Milestone Pharmaceuticals Announces Late-Breaker Oral Presentation of NODE-301 Data at ACC.21

May 17, 2021

- Statistically Significant Improvements in PSVT-Associated Symptoms and Less ER Visits Observed in Patients Treated with Etripamil Compared to Placebo in the NODE-301 Trial -

- Data Presented at the American College of Cardiology's 70th Annual Scientific Session -

MONTREAL and Charlotte, N.C., May 17, 2021 /PRNewswire/ -- Milestone Pharmaceuticals Inc. (Nasdaq: MIST), a biopharmaceutical company focused on the development and commercialization of innovative cardiovascular medicines, today announced the presentation of data related to key secondary endpoints from its Phase 3, multicenter, randomized, double-blind, placebo-controlled NODE-301 trial of etripamil nasal spray, the Company's novel investigational, short-acting calcium channel blocker, in patients with paroxysmal supraventricular tachycardia (PSVT). The oral presentation, titled "Etripamil Nasal Spray Relieves Symptoms And Reduces Emergency Room Interventions In Patients With Paroxysmal Supraventricular Tachycardia (PSVT): Analysis Of Clinical Outcomes In The Node-301 Trial", was featured during a late-breaker session at the American College of Cardiology's 70th Annual Scientific Session (ACC.21) that was held in a virtual format. A copy of the presentation will be available in the Publications section of Milestone's website.

"With current standards of care for the acute termination of PSVT restricted to the burdensome and costly acute care setting, this condition represents an area of particularly high unmet need," said Joseph Oliveto, President and Chief Executive Officer of Milestone Pharmaceuticals. "Etripamil holds the potential to enable patients to treat their episodes in the at-home setting and ultimately take control of their condition. We remain focused on the execution of our ongoing Phase 3 program and our vision to help patients suffering from episodes of SVT."

"Data support the potential for etripamil to improve the patient's experience, both decreasing common PSVT symptoms and reducing the need for emergency room visits relative to placebo," said Bruce Stambler, MD, FHRS, Piedmont Heart Institute, Atlanta, GA, and lead author of the presentation. "Once approved by FDA, etripamil could potentially serve as an effective, meaningful addition to the currently limited PSVT treatment armamentarium."

The NODE-301 trial, which enrolled a total of 431 patients across 65 sites in the U.S. and Canada, was an event-driven Phase 3 efficacy trial of etripamil versus placebo for terminating supraventricular tachycardia (SVT) episodes in the at-home setting. Data presented at ACC.21 build on previously reported data from the NODE-301 trial that showed statistically significant improvements in favor of etripamil over placebo in the important secondary endpoint of patient reported treatment satisfaction, as measured by a treatment satisfaction questionnaire for medication (TSQM-9), including global satisfaction and effectiveness scores, with questions addressing the relief of symptoms commonly associated with an episode of SVT. Treatment effectiveness ($p=0.001$) and global satisfaction ($p=0.007$) scores were greater in patients treated with etripamil than with placebo. Etripamil also had higher scores than placebo related to relief of specific symptoms associated with PSVT, including rapid pulse ($p=0.002$), palpitations ($p<0.001$), shortness of breath ($p=0.008$), dizziness ($p=0.012$), and anxiety ($p=0.006$). In addition, a 51% reduction ($p=0.051$) in the need for an emergency room (ER) visit and a 47% prolongation ($p<0.05$) in time to ER intervention was observed in patients who received etripamil versus placebo.

Enrollment is now underway in the Company's pivotal Phase 3 RAPID trial of etripamil nasal spray in patients with PSVT. This trial, which is targeting a total of 180 adjudicated PSVT events, is expected to randomize approximately 500 patients 1:1 to receive either etripamil nasal spray or placebo. To help maximize the potential treatment effect of etripamil, patients will be directed to administer a second dose of study drug if they do not experience symptom relief within 10 minutes of administration of the first dose of study drug. Under an updated statistical analysis plan, the primary efficacy analysis for both the RAPID trial and the already-completed NODE-301 trial will be time to conversion of SVT over the first 30 minutes following initial study drug administration, with a target p-value of less than 0.05 for each trial. The RAPID and NODE-301 trials could potentially serve to fulfill the efficacy requirement for a future New Drug Application (NDA) for etripamil in patients with PSVT.

