Applied Therapeutics Announces Positive Results from 12-month Interim Analysis of Govorestat (AT-007) in the Ongoing INSPIRE Phase 3 Trial in Sorbitol Dehydrogenase (SORD) Deficiency

February 15, 2024

Interim primary endpoint met; Statistically significant correlation of sorbitol with the CMT-FOM clinical outcome composite (p=0.05)

Sustained, statistically significant reduction in sorbitol in govorestat-treated patients vs. placebo (p<0.001)

Highly statistically significant effects on the CMT Health Index (CMT-HI) patient reported outcome measure (p=0.01), with benefit of govorestat on categories of lower limb function, mobility, fatigue, pain, sensory function, and upper limb function

Company plans to request a pre-NDA meeting with the neurology division of the US FDA regarding potential approval based on current data

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

NEW YORK, Feb. 15, 2024 (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 interim 12-month results from the ongoing Phase 3 INSPIRE trial, in which the primary endpoints and several key secondary endpoints were achieved. The INSPIRE trial is a Phase 3 double-blind placebo-controlled registrational study evaluating the effect of once-daily (QD) oral govorestat (AT-007) in 56 patients aged 16-55 with SORD Deficiency in the US and Europe.

SORD Deficiency 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. Govorestat is a central nervous system penetrant Aldose Reductase Inhibitor, which blocks the conversion of glucose to sorbitol, and has previously been shown to reduce sorbitol levels in patients with SORD Deficiency.

The objective of this pre-specified, 12-month interim analysis was to evaluate early indicators of govorestat treatment effect in order to inform future regulatory discussions and support a potential New Drug Application (NDA) submission, due to the urgent need for treatment and absence of any other options for patients with SORD Deficiency. The 12-month interim analysis was comprised of a clinical efficacy primary endpoint based on correlation of sorbitol with composite clinical outcome measures, and a pharmacodynamic (PD) biomarker primary endpoint based on sorbitol reduction.

Interim Analysis Results:

- Demonstrated statistically significant correlation between sorbitol level and the prespecified CMT-FOM composite clinical endpoint (10-meter walk-run test, 4 stair climb, sit to stand test,6-minute walk test and dorsiflexion) (p=0.05).
- Govorestat treatment provided sustained reduction in sorbitol level in patients with SORD Deficiency over 12 months of treatment, which was statistically significant compared to placebo (p<0.001).
- Govorestat treatment also resulted in a highly statistically significant effect (p=0.01) on the CMT Health Index (CMT-HI), an important patient-reported outcome measure of disease severity and well-being, which was a secondary endpoint in the study. Aspects of the CMT-HI that demonstrated a treatment effect included lower limb function, mobility, fatigue, pain, sensory function, and upper limb function.
- Govorestat was safe and well tolerated, with similar incidence of adverse events between active and placebo-treated groups.

We believe the results from the 12-month interim analysis confirm the role of sorbitol as a key driver of disease severity and progression over time. Clinical outcomes of the ongoing INSPIRE trial are expected to be assessed again at 24 months, where the 10-meter walk run test serves as the primary clinical efficacy endpoint. The Company plans to discuss a potential NDA submission with the U.S. Food and Drug Administration (FDA) based on the clinical data to date.

“Our commitment to bringing first of their kind therapies to rare disease indications with no existing treatment options is at the core of our work,” said Shoshana Shendelman, PhD, Founder and CEO of Applied Therapeutics. “We are excited by the prospect of providing patients with SORD Deficiency with a treatment option that has the potential to slow disease progression and the consistent benefit demonstrated by govorestat.”

“We are thrilled by the results of this 12-month interim analysis, which demonstrate govorestat’s effectiveness in reducing sorbitol levels and improving key functional measures and patient reported outcomes in SORD Deficiency, including lower limb function, upper limb function, fatigue and pain,” said Riccardo Perfetti, MD, PhD, Chief Medical Officer of Applied Therapeutics. “We look forward to meeting with regulatory agencies regarding a path to potential approval based on this data, and endeavor to bring this important treatment to patients as quickly as possible.”

“As a neurologist and neuromuscular specialist, I am delighted to see such strong results from just 12 months of treatment with govorestat for this debilitating disease with no existing treatment options available,” 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 results from this interim analysis

have exceeded my expectations, with a statistically significant impact on how patients feel and function, as measured by the CMT-HI patient reported outcome measure. The ability to reduce sorbitol levels, which we believe to be the pathogenic cause of damage in these patients, coupled with standardized metrics of patient function and well-being are strong indicators of treatment benefit."

Conference Call Information

Applied Therapeutics will host a conference call and webcast on Thursday, February 15, 2024, at 8:30 a.m. ET to discuss the interim analysis of govorestat for the treatment of SORD Deficiency. To access the conference call, please dial +1(844) 481-2912 (local) or +1(412) 317-0695 (international) at least 10 minutes prior to the start of the call 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 of the webcast will be available for 90 days on the Investors section of Applied Therapeutics' website.

About Sorbitol Dehydrogenase (SORD) Deficiency

Sorbitol Dehydrogenase Deficiency (SORD Deficiency) is a rare, progressive, debilitating hereditary neuropathy that affects peripheral nerves and motor neurons. SORD Deficiency is one of the most common forms of recessive hereditary neuropathy and affects approximately 3,300 patients in the U.S. and 4,000 patients in Europe. The disease is caused by a lack of the enzyme sorbitol dehydrogenase, responsible for the metabolism of sorbitol, which causes sorbitol to accumulate at high levels and become toxic to the body. Intracellular sorbitol accumulation results in significant disability, loss of sensory function, neuromuscular dysfunction, and decreased mobility.

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.

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 pre-NDA meeting with the neurology division of the FDA regarding potential approval based on the clinical data to date and (ii) the timing of assessment of clinical outcomes of the INSPIRE trial any potential submission. 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, (xviii) 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.

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