Applied Therapeutics Announces Topline Results from the ARISE-HF Phase 3 Study of AT-001 in Diabetic Cardiomyopathy

January 4, 2024

AT-001 (caficrestat) demonstrated a strong trend in stabilizing cardiac functional capacity, while the placebo group declined over 15 months

AT-001 treatment resulted in a statistically significant difference in cardiac functional capacity in a prespecified subgroup of patients not receiving concomitant treatment with an SGLT2 or GLP-1 (p=0.040) and prevented clinically significant worsening (odds ratio 0.56; p=0.035)

AT-001 demonstrated a favorable safety and tolerability profile

NEW YORK, Jan. 04, 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 the topline results of the ARISE-HF Phase 3 trial of AT-001 (caficrestat) in patients with Diabetic Cardiomyopathy (DbCM) at high risk of progression to overt heart failure.

The primary endpoint of the study was stabilization or improvement in cardiac functional capacity as measured by Peak VO_2 in patients treated with AT-001 1500mg twice daily (BID) as compared to placebo. The placebo-treated group declined by a mean of -0.31 ml/kg/min over 15 months of treatment, while the AT-001 1500mg BID group remained primarily stable, with a mean change of -0.01 ml/kg/min over 15 months. While a trend favored active treatment, the difference between active and placebo treated groups (0.30 ml/kg/min) was not statistically significant (p=0.210).

The ARISE-HF study evaluated the treatment effect of AT-001 as an add-on to diabetes standard of care therapies. Approximately 38% of study subjects were on SGLT2 or GLP-1 therapies for treatment of diabetes, while 62% were not. In a pre-specified subgroup analysis of the primary endpoint in patients not concomitantly treated with SGLT2 or GLP-1 therapies, the placebo group declined by a mean of -0.54 ml/kg/min, while the 1500mg BID AT-001 treated group improved by a mean of 0.08 ml/kg/min over 15 months of treatment, with a difference between groups of 0.62 ml/kg/min (p=0.040). Additionally, in this subgroup analysis, the number of patients who experienced a clinically significant worsening in cardiac functional capacity of 6% or more was substantially higher in the placebo group (46%) as compared to the 1500mg BID AT-001 treated group (32.7%), odds ratio 0.56 (p=0.035). A 6% change in cardiac functional capacity has been shown to predict long-term survival and hospitalization for heart failure. The effect of AT-001 was dose dependent, with the low dose (1000mg BID) demonstrating an intermediate effect between the high dose and placebo.

AT-001 was generally safe and well tolerated, with no substantial differences in serious adverse events between AT-001 treated groups as compared to placebo (14.3% placebo; 12.3% AT-001 1000mg BID; 17.3% AT-001 1500mg BID), no substantial differences in treatment emergent adverse events (79.1% placebo; 81.6% AT-001 1000mg BID; 81% AT-001 1500mg BID) and low incidence of treatment-related discontinuations (3.9% placebo; 9.6% AT-001 1000mg BID; 9.5% AT-001 1500mg BID).

Full study results will be presented at an upcoming medical conference, along with results of the Diabetic Peripheral Neuropathy sub-study, which are still being analyzed.

“AT-001 stabilized cardiac functional capacity as compared to placebo, and prevented clinically significant worsening of disease, an effect which was strengthened in patients not on concomitant treatment with an SGLT2 or GLP-1,” said Riccardo Perfetti, MD, PhD, Chief Medical Officer of Applied Therapeutics. “Given its favorable safety and tolerability profile and oral dosing, we believe that AT-001 represents an important potential tool for physicians in treatment of DbCM patients. We thank the patients and families who participated in the ARISE-HF study and made this important work possible.”

“There are currently no therapies approved for DbCM, and a high unmet need exists for a treatment that can prevent worsening of the condition and progression to overt heart failure,” said James Januzzi, M.D., Principal investigator of the ARISE-HF study and Hutton Family Professor of Cardiology at Massachusetts General Hospital. “Stabilization of cardiac functional capacity is an exciting finding, since declining functional capacity is a leading indicator of progression to overt heart failure.”

Given these encouraging results, the Company plans to focus on identifying an appropriate path forward through partnering in order to bring AT-001 to DbCM patients. Current resources are expected to be focused on the development, regulatory and commercial preparations for the govorestat rare disease program. The Company submitted a New Drug Application (NDA) to the U.S. Food and Drug Administration (FDA) in December 2023 for govorestat for the treatment of Classic Galactosemia. The Marketing Authorization Application (MAA) was validated and accepted for review by the European Medicines Agency (EMA) in December 2023.

About AT-001 (Caficrestat)

AT-001 (caficrestat) is an investigational oral, novel, potent Aldose Reductase inhibitor in Phase 3 clinical development for the treatment of Diabetic Cardiomyopathy. The global ARISE-HF Phase 3 study evaluated the ability of AT-001 to improve or prevent worsening of disease, as measured by changes in cardiac functional capacity, in 675 patients with DbCM at high risk of progression to overt heart failure. The study demonstrated a positive impact of AT-001 treatment, which was statistically significant in a prespecified subgroup of patients not on concomitant treatment with an SGLT2 or GLP-1 inhibitor. AT-001 has been previously studied in a Phase 1/2 study in approximately 120 patients with type 2 diabetes, a subset of which had DbCM.

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 the Company's (i) plan to focus on identifying an appropriate path forward through partnering in order to bring AT-001 to DbCM patients and (ii) expectation for current resources to be focused on the development, regulatory and commercial preparations for the govorestat rare disease program. 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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