Milestone Pharmaceuticals Reports Third Quarter 2022 Financial Results and Provides Clinical and Corporate Update

November 10, 2022

- Phase 3 RAPID trial of etripamil in patients with PSVT achieved primary efficacy endpoint; safety and tolerability data from repeat dose administration consistent with prior studies utilizing single-dose administration of etripamil

- Analyses from etripamil Phase 3 PSVT studies featured during Late-Breaking session at AHA Scientific Sessions 2022 demonstrated significant reductions in emergency department utilization for etripamil-treated patients

- Company plans to submit NDA for etripamil in PSVT to the U.S. FDA in mid-2023 pending Agency feedback

MONTREAL and CHARLOTTE, N.C., Nov. 10, 2022 /PRNewswire/ -- Milestone Pharmaceuticals Inc. (Nasdaq: MIST), a biopharmaceutical company focused on the development and commercialization of innovative cardiovascular medicines, today reported financial results for the third quarter ended September 30, 2022, and provided a clinical and corporate update.

"The positive feedback we received from both clinicians and patient advocacy groups following the presentation of further RAPID data at the American Heart Association (AHA) meeting earlier this week strengthen our conviction that etripamil has the potential to serve as a promising option for patients with paroxysmal supraventricular tachycardia (PSVT)," said Joseph Oliveto, President and Chief Executive Officer of Milestone Pharmaceuticals. "We are keenly focused on preparations for our planned New Drug Application (NDA), which we expect to submit to the U.S. Food and Drug Administration (FDA) in mid-2023 pending agency feedback."

Recent Updates

- **Announcement of Positive Topline Efficacy and Safety Results from Phase 3 RAPID Clinical Trial of Etripamil Nasal Spray in Patients with PSVT.** In October 2022, the Company announced that the Phase 3 RAPID clinical trial of etripamil, a new chemical entity and Milestone's lead investigational product, in patients with PSVT met its primary endpoint, with 64.3% of patients self-administering etripamil converting to sinus rhythm within 30 minutes compared to 31.2% on placebo (HR = 2.62, p<0.001). Safety and tolerability data from the RAPID trial continue to support the potential for at-home use of etripamil, with findings consistent with those observed in prior trials and now including data with an optional repeat dose. The most common randomized treatment emergent adverse events (RTEAEs), adverse events (AEs) which occurred within 24 hours of study drug administration, were related to the nasal administration site. The Company believes that results from the RAPID trial together with data from the already completed NODE-301 trial could fulfill the efficacy requirement for an NDA submission for etripamil in patients with PSVT. Milestone plans to submit an NDA to the U.S. FDA in mid-2023 pending agency feedback.

- **Additional Data from the RAPID Trial Featured During Late-Breaking Session at the American Heart Association (AHA) Scientific Sessions 2022.** More extensive data from the Phase 3 RAPID trial were presented earlier this week at the AHA Scientific Sessions. Data showed statistically significant and clinically meaningful conversion rates in favor of etripamil over placebo at timepoints even beyond the 30-minute mark, including etripamil conversion rates reaching approximately 74% and 80% by 60 and 90 minutes, respectively. Data were presented documenting the faster median time to conversion, 17.2 minutes after administration of etripamil compared to more than 3-fold longer with placebo. In addition, the presentation included detailed pooled analyses of the Phase 3 RAPID and NODE-301 studies that showed significant reductions in emergency department visits and lower use of additional medical interventions in favor of etripamil. A complete evaluation of adjudicated ambulatory electrocardiogram (ECG) measures was also presented, revealing no occurrences of second-degree or greater atrioventricular (AV) block in either arm.

- **Recruitment Continues in the ReVeRA Phase 2 Proof-of-Concept Trial in Patients Experiencing AFib-RVR.** 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 (atrial fibrillation with a rapid ventricular rate). 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 trial is being conducted in Canada in collaboration with the Montreal Heart Institute and other research centers and is imminently planned to expand into other regions. 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. Additionally, based on results from the etripamil program in PSVT, Milestone has started planning a second Phase 2 trial to evaluate at-home self-administered etripamil in patients with AFib-RVR.

