Applied Therapeutics Announces Start of AT-007 Pediatric Galactosemia Study; Releases Additional 40mg/kg Data from Adult Galactosemia Study

June 15, 2020

AT-007 pediatric Galactosemia study (ACTION-Galactosemia Kids) initiated

Additional 40mg/kg adult cohort demonstrates incremental efficacy; data reinforces AT-007 favorable safety and efficacy profile

NEW YORK, June 15, 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 additional supportive biomarker efficacy and safety data for AT-007 in Galactosemia at 40 mg/kg. The company also announced initiation of the AT-007 pediatric trial, ACTION-Galactosemia Kids, in children age 2 to 17.

“From a scientific perspective, it was important to investigate effects of AT-007 at the higher dose, 40mg/kg, to ensure that we are fully informed on the optimal dose for patients,” said Riccardo Perfetti, MD, PhD, Chief Medical Officer of Applied Therapeutics. “The data at 40mg/kg reinforces the favorable safety and efficacy profile of AT-007. We remain excited about the opportunity to offer a potentially life changing therapy to patients with Galactosemia of all ages.”

“The initiation of our pediatric study is an important milestone for the Galactosemia community,” said Shoshana Shendelman, PhD, Founder and CEO of Applied Therapeutics. “We are overwhelmed by the enthusiasm and support from families, and we are truly thankful to all of the clinical trial participants who have contributed to this advancement. We anticipate being fully enrolled on the pediatric study within a matter of weeks.”

ACTION-Galactosemia Adult Trial: 40 mg/kg Dose Results

ACTION-Galactosemia is a Phase 1/2 clinical trial of the CNS penetrant Aldose Reductase inhibitor AT-007 in healthy volunteers and adults with Galactosemia. The biomarker-based pivotal study targeted reduction in plasma galactitol, an aberrant toxic metabolite of galactose formed by Aldose Reductase in Galactosemia patients. Accumulation of galactitol causes long-term complications ranging from CNS dysfunction to cataracts. Previously, Applied Therapeutics reported safety and efficacy data demonstrating a rapid and robust reduction in galactitol from baseline (approximately 50% reduction) at 20mg/kg. The reduction in galactitol at 20mg/kg was statistically significant vs. placebo ($p<0.01$) and did not result in any compensatory increase in other galactose metabolites, such as Gal-1p. Because there were no dose-limiting safety issues at 20mg/kg (and no drug-related adverse events overall), a higher dose cohort at 40mg/kg was initiated to fully explore optimal dosing in adults with Galactosemia. Once-daily 40 mg/kg AT-007 resulted in plasma galactitol reduction of 55%, an incremental improvement in efficacy vs. the 20mg/kg dose. Reduction in galactitol was statistically significant vs. placebo ($p<0.01$). All patients on the 40 mg/kg dose demonstrated significant reduction in galactitol from baseline, and reduction in galactitol was rapid and sustained over the 28-day dosing period. 40mg/kg was safe and well-tolerated with no drug-related adverse events reported, and no compensatory increase in galactose or other metabolites, such as Gal-1p.

90-Day Safety Extension

The 90-day extension study of AT-007 in adult Galactosemia patients remains ongoing. Patients who completed the 40mg/kg cohort have rolled into the 3-month safety extension study. The extension study is open to patients from the core study and to new adult Galactosemia patients. To date, the drug has been shown to be safe and well tolerated, and all patients enrolled in the study remain on treatment.

ACTION-Galactosemia Kids: Pediatric Study Initiated

A placebo-controlled trial of AT-007 in pediatric patients (ACTION-Galactosemia Kids) will begin enrolling this week. Similar to the ACTION-Galactosemia trial in adults, the pediatric study will evaluate safety, pharmacokinetics, and reduction in the toxic biomarker, galactitol. Three age cohorts are being studied in parallel: age 2-6, age 7-12, and age 13-17. An additional cohort of children under 2 years of age may be added following analysis of safety data from the initial pediatric cohorts. The core study is comprised of two parts: a dose range finding segment evaluating up to 7 days of consecutive dosing to determine the optimal dose in children of each age group, followed by a 90 day study evaluating safety and biomarker efficacy. Following completion of the core study, all participants will have the option to participate in a long-term open-label extension (where placebo patients will cross over to active drug). Both the ACTION-Galactosemia adult extension study and the pediatric study are designed to incorporate primarily home health visits in order to limit travel and risk of exposure to COVID-19.

Future Development
Applied Therapeutics plans to submit an NDA for potential approval of AT-007 immediately following completion of the pediatric study, which will also include the 90-day safety data in adults with Galactosemia. A European cohort is also underway to support future European regulatory submission. The company looks forward to sharing MRI/MRS data on galactitol quantitation in the brain at an upcoming medical meeting.

The full ACTION-Galactosemia study data will be available on the Presentations & Publications section of the Applied Therapeutics website at www.appliedtherapeutics.com.

About Applied Therapeutics, Inc.
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-007, is a novel central nervous system penetrant aldose reductase inhibitor (ARI) for the treatment of Galactosemia, a rare pediatric metabolic disease. The Company initiated a pivotal Phase 1/2 clinical trial in June 2019, read out positive top-line biomarker data in adult Galactosemia patients in January 2020 and announced full data from the trial in April

2020. The Company is also developing AT-001, a novel potent 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. 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, as well as novel dual PI3k inhibitors in preclinical development for orphan oncology indications.

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 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 and Pediatric Rare Disease Voucher (PRV) designation 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) our plan to move quickly towards regulatory filing following our pivotal Phase 2 ACTION-Galactosemia study, while preparing for Galactosemia commercial launch and growing our organization, (ii) the design, scope and results of our clinical trials, (iii) the timing of the initiation and completion of our clinical trials, (iv) the likelihood that data from our clinical trials will support future development of our product candidates, and (v) the likelihood of obtaining regulatory approval of our product candidates and qualifying for any special designations, such as orphan drug designation. 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, (i) our plans to develop and commercialize our product candidates, (ii) the initiation, timing, progress and results of our current and future preclinical studies and clinical trials and our research and development programs, (iii) our ability to take advantage of expedited regulatory pathways for any of our product candidates, (iv) our estimates regarding expenses, future revenue, capital requirements and needs for additional financing, (v) our ability to successfully acquire or license additional product candidates on reasonable terms, (vi) our ability to maintain and establish collaborations or obtain additional funding, (vii) our ability to obtain regulatory approval of our current and future product candidates, (viii) our expectations regarding the potential market size and the rate and degree of market acceptance of such product candidates, (ix) our ability to fund our working capital requirements and expectations regarding the sufficiency of our capital resources, (x) the implementation of our business model and strategic plans for our business and product candidates, (xi) our intellectual property position and the duration of our patent rights, (xii) developments or disputes concerning our intellectual property or other proprietary rights, (xiii) our expectations regarding government and third-party payor coverage and reimbursement, (xiv) our ability to compete in the markets we serve, (xv) the impact of government laws and regulations and liabilities thereunder, (xvi) developments relating to our competitors and our industry, (xvii) the impact of the COVID-19 pandemic on the timing and progress of our ongoing clinical trials and our business in general and (xviii) other factors that may impact our financial results. In light of the significant uncertainties in these forward-looking statements, you should not rely upon forward-looking statements as predictions of future events. Although we believe that we have a reasonable basis for each forward-looking statement contained in this press release, we cannot guarantee that the future results, levels of activity, performance or events and circumstances reflected in the forward-looking statements will be achieved or occur at all. 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