Milestone Pharmaceuticals Announces Presentation of Data from Analysis of Etripamil Nasal Spray in Patients Experiencing Atrial Fibrillation with Rapid Ventricular Rate

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- *Self-administration of etripamil in patients experiencing AFib-RVR episodes resulted in a substantial reduction in ventricular rate which was sustained over 60 minutes*

- *Data featured in an oral session at the Heart Rhythm 2023 Annual Meeting*

- *Company to host virtual KOL conference call and webcast to discuss etripamil development for the treatment of AFib-RVR today at 8:00 a.m. ET*

MONTREAL and CHARLOTTE, N.C., May 22, 2023 /PRNewswire/ -- Milestone Pharmaceuticals Inc. (Nasdaq: MIST), a biopharmaceutical company focused on the development and commercialization of innovative cardiovascular medicines, today announced promising data from an ad hoc analysis of a subset of patients experiencing atrial fibrillation with rapid ventricular rate (AFib-RVR) in the NODE-303 study, which evaluated etripamil, the Company's investigational calcium channel blocker, in patients with paroxysmal supraventricular tachycardia (PSVT). The data were featured during an oral session at the Heart Rhythm 2023 Annual Meeting.

"Data from this unplanned analysis represent the first direct clinical evidence of the impact of etripamil on heart rate in patients experiencing an event of AFib-RVR," said Joseph Oliveto, President and Chief Executive Officer of Milestone Pharmaceuticals. "We look forward to sharing topline results from our ongoing Phase 2, placebo-controlled study in patients with AFib-RVR, which we expect to report in the second half of 2023. We are firmly committed to our mission of unlocking the full potential of etripamil to serve as a self-administered, on-demand treatment for patients facing episodic cardiovascular conditions associated with rapid heart rate."

"AFib-RVR frequently causes severe symptoms and anxiety. Slowing the heart rate quickly can offer considerable relief from both symptoms and associated concerns. Etripamil nasal spray, an investigational treatment, would be the only self-administered medication available which suits this purpose," said lead author Paul Dorian, MD, MSC, Professor of Medicine & Pharmacology, University of Toronto; Staff Cardiac Electrophysiologist, St. Michael's Hospital. "These initial results are encouraging and support further clinical development of etripamil and highlight the potential of etripamil to offer patients a valuable option to manage their AFib-RVR episodes outside of the stressful and costly acute-care setting."

Overview of Data

The open-label Phase 3 NODE-303 global safety study evaluated self-administered etripamil in patients with PSVT. Based on expert review of ambulatory electrocardiogram (ECG) data collected for 1024 treated episodes, 21 of the episodes in 18 patients were determined to be attributed to AFib-RVR rather than PSVT.

Of the 21 AFib-RVR episodes analyzed, 17 had a ventricular rate (VR) ≥110 bpm at baseline. After self-administering etripamil, average-reductions in VR from baseline were determined throughout the 60-minute post-administration window, with 6 episodes converting to sinus rhythm. Results demonstrate a maximum reduction (± SEM) of -27.4 ± 6.1 bpm at 22 minutes, and -16.2 ± 5.6 bpm at 60 minutes.

The safety and tolerability data from the analysis of these AFib-RVR episodes were consistent with those observed across prior studies in PSVT. The most common treatment-related adverse events (AEs) were related to the nasal administration site. Overall, the majority of AEs were reported as mild to moderate, and there were no reported serious AEs related to etripamil. Results of this ad hoc analysis may be limited due to time of study-drug administration variability related to the start of ECG recording and enrollment of patients with an existing history of supraventricular tachycardia, which may not be representative of the entire AFib population.

Enrollment continues in ReVeRA, Milestone's Phase 2 double-blind, placebo-controlled, proof-of-concept trial of etripamil nasal spray in emergency-department patients experiencing AFib-RVR. The trial, in which patients are randomized 1:1 to receive either 70 mg of etripamil or placebo, is designed to assess the safety and efficacy of etripamil nasal spray to reduce elevated ventricular rates in patients with symptomatic AFib-RVR. The primary endpoint will assess reduction in ventricular rate, with key secondary endpoints including the time to achieve the maximum reduction in rate and duration of the effect. Milestone expects to report topline data from this trial in the second half of 2023.

Conference Call and Webcast

The Company will host a virtual Key Opinion Leader (KOL) event today, Monday, May 22, 2023 at 8:00 a.m. ET. The event will feature a review of the HRS data, as well as an overview of AFib-RVR, the current treatment landscape, characteristics of etripamil, and commentary on next steps for Milestone's etripamil clinical development program. Joining the Company's management team will be Paul Dorian, MD, MSC, Professor of Medicine, Departments of Medicine and Pharmacology, University of Toronto; Staff Cardiac Electrophysiologist, St. Michael's Hospital, and Jonathan P. Piccini, MHS, MD, FHRS, Professor of Medicine & Population Health, Director, Cardiac Electrophysiology, Duke University & Duke Clinical Research Institute.

