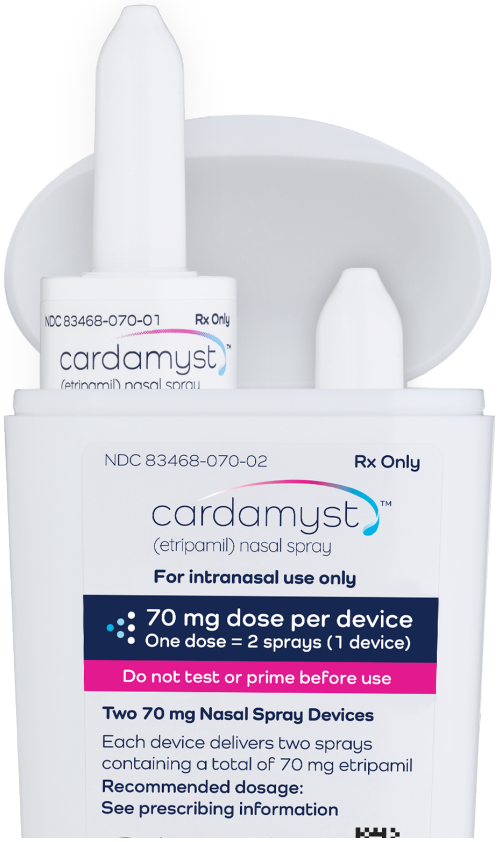
Milestone Receives FDA Approval of CARDAMYST™ (etripamil) as First and Only Self-Administered Nasal Spray for Adults with Paroxysmal Supraventricular Tachycardia (PSVT)

December 12, 2025

- *First FDA approved treatment in 30+ years for more than 2 million Americans with PSVT*
- *Novel nasal spray designed to rapidly resolve episodes of PSVT and restore sinus rhythm*
- *FDA approval in PSVT enables development of AFib-RVR under sNDA pathway*
- *Milestone well-capitalized to launch and commercialize CARDAMYST with existing capital and royalty financing*
- *Conference call and webcast December 15, 8:00 a.m. ET*

MONTREAL and CHARLOTTE, N.C., Dec. 12, 2025 (GLOBE NEWSWIRE) -- Milestone® Pharmaceuticals Inc. (Nasdaq: MIST) today announced that the U.S. Food and Drug Administration (FDA) approved its first commercial product, CARDAMYST™ (etripamil) nasal spray, a prescription medication for the conversion of acute symptomatic episodes of paroxysmal supraventricular tachycardia (PSVT) to sinus rhythm in adults. This approval marks the first time that more than two million Americans with PSVT will have a rapid-acting treatment option they can self-administer outside the emergency department or other healthcare setting. CARDAMYST is expected to be available in retail pharmacies in the first quarter of 2026.



CARDAMYST nasal spray is a novel and rapid-acting calcium channel blocker delivered when needed to treat often highly symptomatic and unpredictable episodes of PSVT. With CARDAMYST, adults with PSVT can be prepared wherever and whenever episodes occur, providing them with active management and a greater sense of control of their condition.

“CARDAMYST is a novel at-the-ready treatment option that addresses the unpredictable impact of PSVT by offering patients the freedom to manage episodes anytime and anywhere,” said Joseph Oliveto, President and Chief Executive Officer of Milestone Pharmaceuticals. “The FDA approval of CARDAMYST is a watershed moment for Milestone and a gratifying event for our team members, patients, clinical investigators, and health care providers who participated in the development program, all of whom I sincerely thank for their dedication, counsel, and collaboration toward this important achievement.”

“Some people with PSVT have endured years of anxiety, fearing their next episode and the stress and disruption of emergency department visits,” said James Ip, M.D., FACC, FHRS, an etripamil investigator. “CARDAMYST will give many of them the ability to administer a medication themselves that can quickly stop their PSVT episode and potentially avoid a hospital trip or a call to emergency services.”

