Applied Therapeutics Announces Positive Sorbitol Reduction Data From the Ongoing Phase 3 INSPIRE Trial in Sorbitol Dehydrogenase (SORD) Deficiency

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- *The ongoing Phase 3 INSPIRE trial 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 age 16-55 in the US and Europe*
- *AT-007 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)*
- *Company to host conference call to discuss results at 8:30am Eastern*

NEW YORK, Feb. 16, 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 positive sorbitol reduction data from the ongoing global Phase 3 INSPIRE trial. The INSPIRE trial is a Phase 3 double-blind placebo-controlled registrational study evaluating the effect of once-daily oral AT-007 in approximately 50 patients age 16-55 with SORD Deficiency in the US and Europe. SORD Deficiency (also called SORD Neuropathy or CMT-SORD) is a debilitating hereditary axonal neuropathy caused by mutations in the Sorbitol Dehydrogenase gene, leading to an inability to metabolize the sugar sorbitol, and resulting in accumulation of high levels of toxic sorbitol, which causes motor neuron degeneration and loss of mobility and motility. AT-007 (govorestat) is a central nervous system penetrant Aldose Reductase Inhibitor, which blocks conversion of glucose to sorbitol, and has previously been shown to reduce sorbitol levels in an open-label pilot study in patients with SORD Deficiency.

In a pre-specified interim analysis of the ongoing Phase 3 INSPIRE trial, AT-007 reduced sorbitol levels by a mean of approximately 52% (or approximately 16,000ng/ml) over 90 days of treatment (p<0.001 vs. placebo) in patients with SORD Deficiency.

At baseline, the mean blood sorbitol level of SORD patients was approximately 29,000ng/ml, with a range of approximately 22,000ng/ml-38,000ng/ml. In the INSPIRE trial, a baseline cross-sectional analysis of the relationship between sorbitol level, age (or duration of disease) and clinical outcome measures demonstrated a statistically significant correlation between sorbitol level and key clinical outcome measures, including 10-meter-walk/run speed, 4-stair climb speed, and sit-to-stand test (p<0.05). Taken together with the biology of the disease and strong supportive animal model data, the Company believes that compelling data exists demonstrating that sorbitol reduction is reasonably likely to predict effect on clinical outcomes over time. The Company is working with the FDA to determine the appropriate regulatory path forward, as well as data required for an NDA submission, with the shared goal of bringing a safe and effective treatment to patients with SORD Deficiency as expeditiously as possible.

The INSPIRE study will continue in blinded format to the 12-month interim clinical outcomes assessment. If the primary clinical outcome measure (10-meter-walk/run) reaches statistical significance at 12 months, the study will be completed and unblinded. If not, the study will continue in blinded format to 24 months, where clinical outcomes will be assessed again in a final statistical analysis. AT-007 continues to be safe and well tolerated to date.

“The results of the interim sorbitol analysis are quite compelling, and we believe the reduction in sorbitol level with AT-007 is clinically meaningful,” said Riccardo Perfetti, MD, PhD, Chief Medical Officer of Applied Therapeutics.

“The role of sorbitol in disease pathogenesis in SORD Deficiency is clear,” said Michael Shy, MD, Director of the Division of Neuromuscular Medicine at Carver College of Medicine, University of Iowa Medical Center, and Principal Investigator on the INSPIRE Phase 3 trial. “The reduction in sorbitol level seen thus far with AT-007 is impressive, and is predicted to translate into clinical benefit.”

“This is exciting data for patients with SORD Deficiency,” said Amy Gray, CEO of the Charcot-Marie-Tooth Association. “We will continue to work closely with Applied Therapeutics and the patient community to ensure that patients have a safe and effective treatment option available for this devastating disease.”

“SORD Deficiency is a degenerative disease, and there are currently no approved treatment options,” said Allison Moore, Founder and CEO of the Hereditary Neuropathy Foundation. “We are committed to working with Applied Therapeutics, the FDA and the patient community to ensure that all stakeholders understand the urgency surrounding SORD Deficiency and other hereditary neuropathies, and the importance of making treatments available as quickly as possible.”

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.

Additional Information

For additional information that management believes to be useful for investors, please refer to the latest company presentation posted on the Investors & Media section of the Company’s website, www.appliedtherapeutics.com.

About AT-007

AT-007 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 clinical trials, AT-007 significantly reduced plasma galactitol levels vs. placebo in adults and children with Galactosemia. AT-007 is currently being studied in a Phase 3 clinical outcomes trial (ACTION-Galactosemia Kids) in children ages 2-17 with Galactosemia, as well as a long-term open-label study in adults with Galactosemia. In a pilot study in adults with SORD Deficiency, AT-007 significantly reduced blood sorbitol levels. AT-007 is currently being studied in a Phase 3 trial (INSPIRE) investigating biomarker efficacy and clinical outcomes in adults and children 16 years and older with SORD Deficiency. The drug has been generally safe and well tolerated in all clinical studies to date.

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-007, 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 belief that sorbitol reduction is reasonably likely to predict effect on clinical outcomes over time and (ii) the expected timing for completion of the study and submission of an NDA. 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) the impact of the COVID-19 pandemic on the timing and progress of our ongoing clinical trials and our business in general 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.

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