To access a live or recorded webcast of the KOL event and accompanying slides, please visit the News & Events section of Milestone's website at www.milestonepharma.com. To access the live call by phone, dial (877) 870-4263 (domestic) or (412) 317-0790 (international) and ask to be connected to the Milestone Pharmaceuticals call. The recorded webcast and slides will be available on the Company's website following the call.

About Atrial Fibrillation with Rapid Ventricular Rate

Atrial fibrillation (AFib) is a common arrhythmia marked by an irregular and often rapid heartbeat. AFib is estimated to affect five million patients in the United States, a prevalence projected by the Centers for Disease Control to increase to twelve million patients by 2030. Atrial fibrillation with rapid ventricular rate (AFib-RVR) is a condition that many patients with AFib experience and includes episodes of abnormally high heart rate, often with

symptoms of palpitations, shortness of breath, dizziness, and weakness. Oral calcium channel blockers and/or beta blockers are used to reduce the heart rate in this condition. When AFib-RVR occurs, symptoms are often burdensome enough to cause patients to seek acute care in the emergency department, where standard-of-care procedures include intravenous administration of calcium channel blockers or beta blockers, or electrical cardioversion, under medical supervision. Milestone's initial market research indicates that 30-40% of patients with AFib experience one or more symptomatic episodes of RVR per year that require treatment, suggesting a target addressable market of approximately three to four million patients in 2030 for etripamil in patients with AFib.

About Paroxysmal Supraventricular Tachycardia

Paroxysmal Supraventricular Tachycardia (PSVT) is a highly symptomatic and impactful heart arrhythmia characterized by unpredictable attacks of a racing heart that afflicts approximately two million Americans. Symptoms of PSVT, including palpitations, chest pressure, and shortness of breath are often debilitating, causing the patient to stop their current activities or avoid pursuits altogether. The impact and morbidity from an attack can be especially detrimental in patients with underlying cardiovascular or medical conditions, such as heart failure, obstructive coronary disease, or dehydration. The uncertainty of when an episode of SVT will strike or how long it will persist can provoke anxiety in patients, which can have a negative impact on their day-to-day life. Many doctors are unsatisfied by the lack of effective treatment options besides a prolonged, unpleasant, and costly trip to the emergency department or, for some patients, an invasive ablation procedure.

About Etripamil

Etripamil, Milestone's lead investigational product, is a novel calcium channel blocker nasal spray. It is designed to be a rapid-response therapy that is self-administered by the patient, without the need for direct medical oversight, and is being developed for elevated and often highly symptomatic heart rate attacks associated with PSVT and AFib-RVR. If approved, etripamil is intended to provide health care providers with a new tool to enable virtual care and patient self-management, and to impart upon the patient a greater sense of control over their condition. Milestone is conducting a comprehensive development program for etripamil, with Phase 3 trials completed and an NDA soon to be submitted in the third quarter of 2023 in paroxysmal supraventricular tachycardia (PSVT). Milestone also has a Phase 2 proof-of-concept trial that is ongoing in patients experiencing atrial fibrillation with 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 recently completed its Phase 3 clinical-stage program for the treatment of paroxysmal supraventricular tachycardia (PSVT) and is in a Phase 2 proof-of-concept trial for the treatment of patients with atrial fibrillation with rapid ventricular rate (AFib-RVR). Milestone Pharmaceuticals operates in Canada and the United States. For more information, visit www.milestonepharma.com and follow Milestone 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 "believe," "continue," "could," "demonstrate," "designed," "develop," "estimate," "expect," "may," "pending," "plan," "potential," "progress," "will" 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 to serve as a promising therapy for PSVT patients; the timing of the NDA submission for etripamil nasal spray; the potential for clinical trial data from the Phase 2 ReVeRA program in the second half of 2023 etripamil's further clinical development and potential to offer patients a valuable option to manage their AFib-RVR episodes; and our ability to continue enrollment in ReVeRA. 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, evaluation and results of our clinical trials; risks and uncertainty related to the complexity inherent in cleaning, verifying and analyzing trial data; and whether the clinical trials will validate the safety and efficacy of etripamil for PSVT or other indications, among others, general economic, political, and market conditions, including deteriorating market conditions due to investor concerns regarding inflation and Russian hostilities in Ukraine and overall fluctuations in the financial markets in the United States and abroad, risks related to pandemics and public health emergencies, and risks related the sufficiency of Milestone's capital resources and its ability to raise additional capital in the current economic climate. 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, 2022, under the caption "Risk Factors," as such discussion may be updated from time to time by subsequent filings it may make with the U.S. Securities & Exchange Commission. 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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