CARDAMYST Clinical Data

The FDA approval of CARDAMYST is supported by a robust clinical trial program based on safety data from more than 1,800 participants and more than 2,000 episodes of PSVT. This includes the successful Phase 3 RAPID trial, a global, randomized, double-blind comparison of CARDAMYST vs. placebo, published in *The Lancet* in 2023. In clinical studies, participants using CARDAMYST were two times more likely to convert symptomatic PSVT to sinus rhythm and did so more than three times faster compared with placebo. The RAPID trial achieved its primary endpoint with 64% of those who self-administered CARDAMYST (N=99) converting from supraventricular tachycardia (SVT) to sinus rhythm within 30 minutes compared to 31% on placebo (N=85) (HR = 2.62; p<0.001). At one hour, the benefit was demonstrated in 73% of participants. In addition, significant reductions in time to conversion in those who took CARDAMYST were evident early and durable, with a median time to conversion of 17 minutes (95% CI: 13.4, 26.5) for those treated with CARDAMYST vs. 54 minutes (95% CI: 38.7, 87.3) for those treated with placebo.

A consistent safety profile and treatment effects were observed across all subgroups, including participants concurrently on beta blockers or calcium channel blockers. The most frequent adverse events occurring in ≥5% of participants in randomized clinical trials were mild-to-moderate and transient in nature, including local-site nasal discomfort, nasal congestion, rhinorrhea, throat irritation, and epistaxis. Less than 2% of trial participants discontinued therapy due to adverse events.

For more safety information about CARDAMYST, please see Important Safety Information below. For the latest information about the product availability, please see https://milestonepharma.com/.

PSVT, also called SVT, is characterized by episodes of abnormally fast heart rate. Most people with PSVT experience multiple sustained episodes that require treatment on an annual basis. Until now, successful treatment options typically required IV administration in healthcare settings, creating stress and costs for patients and their insurers. CARDAMYST offers a new approach to treat episodes of PSVT, enabling adults to self-administer the medication at the onset of symptoms. For more information, please visit SVTHearttoHeart.com.

“Our goal is that CARDAMYST will become a trusted and essential solution for healthcare providers and their patients,” said Lorenz Muller, Chief Commercial Officer of Milestone. “Our team is focused on making CARDAMYST available to adults with PSVT as quickly as possible, including actively working to secure insurance coverage and begin the distribution of the product through retail pharmacies.”

Annette Greene, CARDAMYST clinical trial participant and administrator of the Supraventricular Tachycardia Group on Facebook, with more than 30,000 members, said, “Adults with SVT have been waiting a long time for the day when they can confidently self-administer CARDAMYST to treat their SVT episodes. It is very exciting that the day has become a reality.”

Regarding future R&D, Milestone is poised to enter a Phase 3 program in atrial fibrillation with rapid ventricular rate (AFib-RVR), particularly on the strength of the successful ReVeRA Phase 2 trial in AFib-RVR, results of which were published in *Circulation: Arrhythmia and Electrophysiology*. Incorporating FDA’s guidance, Milestone has developed a Phase 3 registrational program to evaluate self-administered etripamil as a potential treatment for patients with AFib-RVR. When completed, the Company will be following a supplemental New Drug Application (sNDA) regulatory approval pathway for a potential second indication for etripamil in AFib-RVR. As such, Milestone will leverage the approved PSVT indication and the PSVT program data, along with a single pivotal Phase 3 study in patients with AFib-RVR.

About Paroxysmal Supraventricular Tachycardia

An estimated two million people in the United States are currently diagnosed with PSVT, a type of arrhythmia or abnormal heart rhythm. PSVT is characterized by episodes of sudden onset rapid heartbeats often exceeding 150 to 200 beats per minute. The heart rate spike is unpredictable and may last several hours. The rapid heart rate often causes disabling severe palpitations, shortness of breath, chest discomfort, dizziness or lightheadedness, and distress, forcing people with PSVT to limit their daily activities. The uncertainty of when an episode of PSVT will strike or how long it will persist can provoke anxiety and negatively impact the day-to-day life between episodes of people with PSVT. The impact and morbidity from

an attack can be especially detrimental in people with underlying cardiovascular or medical conditions, such as heart failure, obstructive coronary disease, or dehydration. Many health care providers are dissatisfied with the lack of effective treatment options with people with PSVT, often requiring prolonged, burdensome, and costly trips to the emergency department or even invasive cardiac ablation procedures.

