Milestone Pharmaceuticals Announces Publication of Results from Phase 3 RAPID Clinical Trial of Etripamil Nasal Spray in Patients with PSVT in The Lancet

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- *Primary endpoint met, with 64.3% of patients who self-administered etripamil converting from supraventricular tachycardia to sinus rhythm within 30 minutes compared to 31.2% on placebo (HR = 2.62, p<0.001)*

- *Significant improvement in multiple symptoms of supraventricular tachycardia in patients receiving etripamil compared to placebo*

- *Safety and tolerability profile of repeat-dose regimen consistent with previously studied single-dose self-administration and supportive of NDA submission*

- *NDA submission for etripamil in patients with PSVT on track for 3Q23*

MONTREAL and CHARLOTTE, N.C., June 20, 2023 /PRNewswire/ -- Milestone Pharmaceuticals Inc. (Nasdaq: MIST), a biopharmaceutical company focused on the development and commercialization of innovative cardiovascular medicines, today announced the publication of results in *The Lancet* from the Phase 3 RAPID clinical trial evaluating etripamil nasal spray, the Company's investigational calcium channel blocker, in patients with paroxysmal supraventricular tachycardia (PSVT).

"PSVT places a significant burden on both patients and the healthcare system, with currently available acute therapies often marked by low effectiveness or undesirable side effects, and limited to the costly and inconvenient acute-care setting," said Bruce Stambler, M.D., Lead Author, Piedmont Heart Institute, Atlanta, GA. "With patients experiencing PSVT on the etripamil regimen having a much faster and greater degree of conversion to sinus rhythm compared to placebo, these results from the RAPID trial strongly support the potential for etripamil to offer patients a rapid, effective, and safe at-home intervention to manage their episodes whenever they occur."

"Publication of these results in *The Lancet*, a high-impact, international journal, underscores our confidence in the potential for etripamil to deliver value to the healthcare system through a reduction in utilization of emergency- and acute-care services and, importantly, to have a meaningful impact on the patients burdened with this unpredictable and serious condition," said David Bharucha, M.D., Ph.D., F.A.C.C., Chief Medical Officer of Milestone Pharmaceuticals. "We believe that self-administered etripamil could serve as the first approved supraventricular tachycardia treatment for use outside of the healthcare setting. We remain on track for an NDA submission in the third quarter of 2023."

The publication, titled "*Self-administered Intranasal Etripamil Using a Symptom-Prompted, Repeat-Dose Regimen for Atrioventricular-Nodal Dependent Supraventricular Tachycardia: The Randomised, Controlled RAPID Trial*," is available via the following link: https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(23)00776-6/fulltext.

Phase 3 RAPID Trial

The multi-center, randomized, double-blind, placebo-controlled RAPID trial enrolled 706 patients across clinical sites in North America and Europe. Patients were randomized 1:1 to self-administer a nasal spray of etripamil or placebo, as prompted by symptoms of PSVT, without medical monitoring and when an episode occurred in the course of daily activities. To maximize the potential treatment effect of etripamil, patients who did not experience PSVT-symptom relief within 10 minutes were directed to self-administer a repeat dose of study drug. Pre- and post-drug ambulatory electrocardiographic (ECG) data were independently adjudicated in this event-driven trial.

Key findings from the trial featured in the publication, which support the potential self-administration of etripamil outside of the healthcare setting, are summarized below:

- The RAPID trial achieved its primary endpoint, with patients taking etripamil demonstrating a highly statistically significant and clinically meaningful difference in time to supraventricular tachycardia conversion compared to placebo. A Kaplan Meier analysis showed a statistically significantly greater proportion of patients who took etripamil converted within thirty minutes compared to placebo (64.3% vs. 31.2%; hazard ratio [HR] = 2.62; 95% CI 1.66, 4.15; p<0.001).
- Significant reductions in time to conversion in patients who took etripamil were evident early and were durable, persisting throughout the observation window of the study compared to placebo, with a median time to conversion of 17.2 minutes (95% CI= 13·4, 26·5) for patients treated with etripamil versus 53.5 minutes (95% CI= 38.7, 87.3) for patients treated with placebo.
- Data demonstrated statistically significant improvement in multiple defined symptoms of PSVT in patients receiving etripamil compared to placebo, using a patient-reported outcome (PRO) questionnaire.
- Reduction in emergency-department visits and, for example, need for intravenous treatments, was observed, though not with statistical significance in this dataset alone.
- The safety and tolerability data from the RAPID trial continue to support the potential self-administration of etripamil, with findings consistent with those observed in prior trials. The most common randomized treatment emergent adverse events (RTEAEs), which are adverse events (AEs) that occurred within 24 hours of study drug administration, were related to the nasal administration site. Overall, the majority of RTEAEs were reported as mild (68%) to moderate (31%). There were no reported serious AEs related to etripamil.

As previously communicated, Milestone plans to submit a New Drug Application (NDA) filing in the third quarter of 2023.

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 potential for self-administered etripamil to serve as the first approved supraventricular tachycardia treatment for use outside of the healthcare setting; the timing of the NDA submission for etripamil nasal spray; and further clinical development of etripamil and continued success with future clinical trials. 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 and its quarterly report on Form 10-Q for the quarter ended March 31, 2023, in each case 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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View original content:https://www.prnewswire.com/news-releases/milestone-pharmaceuticals-announces-publication-of-results-from-phase-3-rapid-clinical-trial-of-etripamil-nasal-spray-in-patients-with-psvt-in-the-lancet-301854596.html

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