adult Galactosemia patients. ACTION-Galactosemia is a double-blind placebo-controlled trial evaluating safety and pharmacokinetics of AT-007 in healthy volunteers, as well as safety, pharmacokinetics, and biomarker effects in adult Galactosemia patients over 28 days of once daily oral dosing. The key biomarker outcome of the study was reduction in galactitol, an aberrant toxic metabolite of galactose, formed by Aldose Reductase in Galactosemia patients.

AT-007 treatment resulted in a statistically significant and robust reduction in plasma galactitol vs placebo in adult Galactosemia patients. Reductions in galactitol were dose dependent, with higher concentrations of AT-007 resulting in a greater magnitude of reduction in galactitol. At the highest dose tested (20mg/kg), AT-007 significantly reduced plasma galactitol 45-54% from baseline vs. placebo ($p<0.01$). Galactitol reduction was rapid and sustained over time. No substantial change from baseline was observed in placebo treated patients. AT-007 was well tolerated, with no drug-related adverse events noted to date in Galactosemia patients or in the 72 healthy volunteers treated in Part 1 of the trial.

The company will present full data from the ACTION-Galactosemia trial at the Society for Inherited Metabolic Disorders Annual Meeting, April 26 – 29, 2020.

Applied Therapeutics will continue to characterize AT-007 long-term safety in adult Galactosemia patients and intends to initiate a pediatric study in 2020.

Based on these results reported today, Applied Therapeutics believes that AT-007 represents a potentially compelling new therapeutic option for patients with Galactosemia. The company plans to utilize recent FDA guidance permitting biomarker-based development in low prevalence, slowly progressing rare metabolic diseases, such as Galactosemia, and expects to file for regulatory approval in the second half of 2020.

“We are thrilled with these results,” said Riccardo Perfetti, MD, PhD, Chief Medical Officer of Applied Therapeutics. “Galactosemia is a devastating disease with no treatments currently available. We have long known that dietary restriction alone does not prevent chronic complications of disease. These results provide hope for patients and families that action through drug treatment with AT-007 can potentially change the course of the disease, transforming patients’ lives.”

“The Galactosemia program is an example of our overall strategy to apply technological breakthroughs to areas of high unmet need,” said Shoshana Shendelman, PhD, Founder, CEO and Chair of the Board. “By employing new regulatory pathways and using biomarkers early in development, we are able to bring critical drugs to patients who desperately need them quickly and effectively. The ACTION-Galactosemia data presented today is our first pivotal study readout - but it’s just the beginning. We are continuing to advance our pipeline of novel drug candidates in other disease indications and look forward to sharing additional successful data readouts in the future.”

About Galactosemia
Galactosemia is a rare metabolic disease that affects how the body processes a simple sugar called galactose, and for which there is no known cure or approved treatment available. Galactose is found in foods, but the human body also naturally produces galactose on its own, so dietary restriction can't prevent complications of disease. It is estimated that the U.S. Galactosemia population is approximately 2,800 patients, based on newborn screening data identifying 2,500 infants through 2014, and the estimated birth rate of 80 patients per year. High levels of galactose circulating in the blood and tissues of Galactosemia patients enables Aldose Reductase to convert galactose to a toxic metabolite, called galactitol, which causes long-term complications ranging from CNS dysfunction to cataracts.

About AT-007
AT-007 is a central nervous system (CNS) penetrant Aldose Reductase inhibitor (ARI) in clinical development for treatment of Galactosemia. AT-007 has been studied in in an animal model of Galactosemia, which demonstrated that AT-007 reduces toxic galactitol levels and prevents disease complications. Applied Therapeutics is conducting a biomarker based development program in patients with Galactosemia, based on the recently released draft industry guidance on drug development for low prevalence, slowly progressing rare metabolic diseases. The company received Orphan Designation for AT-007 for Galactosemia in May 2019.

Conference Call at 8:30 a.m. ET
Applied Therapeutics will hold a conference call to discuss the topline results of the ACTION-Galactosemia study today, January 8, 2020 at 8:30 a.m. ET. The live event will be available on the investor page of the Applied Therapeutics website at http://ir.appliedtherapeutics.com or by calling (800) 369-8554 (toll-free domestic) or (409) 937-8917 (international) five minutes prior to the start time and entering passcode 5320779. A replay of the call

will be available on the Applied Therapeutics website approximately two hours after the completion of the call and will be archived for 30 days.

About Applied Therapeutics

Applied Therapeutics is a clinical-stage biopharmaceutical company developing a pipeline of novel drug candidates against validated molecular targets in indications of high unmet medical need. The company's lead drug candidate, AT-001, is a novel aldose reductase inhibitor (ARI) that is being developed for the treatment of Diabetic Cardiomyopathy, or DbCM, a fatal fibrosis of the heart. The company initiated a Phase 3 registrational study in DbCM in September 2019. Applied Therapeutics is also developing AT-007, a central nervous system penetrant ARI, for the treatment of Galactosemia, a rare pediatric metabolic disease, and initiated a Phase 1/2 clinical trial in June 2019. The preclinical pipeline also includes AT-003, an ARI designed to cross through the back of the eye when dosed orally, for the treatment of diabetic retinopathy, expected to advance into a Phase 1 study in 2020.

Forward-looking Statements

This press release contains "forward-looking statements" that involve substantial risks and uncertainties for purposes of the safe harbor provided by the Private Securities Litigation Reform Act of 1995. Any statements, other than statements of historical fact, included in this press release regarding strategy, future operations, prospects, plans and objectives of management, including words such as "may," "will," "expect," "anticipate," "plan," "intend," and similar expressions (as well as other words or expressions referencing future events, conditions or circumstances) are forward-looking statements. These include, without limitation, statements regarding (i) the design, scope and results of our clinical trials, (ii) the timing of the initiation and completion of our clinical trials, (iii) the likelihood that data from our clinical trials will support future development of our product candidates, (iv) the likelihood of obtaining regulatory approval of our product candidates and qualifying for any special designations, such as orphan drug designation, (v) our cash runway and the timing of our clinical development plan. Forward-looking statements in this release involve substantial risks and uncertainties that could cause actual results to differ materially from those expressed or implied by the forward-looking statements, and we, therefore cannot assure you that our plans, intentions, expectations or strategies will be attained or achieved. Such risks and uncertainties include, without limitation, the uncertainties inherent in the initiation, execution and completion of clinical trials, in the timing of availability of trial data, in the results of the clinical trials, in the actions of regulatory agencies, in the commercialization and acceptance of new therapies. Factors that may cause actual results to differ from those expressed or implied in the forward-looking statements in this press release are discussed in our filings with the U.S. Securities and Exchange Commission, including the "Risk Factors" contained therein. Except as otherwise required by law, we disclaim any intention or obligation to update or revise any forward-looking statements, which speak only as of the date they were made, whether as a result of new information, future events or circumstances or otherwise.

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Source: Applied Therapeutics