Milestone Pharmaceuticals Enrolls First Canadian Study Participant in ReVeRA-301 Phase 3 Pivotal Trial Evaluating Etripamil Nasal Spray for AFib-RVR

September 24, 2026

Montreal Heart Institute Joins Multinational Study Evaluating a Self-Administered 70 mg Repeat-Dose Regimen of Etripamil

MONTREAL and CHARLOTTE, N.C., Sept. 24, 2026 (GLOBE NEWSWIRE) -- Milestone® Pharmaceuticals Inc. (Nasdaq: MIST), a biopharmaceutical company focused on the development and commercialization of innovative cardiovascular medicines, today announced that the Montreal Heart Institute, recently activated as the first Canadian clinical trial site for the ReVeRA-301 Phase 3 pivotal trial evaluating etripamil nasal spray for the treatment of atrial fibrillation with rapid ventricular rate (AFib-RVR), has enrolled their first patient. The expansion into Canada advances the multinational study toward its target of 150 patients with treated AFib-RVR events. ReVeRA-301 is evaluating the same 70 mg repeat-dose regimen that is U.S. Food and Drug Administration (FDA)-approved for paroxysmal supraventricular tachycardia (PSVT) as CARDAMYST® (etripamil) nasal spray.

“Activating clinical trial sites and enrolling study participants in Canada are important steps toward advancing ReVeRA-301 and reflect the momentum behind our global enrollment efforts following the recent first enrolled patient in the United States,” said David Bharucha, M.D., PhD, FACC, Chief Medical Officer of Milestone Pharmaceuticals. “We are honored to continue our work with the strong Canadian community of cardiovascular investigators and centers with deep experience in atrial fibrillation research.”

“Following the promising Phase 2 data, we are pleased to advance etripamil into this pivotal Phase 3 trial in AFib-RVR,” said Adrian Petzl, M.D., Cardiologist-Electrophysiologist, Montreal Heart Institute, and investigator on ReVeRA-301. “The ability to intervene promptly with a self-administered therapy outside of the emergency department could represent a meaningful change for patients living with this condition. We are excited that the Montreal Heart Institute is at the forefront of this global research initiative.”

About ReVeRA-301

ReVeRA-301 is a Phase 3 multinational, multi-center, randomized, double-blind, placebo-controlled study to evaluate the effects of etripamil nasal spray in approximately 150 patient events with AFib-RVR. Prompted by symptoms, patients will self administer, in a medically unsupervised setting (e.g., at home), the same 70 mg dose of etripamil and repeat-dose regimen that supports the current FDA indication for the treatment of PSVT. Based on safety data demonstrated to date, Milestone is currently pursuing a single-study supplemental new drug application (sNDA) registration pathway for the treatment of AFib-RVR. The primary endpoint for ReVeRA-301 is reduction in ventricular rate (VR) within 30 minutes. The study will also evaluate a key secondary endpoint of symptom improvement via patient-reported outcomes. Clinical trial sites and enrollment information can be found at https://clinicaltrials.gov.

The trial advances research from ReVeRA-201, a multi-center Phase 2, randomized controlled study of the efficacy and safety of etripamil nasal spray for the acute reduction of symptomatic AFib-RVR in an emergency room setting. The clinical trial showed that a single dose of etripamil nasal spray at 70 mg reduced VR and improved both relief of symptoms and treatment satisfaction.

About Atrial Fibrillation with Rapid Ventricular Rate (AFib-RVR)

Atrial fibrillation (AFib) is the most common sustained arrhythmia, affecting over 6 million people in the United States. The prevalence of AFib in Canada is similarly problematic to that in the United States. The Canadian Cardiovascular Society estimates that AFib affects approximately 1-2% of the population, up to approximately 800,000 people in Canada, and represents a substantial and growing public health burden. AFib presents with an irregular heart rate and is classified as paroxysmal, persistent, or permanent. When there is a rapid heart rate during AFib, it is referred to as “atrial fibrillation with rapid ventricular rate (AFib-RVR).”

Market research indicates that 30-40% of patients with AFib experience at least one episode of RVR per year requiring urgent medical attention. These episodes commonly cause palpitations, shortness of breath, and weakness. While AFib is rarely life-threatening, it is a serious condition that often requires treatment and increases the risk of serious complications if not properly managed. Current options for acute AFib-RVR management are limited and often involve an emergency department visit for IV beta blockers, IV calcium channel blockers, or electrical cardioversion.

