Milestone Pharmaceuticals Announces New Data from Phase 3 RAPID Trial of Etripamil Nasal Spray in Patients with PSVT During Late-Breaking Session at the AHA Scientific Sessions 2022

November 07, 2022

- *Trial met its primary endpoint, with 64.3% of patients receiving etripamil converting to sinus rhythm within 30 minutes compared to 31.2% on placebo (HR = 2.62, p<0.001)*
- *Median time to conversion was 17 minutes for patients treated with etripamil – three times faster than placebo*
- *Analyses of pooled data show significant reductions in medical interventions and visits to the emergency department for patients who took etripamil*
- *Safety and tolerability data are consistent with previous trials, supporting potential self-administration of the optional repeat dose regimen*

MONTREAL and CHARLOTTE, N.C., Nov. 7, 2022 /PRNewswire/ -- Milestone Pharmaceuticals Inc. (Nasdaq: MIST), a biopharmaceutical company focused on the development and commercialization of innovative cardiovascular medicines, today announced the presentation of new data from the Phase 3 RAPID clinical trial of etripamil, the Company's investigational calcium channel blocker, in patients with paroxysmal supraventricular tachycardia (PSVT) in the at-home setting. The presentation, titled "Self-administered Etripamil for Termination of Spontaneous Paroxysmal Supraventricular Tachycardia: Primary Analysis from the RAPID Study", was featured during a Late-Breaking Clinical Trials session at the American Heart Association (AHA) Scientific Sessions 2022 held November 5-7 in Chicago, IL and virtually. Etripamil, a new chemical entity, is Milestone's lead investigational product. A copy of the presentation will be available in the Publications section of Milestone's website.

"The unpredictable nature of PSVT places an overwhelming burden on patients who lack effective at-home interventions to manage their episodes," said James Ip, M.D., Associate Professor and Director of Cardiac Pacing and Implantable Devices, Division of Cardiology, Weill Cornell Medicine, New York Presbyterian Hospital, the study's presenter and a RAPID investigator. "Data from the RAPID trial demonstrate that patients on the etripamil regimen had both a greater degree of conversion and a much faster conversion than those taking placebo. These findings further support that etripamil could offer patients a meaningful intervention for their condition outside of the more costly and inconvenient acute-care setting."

"Further analyses featured in today's late-breaking session, showing reduced emergency department utilization, continue to support our conviction that etripamil has the potential to empower patients to take control over their condition as well as to provide value to the healthcare system," said Joseph Oliveto, President and Chief Executive Officer of Milestone Pharmaceuticals. "We are now focused on seeking guidance from the U.S. Food and Drug Administration (FDA) to bring this important first-of-its-kind therapy to as many appropriate patients as possible."

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 a nasal spray of etripamil or placebo, as prompted by symptoms of PSVT and without medical monitoring. 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. The RAPID trial achieved its primary endpoint, with patients taking etripamil demonstrating a highly statistically significant and clinically meaningful difference in time to PSVT 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). By 90 minutes post-study drug administration, 80.6% of etripamil patients converted versus 60.7% of placebo patients (HR = 1.93; 95% CI 1.349, 2.752; p<0.001) and statistical significance was maintained throughout the five-hour observation window. Significant reductions in time to conversion in patients who took etripamil were evident early and persisted throughout the observation window of the study compared to placebo. The median time to conversion for patients in RAPID who received etripamil was 17.2 minutes compared to 53.3 minutes for patients on placebo.

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. Independently adjudicated ECG data show no cases of 2nd or 3rd degree heart block or significant pauses during at-home drug administration. To date, the Company's overall PSVT clinical program has resulted in more than 1,600 unique patient exposures to etripamil doses of ≥70 mg.

In the RAPID study, patients who were treated with etripamil sought additional medical interventions less frequently (15% vs. 25%; p=0.103) and had fewer emergency department visits (14% vs. 21%; p=0.209) than patients in the placebo arm. These findings were consistent with the Company's previously completed Phase 3 NODE-301 study, in which patients who were treated with etripamil also sought additional medical interventions less frequently (14% vs. 27%; p=0.119) and saw a reduction in emergency department visits (13% vs. 25%; p=0.076) compared to patients in the placebo arm. Notably, analyses of pooled data from the NODE-301 and RAPID trials show that etripamil treatment provided a statistically significant reduction in both the use of additional medical interventions and visits to the emergency department.

As previously communicated, the Company believes results from the RAPID trial together with the data from the already completed NODE-301 trial

could fulfill the efficacy requirement for a New Drug Application (NDA) submission for etripamil in patients with PSVT. The Company plans to submit an NDA application in mid-2023 pending agency feedback.

About Paroxysmal Supraventricular Tachycardia

Paroxysmal supraventricular tachycardia (PSVT) is a condition affecting approximately two million Americans that is characterized by intermittent episodes of a rapid heartbeat that starts and stops suddenly. Episodes of supraventricular tachycardia (SVT) are often associated with symptoms such as palpitations, sweating, chest pressure or pain, shortness of breath, sudden onset of fatigue, lightheadedness or dizziness, fainting, and anxiety. Certain intravenous medications, including adenosine, beta-blockers and calcium channel blockers, have long been used for the acute treatment of PSVT. However, these medications must be administered under medical supervision, usually in an emergency department or other acute care setting.

About Etripamil

Etripamil, a new chemical entity, is Milestone's lead investigational product. It is a novel calcium channel blocker designed to be a rapid-response therapy for episodic cardiovascular conditions. As a nasal spray that is self-administered by the patient, etripamil has the potential to shift the current treatment experience for many patients from the emergency department to a medically unsupervised 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 that is underway in patients with 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 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 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 "announce," "assume," "believe," "continue," "could," "demonstrate," "develop," "estimate," "expect," "further," "may," "ongoing," "potential," "progress" "support," "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 design, progress, timing, scope and results of the RAPID trial; Milestone's ability to execute on the remainder of the PSVT program; the timing of release of unblind RAPID results and topline data with respect to the Company's RAPID trial; the ability of the results from the RAPID study to actually fulfill the efficacy requirements of Milestone's NDA application and the timing of agency feedback on such application; Milestone's ongoing plans to study etripamil in atrial fibrillation patients, the sufficiency of Milestone's current cash resources to support its operations, and estimates about the addressable market and commercial potential for treatments of atrial fibrillation with rapid ventricular rate. 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; 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, as well as risks related to pandemics and public health emergencies, including those related to the ongoing COVID-19 pandemic, 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, 2021, under the caption "Risk Factors," as such discussion may be updated from time to time by subsequent filings we 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.

Contact:

David Pitts
Argot Partners
212-600-1902
milestone@argotpartners.com

View original content to download multimedia:https://www.prnewswire.com/news-releases/milestone-pharmaceuticals-announces-new-data-from-phase-3-rapid-trial-of-etripamil-nasal-spray-in-patients-with-psvt-during-late-breaking-session-at-the-aha-scientific-sessions-2022-301669662.html

SOURCE Milestone Pharmaceuticals, Inc.