Applied Therapeutics Announces Full Enrollment in the Registrational Phase 3 ARISE-HF Trial of AT-001 in Diabetic Cardiomyopathy

October 25, 2022

- *ARISE-HF is a global registrational study in 675 patients with Diabetic Cardiomyopathy (DbCM), evaluating the potential of AT-001 to improve or prevent worsening of cardiac function vs. placebo*
- *Primary study endpoint is cardiac functional capacity (measured by Peak VO_2) at 15 months*
- *DbCM is a form of heart failure affecting approximately 20% of Type 2 Diabetes patients (~6M patients in the US and ~5M in EU), which represents a significant commercial market opportunity*
- *There are currently no treatments approved for DbCM, and AT-001 has the potential to be the first therapy approved*

NEW YORK, Oct. 25, 2022 (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 full enrollment in the Phase 3 registrational ARISE-HF trial, studying AT-001, a selective Aldose Reductase inhibitor, in patients with Diabetic Cardiomyopathy (DbCM).

The ARISE-HF study is a randomized double-blind placebo-controlled Phase 3 registrational trial. The study enrolled 675 patients with DbCM at high risk of progression to overt heart failure in the US, EU, UK, Canada, Australia and Hong Kong. The primary endpoint is cardiac functional capacity (as measured by Peak VO_2) at 15 months of treatment. Topline data is expected around year-end 2023 or early 2024, and if positive, the company plans to submit for potential regulatory approval. Patients will continue in blinded format for an additional 12 months of treatment (up to 27 months total) to produce secondary endpoint data on progression to overt heart failure, hospitalization, morbidity and mortality, which is not anticipated for regulatory approval, but will support long-term market access. The ARISE-HF trial also includes an embedded sub-study in patients with both DbCM and Diabetic Peripheral Neuropathy evaluating the impact of AT-001 on neuropathy progression.

AT-001 is a novel, potent, highly selective Aldose Reductase inhibitor. Aldose Reductase is a well validated molecular target, and over-activation of this enzyme is known to result in many diabetic complications, including Diabetic Cardiomyopathy and Diabetic Peripheral Neuropathy. In the ARISE-HF study, AT-001 is dosed twice daily in oral capsules as an add-on to other Type 2 Diabetes standard of care medications. AT-001 is safe and well tolerated to date, with approximately 80 patients having already completed the primary endpoint at 15 months of treatment in the study.

Diabetic Cardiomyopathy is a specific form of heart failure affecting approximately 20% of patients with Type 2 Diabetes (or 1 in 5 people living with diabetes). There are no treatments approved for DbCM to date, and AT-001 has the potential to be the first therapy approved to treat this devastating disease. DbCM is diagnosed via cardiac echo abnormalities or elevated cardiac biomarkers (via a simple blood test) in the absence of coronary artery disease or uncontrolled hypertension. Patients with DbCM have decreased cardiac functional capacity at the time of diagnosis, leading to early symptoms of disease, which continues to progressively worsen over time, resulting in overt heart failure and death.

“Diabetic Cardiomyopathy is a devastating disease that we see every day in clinical practice, but until now have had no treatments to offer patients,” said James Januzzi, MD, Hutter Family Professor of Medicine at Harvard Medical School, cardiologist at Massachusetts General Hospital and Lead Investigator on the ARISE-HF trial. “The ARISE-HF study is a huge step forward in advancing AT-001 as a potential treatment for patients with DbCM. This could be life-saving for millions of people. The global study team is an impressive group of leaders in cardiology and diabetology, and I’m excited to be a part of such a ground-breaking trial.”

“Diabetic Cardiomyopathy is a major health issue, which continues to expand with increasing prevalence of Type 2 Diabetes,” said Riccardo Perfetti, MD, PhD, Chief Medical Officer of Applied Therapeutics. “We look forward to the study readout next year, and the potential to offer the first approved treatment for DbCM to patients.”

About AT-001
AT-001 is an investigational oral, novel, potent Aldose Reductase inhibitor in Phase 3 clinical development for the treatment of Diabetic Cardiomyopathy. The global ARISE-HF study is currently ongoing, and is designed to evaluate 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. 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, 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 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) the timing of topline data, which is expected around year-end 2023 and (ii) the company’s plans to submit for potential regulatory approval. 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.

Contacts:

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

Media:
media@appliedtherapeutics.com

Applied Therapeutics, Inc.