Applied Therapeutics Announces Clinical Benefit of Govorestat (AT-007) in ACTION-Galactosemia Kids Trial; Company Plans to Meet with FDA Regarding Potential NDA Submission

April 24, 2023

- Govorestat demonstrated consistent long-term clinical outcomes benefit across a range of functional measures in the ACTION-Galactosemia Kids trial, confirming prior biomarker data
- Govorestat treatment improved activities of daily living, behavior, cognition, fine motor skills, adaptive skills and tremor vs. placebo
- Company plans to request a pre-NDA meeting with the FDA as soon as possible to discuss a potential NDA submission in second half of 2023; plans to submit a Marketing Authorization Application (MAA) with the European Medicines Agency (EMA) in mid-2023

NEW YORK, April 24, 2023 (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 results from the ACTION-Galactosemia Kids study of govorestat (AT-007), a novel, oral, small molecule, central nervous system (CNS) penetrant Aldose Reductase inhibitor (ARI).

“We believe Govorestat has demonstrated compelling evidence of clinical benefit alongside a favorable safety profile in patients with Galactosemia,” said Shoshana Shendelman, PhD, CEO, Founder and Chair of the Board of Applied Therapeutics. “We look forward to working collaboratively with regulators to ensure that this important treatment is available to patients with Galactosemia as quickly as possible. We plan to request a pre-NDA meeting with the FDA, and we have already received feedback from the EMA supportive of a submission in Europe.”

“Govorestat has demonstrated consistent results on improvement in galactitol biomarker levels in both adults and children and on long-term clinical and functional outcomes in children with Galactosemia,” said Riccardo Perfetti, MD, PhD, Chief Medical Officer of Applied Therapeutics. “We would like to thank all of the patients, investigators, and caregivers who participated in the ACTION-Galactosemia Kids study.”

“In the ACTION-Galactosemia Kids trial, treatment with govorestat affected clinically meaningful aspects of the disease, including activities of daily living, behavioral symptoms, cognition, adaptive skills and tremor,” said Janet Thomas, MD, Director of Clinical Research, Section of Clinical Genetics and Metabolism, Children’s Hospital Colorado. “This is exciting news. Until now, physicians have had no pharmacological options available for Galactosemia, and I look forward to being able to provide this therapy to my patients in the future.”

“The Galactosemia community has been waiting for a treatment for a long time, and we are thrilled with the results from the ACTION-Galactosemia Kids trial. Govorestat clearly improves critical characteristics of this disease - like our children’s abilities to feed themselves, dress themselves, understand what they are being taught in school, interact with other children - all of which impact our daily lives.” said Brittany Cudzilo, Vice President of the Galactosemia Foundation.

The ACTION-Galactosemia Kids Phase 3 study was designed to evaluate the impact of govorestat treatment vs. placebo on clinical outcomes over time in 47 children age 2-17 with Galactosemia. The primary endpoint, the Global Statistical Test, was a composite sum of change comprised of four endpoints: OWLS-2 Oral Expression (OE), OWLS-2 Listening Comprehension (LC), BASC-3 Behavior Symptoms Index (BSI) and the BASC-3 Activities of Daily Living (ADL). An additional pre-specified sensitivity analysis included cognition in the primary endpoint (NIH-Toolbox Cognition Battery). Additional clinical outcomes were assessed as secondary endpoints, including adaptive skills and tremor. Clinical outcomes were assessed every 6 months by a firewalled independent Data Monitoring Committee (DMC).

- Treatment with govorestat demonstrated consistent and sustained clinical benefit on activities of daily living, behavioral symptoms, cognition, adaptive behavior and tremor.
- While statistical significance defined as a p value of <0.05 was not met on the primary endpoint, systematic improvement over time was demonstrated for the overall primary endpoint (p=0.1030) and for a pre-specified sensitivity analyses including cognition (p=0.0698).
- Individual speech and language components of the primary endpoint were not impacted, which is suspected to be due to lack of progression in the placebo group and concomitant speech therapy received by almost all children in the trial. Of note, patients with severe speech deficits showed a favorable trend towards improvement with govorestat vs. placebo.
- A post-hoc analysis of the global statistical test including behavior and activities of daily living but excluding speech & language components (OWLS-OE and OWLS-LC) demonstrated a highly statistically significant benefit of active treatment vs. placebo (p=0.0205), which strengthened over time.
- Govorestat provided a statistically significant benefit on tremor at 18 months (p=0.0428), as measured by the Archimedes Spiral Drawing Test, and adaptive skills as assessed by the BASC-3 Adaptive Skills Index (p=0.0265).
- Consistent with prior reported data, improvement in galactitol levels was sustained throughout the trial with no impact on Gal-1p or galactose, further establishing the causal role of galactitol in disease pathogenesis.
- Govorestat continued to be safe and well-tolerated in all age groups; there were no treatment-related serious adverse

events (SAEs) reported.