About CARDAMYST in the United States

CARDAMYST® (etripamil) nasal spray is approved by the U.S. Food and Drug Administration (FDA) for the conversion of acute symptomatic episodes of paroxysmal supraventricular tachycardia (PSVT) to sinus rhythm in adults. It is a novel calcium channel blocker nasal spray designed as a self-administered rapid response therapy for patients, thereby bypassing the need for immediate medical oversight. The product is intended to provide health care providers with a new treatment option to enable on-demand care and patient self-management. This portable treatment may provide patients with active management and a greater sense of control over their condition. CARDAMYST is well studied with a robust clinical trial program that includes a completed Phase 3 clinical-stage program for the treatment of PSVT. Currently, etripamil is in Phase 2 development for treatment of PSVT in pediatric patients and Phase 3 development for control of acute atrial fibrillation with rapid ventricular rate (AFib-RVR) in adults. For more information, please visit CARDAMYST.com.

U.S. FDA Indication
CARDAMYST is indicated for the conversion of acute symptomatic episodes of paroxysmal supraventricular tachycardia (PSVT) to sinus rhythm in adults.

IMPORTANT SAFETY INFORMATION FOR CARDAMYST (etripamil)

What is CARDAMYST?

CARDAMYST is a prescription medicine used to help restore normal sinus heart rhythm in adults who have symptoms of sudden episodes of fast heartbeat called paroxysmal supraventricular tachycardia (PSVT).

It is not known if CARDAMYST is safe and effective in children.

Do not use CARDAMYST if you:

- are allergic to CARDAMYST or any of its ingredients. See the Patient Information for a complete list of ingredients in CARDAMYST.
- have limitations in activities due to heart failure (moderate to severe heart failure).
- have Wolff-Parkinson-White (WPW) syndrome, Lown-Ganong-Levine syndrome, or an abnormal heart rhythm pattern called pre-excitation (delta wave) on an electrocardiogram (ECG).
- have sick sinus syndrome without a permanent pacemaker.
- have second degree or higher atrioventricular (AV) block.

Before using CARDAMYST, tell your healthcare provider about all of your medical conditions, including if you:

- have a history of fainting.
- have low blood pressure.
- are pregnant or plan to become pregnant. It is not known if CARDAMYST will harm your unborn baby.
- are breastfeeding or plan to breastfeed. It is not known if CARDAMYST passes into your breast milk. You should stop breastfeeding for 12 hours after treatment with CARDAMYST. During this time, pump and throw away your breast milk. Talk to your healthcare provider about the best way to feed your baby after using CARDAMYST.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

What are the possible side effects of CARDAMYST?

CARDAMYST may cause serious side effects, including:

- Fainting due to CARDAMYST effects on blood pressure, heart rate, and electrical activity of the heart. CARDAMYST may cause dizziness and fainting, especially in people with a history of fainting and certain heart problems, or people with a history of fainting during an episode of PSVT. Use CARDAMYST while sitting in a safe area where you will not fall if you become dizzy or lightheaded. Lie down if you feel dizzy or lightheaded after using CARDAMYST. If fainting occurs after using CARDAMYST, caregivers should place you on your back and seek medical help.

The most common side effects of CARDAMYST include:

• nasal discomfort • nasal congestion • runny nose	• throat irritation • nosebleed

These are not all of the possible side effects for CARDAMYST. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

Please see the full Prescribing Information
https://milestonepharma.com/etripamilprescribinginformation.pdf for CARDAMYST.

About Milestone Pharmaceuticals

Milestone Pharmaceuticals Inc. (Nasdaq: MIST) is an emerging commercial-stage biopharmaceutical company advancing innovative cardiovascular medicines to benefit people living with certain heart conditions. Milestone's lead product is CARDAMYST® (etripamil) nasal spray, a novel calcium channel blocker, which is FDA-approved for the conversion of acute symptomatic episodes of paroxysmal supraventricular tachycardia (PSVT) to sinus rhythm in adults. Etripamil is also in Phase 3 development for the control of symptomatic episodic attacks associated with AFib-RVR. https://milestonepharma.com/

Cautionary Note on 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," "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: Milestone's business strategy and plans; the design, timing, and enrollment of the ReVeRA-301 Phase 3 clinical trial for AFib-RVR, including the anticipated number of patients and sites; the potential for etripamil to serve as a treatment option for patients with AFib-RVR, including as a self-administered therapy; the commercialization and market adoption of CARDAMYST; the development of etripamil for additional indications, including Phase 2 development in pediatric PSVT patients; expectations regarding the efficacy and safety of etripamil for AFib-RVR based on Phase 2 findings; the timing and outcomes of future interactions with U.S. and foreign regulatory bodies, including the FDA; and other statements not related to historical facts. 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 Milestone's 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, international tariffs and conflicts, and overall fluctuations in the financial markets in the United States and abroad, risks related to pandemics and public health emergencies, and risks related to 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 (SEC), including in its annual report on Form 10-K for the year ended December 31, 2025, under the caption "Risk Factors," as such discussions may be updated from time to time by subsequent filings Milestone may make with the SEC. 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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