About NODE-301

The NODE-301 trial is a Phase 3, multicenter, randomized, double-blind, placebo-controlled trial of etripamil, the Company's lead investigational product, etripamil. The study is designed for a population of those PSVT patients who historically experience SVT episodes lasting 20 minutes or longer or episodes requiring termination in the emergency department. Following an in-office test dose of etripamil, 97.5% of patients were randomized (2:1) to receive either 70 mg of etripamil or placebo. Upon onset of PSVT symptoms, patients applied a wireless cardiac monitor to their chest to record heart rhythm, performed a vagal maneuver, and, if symptoms persisted, administered study drug. Of the 198 patient-reported events for which study drug was administered, a total of 156 were confirmed to be SVT events by a central independent adjudication committee and used to assess the study's efficacy endpoints.

The primary endpoint of the NODE-301 study is time to conversion of an SVT episode to sinus rhythm after the administration of study drug, as confirmed by a central independent adjudication committee. The NODE-301 trial did not meet its primary endpoint. Secondary study endpoints include relief of symptoms commonly associated with an episode of SVT such as heart palpitations, chest pain, anxiety, shortness of breath, dizziness, or fainting, and rating of treatment satisfaction questionnaire for medication (TSQM).

About Paroxysmal Supraventricular Tachycardia

Paroxysmal supraventricular tachycardia (PSVT) is a rapid heart rate condition characterized by intermittent episodes of supraventricular tachycardia (SVT) that start and stop suddenly and without warning which affects approximately two million Americans. Episodes of SVT are often associated with symptoms including palpitations, sweating, chest pressure or pain, shortness of breath, sudden onset of fatigue, lightheadedness or dizziness,

fainting, and anxiety. Certain calcium channel blockers have long been approved for the treatment of PSVT as well as other cardiac conditions. However, calcium channel blockers approved for the termination of SVT episodes must be administered intravenously under medical supervision, usually in an emergency department or other acute care setting.

About Etripamil

Etripamil, Milestone's lead investigational product, is a novel calcium channel blocker designed to be a rapid-response therapy for episodic cardiovascular conditions. As a nasal spray that is intended to be self-administered by the patient, etripamil has the potential to shift the current treatment experience for many patients from the emergency department to the at-home setting. Milestone is conducting a comprehensive development program for etripamil, with Phase 3 trials ongoing in paroxysmal supraventricular tachycardia (PSVT) and a Phase 2 proof-of-concept trial is now underway in patients with atrial fibrillation and rapid ventricular rate (AFib-RVR).

About Milestone Pharmaceuticals

Milestone Pharmaceuticals Inc. (Nasdaq: MIST), is a biopharmaceutical company focused on the development and commercialization of innovative cardiovascular medicines. Milestone's lead product candidate etripamil is currently in a Phase 3 clinical-stage program for the treatment of paroxysmal supraventricular tachycardia (PSVT) and in a Phase 2 proof-of-concept trial for the treatment of patients with atrial fibrillation and rapid ventricular rate (AFib-RVR). Milestone Pharmaceuticals operates in Canada and the United States. For more information, visit www.milestonepharma.com and follow the Company on Twitter at @MilestonePharma.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Words such as "may," "will," "expect," "plan," "anticipate," "estimate," "potential," "intend" and similar expressions (as well as other words or expressions referencing future events, conditions or circumstances) are intended to identify forward-looking statements. These forward-looking statements are based on Milestone's expectations and assumptions as of the date of this press release. Each of these forward-looking statements involves risks and uncertainties. Actual results may differ materially from these forward-looking statements. Forward-looking statements contained in this press release include statements regarding the potential of etripamil as a promising therapy for PSVT patients, the design, progress, timing, scope and results of the RAPID trial, and Milestone's ability to execute on the remainder of the PSVT program. Important factors that could cause actual results to differ materially from those in the forward-looking statements include, but are not limited to, the risks inherent in biopharmaceutical product development and clinical trials, including the lengthy and uncertain regulatory approval process, uncertainties related to the timing of initiation, enrollment, completion and evaluation of clinical trials, and whether the clinical trials will validate the safety and efficacy of etripamil for PSVT or other indications, among others, as well as risks related to pandemics and public health emergencies, including those related to COVID-19, and risks related the sufficiency of Milestone's capital resources and its ability to raise additional capital. These and other risks are set forth in Milestone's filings with the U.S. Securities and Exchange Commission, including in its annual report on Form 10-K for the year ended December 31, 2020, under the caption "Risk Factors." Except as required by law, Milestone assumes no obligation to update any forward-looking statements contained herein to reflect any change in expectations, even as new information becomes available.

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