This data will be submitted for presentation at an upcoming medical conference.

The Company believes that there is compelling evidence of clinical efficacy and plans to move toward registration of govorestat for Galactosemia. The trial will be unblinded and placebo patients will be crossed to active treatment.

The Company will host a conference call to discuss the results today at 8:30am Eastern.

To access the conference call, please dial (833) 630-1956 (local) or (412) 317-1837 (international) at least 10 minutes prior to the start time and ask to be joined into the Applied Therapeutics call. A live webcast of the call will be accessible on the Events page under the Investor Relations section of the Applied Therapeutics website at www.appliedtherapeutics.com. A replay will be available on the Company's website approximately two hours after the event.

About Galactosemia
Galactosemia is a rare genetic metabolic disease resulting in an inability to metabolize the simple sugar galactose. Galactose is found in foods, but is also produced endogenously by the body. When not metabolized properly, galactose is converted to the toxic metabolite, galactitol, which causes neurological complications, including deficiencies in speech, cognition, behavior, and motor skills, and also results in juvenile cataracts and ovarian insufficiency (in women). There are approximately 3,000 patients with Galactosemia in the US and 80 new births per year, and approximately 4,000 patients with Galactosemia in the EU and 120 new births per year.

About Govorestat (AT-007)
Govorestat is a central nervous system (CNS) penetrant Aldose Reductase inhibitor (ARI) in development for the treatment of several rare neurological diseases, including Galactosemia, SORD Deficiency, and PMM2-CDG.

In a study in children with Galactosemia aged 2-17, treatment with govorestat demonstrated clinical benefit on activities of daily living, behavioral symptoms, cognition, fine motor skills and tremor. Govorestat also significantly reduced plasma galactitol levels in both adults and children with Galactosemia. Galactitol is a toxic metabolite responsible for tissue damage and long-term complications in Galactosemia.

Govorestat is also being studied in the ongoing Phase 3 INSPIRE trial, which is evaluating the effect of AT-007 vs. placebo in patients with SORD Deficiency on sorbitol reduction as well as clinical outcomes in approximately 50 patients aged 16-55 in the US and Europe. In an interim analysis, govorestat reduced sorbitol by a mean of 52%, or approximately 16,000 ng/ml, over a 90-day period, which was highly statistically significant vs. placebo ($p<0.001$).

Govorestat has received Orphan Medicinal Product Designation from the European Medicines Agency (EMA) for both Galactosemia and SORD Deficiency. Govorestat has also received Orphan Drug Designation from the U.S. Food and Drug Administration (FDA) for the treatment of Galactosemia, PMM2-CDG, and SORD Deficiency; Pediatric Rare Disease designation for Galactosemia and PMM2-CDG; and Fast Track designation for Galactosemia.

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, govorestat, is a novel central nervous system penetrant Aldose Reductase Inhibitor (ARI) for the treatment of CNS rare metabolic diseases, including Galactosemia, SORD Deficiency, and PMM2-CDG. The Company is also developing AT-001, a novel potent ARI, for the treatment of Diabetic Cardiomyopathy, or DbCM, a fatal fibrosis of the heart. 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.

To learn more, please visit www.appliedtherapeutics.com and follow the company on Twitter @Applied_Tx.

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 the strategy, future operations, prospects, plans and objectives of management, including words such as "may," "will," "expect," "anticipate," "plan," "intend," "predicts" 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 Company's plans to request a pre-NDA meeting with the FDA to discuss a potential NDA submission in the second half of 2023; plans to submit a Marketing Authorization Application (MAA) with the European Medicines Agency (EMA) in mid-2023 and (ii) the Company's belief with respect to the clinical benefits of govorestat. 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, market 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 and advance product candidates into, and successfully complete, clinical studies, (vi) our ability to maintain and establish collaborations or obtain additional funding, (vii) our ability to obtain and timing of regulatory approval of our current and future product candidates, (viii) the anticipated indications for our product candidates, if approved, (ix) our expectations regarding the potential market size and the rate and degree of market acceptance of such product candidates, (x) our ability to fund our working capital requirements and expectations regarding the sufficiency of our capital resources, (xi) the implementation of our business model and strategic plans for our business and product candidates, (xii) our intellectual property position and the duration of our patent rights, (xiii) developments or disputes concerning our intellectual property or other proprietary rights, (xiv) our expectations regarding government and third-party payor coverage and reimbursement, (xv) our ability to compete in the markets we serve, (xvi) the impact of government laws and regulations and liabilities thereunder, (xvii) developments relating to our competitors and our industry, (xvii) our ability to achieve the anticipated benefits from the agreements entered into in connection with our partnership with Advanz Pharma and (xiv) 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.

Contacts

Investors:
Maeve Conneighton
(212) 600-1902
appliedtherapeutics@argotpartners.com

Media:
media@appliedtherapeutics.com

Applied Therapeutics, Inc.