About Atrial Fibrillation with Rapid Ventricular Rate

An estimated ten million Americans suffer from atrial fibrillation (AFib), a common arrhythmia marked by an irregular, disruptive and often rapid heartbeat. A subset of patients with AFib experience episodes of abnormally high heart rate most often accompanied by palpitations, shortness of breath, dizziness, and weakness. While these episodes, known as AFib-RVR, may be treated by oral calcium channel blockers and/or beta blockers, patients frequently seek acute care in the emergency department to address symptoms. In 2016, nearly 800,000 patients were admitted to the emergency department due to AFib symptoms where treatment includes medically supervised intravenous administration of calcium channel blockers or beta blockers, or electrical cardioversion. With little available data for AFib-RVR, Milestone's initial market research indicates that 30% to 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-RVR.

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 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
- throat irritation
- nosebleed

- runny nose

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.

Milestone Well-Capitalized to Launch and Commercialize CARDAMYST

Milestone is well-capitalized to launch and commercialize CARDAMYST with existing capital and royalty financing. As of September 30, 2025, Milestone had cash, cash equivalents, and short-term investments of $82.6 million. In addition in March 2023, Milestone entered into the Royalty Purchase Agreement with RTW Investments, LP and certain of its affiliates (RTW), pursuant to which RTW agreed to purchase, following the FDA approval (subject to certain conditions) of etripamil on or prior to September 30, 2025 (Approval Date), the right to receive a tiered royalty payments on the annual net product sales of etripamil in the United States, in exchange for a purchase price of $75.0 million. On July 10, 2025, Milestone amended its Royalty Purchase Agreement (the Amendment) to provide for a three-month extension of the Approval Date.

Pursuant to the Amendment, in order to receive the $75.0 million purchase price, Milestone must receive marketing approval of etripamil from the FDA on or prior to December 31, 2025, and satisfy the other customary closing conditions. Milestone anticipates that the FDA approval announced today will satisfy the requirements for Milestone to receive the $75.0 million purchase price.

Conference Call and Live Webcast

Milestone management will host a conference call and live audio webcast with slides at 8:00 a.m. ET on Monday, December 15, 2025, to discuss the FDA approval of CARDAMYST. To access the call, please dial 1-877-407-0792 (domestic) or 1-201-689-8263 (international) and refer to conference ID 13756738, or click on Call me™link and request a return call. The Call me™ link will be made active 15 minutes prior to scheduled start time. The webcast and slides can be accessed live on this link and also on the “News & Events” page of the Milestone Corporate Website at https://milestonepharma.com/. The archived webcast will also be available on Milestone's website following the call.

About Milestone Pharmaceuticals

Milestone Pharmaceuticals Inc. (Nasdaq: MIST) is a biopharmaceutical company developing and commercializing 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 development for the treatment of symptomatic episodic attacks associated with AFib-RVR.

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: expectations on the timing of CARDAMYST for PSVT being available to patients in retail pharmacies; CARDAMYST’s potential as a novel treatment option to help patients with PSVT; Milestone’s ability to make CARDAMYST quickly available to PSVT patients following FDA approval; the success of Milestone’s launch infrastructure; the timing of patient enrollment in the Phase 3 study of etripamil for AFib-RVR and expectations regarding the Phase 3 study in patients with AFib-RVR; 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, whether our future interactions with the FDA will have satisfactory outcomes; whether and when, if at all, our NDA for etripamil will be approved by the FDA; 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, international tariffs, Russian hostilities in Ukraine and ongoing disputes in Israel and Gaza 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 (SEC), including in its annual report on Form 10-K for the year ended December 31, 2025 and its quarterly report on Form 10-Q for the quarter ended September 30, 2025, in each case 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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A photo accompanying this announcement is available at https://www.globenewswire.com/NewsRoom/AttachmentNg/1cd3bcec-2019-4e39-b90e-aab21bcd97ac.

Source: Milestone Pharmaceuticals Inc.

CARDAMYST(TM)

CARDAMYST(TM), the brand name for etripamil, is now approved by the U.S. Food and Drug Administration