- **Successful Completion of RAPID Phase 3 Clinical Trial Triggers Milestone Payment from Ji Xing Pharmaceuticals Limited.** The positive results of the RAPID Phase 3 clinical trial have triggered a $3.5 million payment from Milestone's partner, Ji Xing Pharmaceuticals Limited (Ji Xing). In May 2021, Milestone and Ji Xing entered into an exclusive license agreement to develop and commercialize etripamil for PSVT in Greater China. Under the terms of the agreement, Milestone granted Ji Xing an exclusive license to develop and, if regulatory approval is obtained, commercialize etripamil in patients with PSVT in Greater China. Milestone is eligible to receive up to $107.5 million in milestone payments and royalties on future sales of etripamil in Greater China. Under the terms of the agreement, Milestone will supply etripamil and delivery devices to Ji Xing. Ji Xing will be responsible for development and commercialization costs in Greater China

Third Quarter 2022 Financial Results

- As of September 30, 2022, Milestone had cash, cash equivalents, and short-term investments of $77.2 million and 30.4 million common shares and 12.3 million common shares issuable upon exercise of pre-funded warrants outstanding. We expect our current cash, cash equivalents, and short-term investments to fund operations through 2023.

- We generated revenue of $1.5 million from milestone payments under the License Agreement for the three months and nine months ended September 30, 2022 compared to no revenue in the three months ended September 30, 2021 and revenue of $15 million from upfront payments under the License Agreement during the nine months ended September 30, 2021.

- Research and development (R&D) expense for the third quarter of 2022 was $9.8 million, which was consistent with $9.7 million for the same period in the prior year. For the nine months ended September 30, 2022, R&D expense was $29.3 million compared with $27.8 million for the prior year period. The $1.5 million increase in R&D expense in the nine months ended September 30, 2022 is the result of clinical personnel related costs and clinical consulting fees. Regulatory costs increased due to personnel related costs.

- General and administrative (G&A) expense for the third quarter of 2022 was $4.0 million, compared with $3.0 million for the prior year period. The difference is primarily the result of increase in personnel-related costs and consulting fees for general and administrative expenses. For the nine months ended September 30, 2022, G&A expense was $11.6 million compared with $8.6 million for the prior year period. The $3.0 million increase in G&A expense in the nine months ended September 30, 2022 is primarily the result of increased personnel related costs and consulting fees for general and administrative expenses.

- Commercial expense for the third quarter of 2022 was $2.7 million, compared with $1.6 million for the prior year period. The difference is primarily the result of an increase in costs associated with consulting and marketing analytics. For the nine months ended September 30, 2022, commercial expense was $6.5 million compared with $4.8 million for the prior year period. The $1.7 million increase in commercial expense for the nine months ended September 30, 2022 over the same period in the prior year is primarily the result of personnel related costs and consulting fees.

- For the third quarter of 2022, operating loss was $14.6 million, compared to operating loss of $14.2 million for the prior year period. For the nine months ended September 30, 2022, Milestone's operating loss was $45.2 million, compared to $26.0 million in the prior year period.

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 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 within the next 10 years. Atrial fibrillation with rapid ventricular rate (AFib-RVR) is a condition that some patients with AFib experience and includes episodes of abnormally high heart rate, often with symptoms such as palpitations, shortness of breath, dizziness and weakness. Oral calcium channel blockers and/or beta blockers are commonly used to reduce the heart rate in this condition. When AFib-RVR occurs, symptoms often 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 under medical supervision. Milestone's 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 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 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 clinical trial data from the phase 3 RAPID clinical trial of etripamil nasal spray in patients with PSVT to support an NDA in mid-2023 pending agency feedback, the design, progress, timing, scope, recruitment and results of the RAPID and ReVeRA trials; Milestone's ability to execute on the remainder of the PSVT program; the receipt of milestone payments from Ji Xing, 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, 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, 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.

CONSOLIDATED STATEMENTS OF LOSS
(Unaudited, in thousands of US dollars, except share and per share data)

	Three months ended September 30,		Nine months ended September 30,	
	2022	2021	2022	2021
Revenue	$ 1,500	$ —	$ 1,500	$ 15,000
Operating expenses				
Research and development, net of tax credits	9,826	9,733	29,251	27,755
General and administrative	4,034	2,961	11,595	8,612
Commercial	2,670	1,579	6,537	4,788
Loss from operations	(15,030)	(14,273)	(45,883)	(26,155)
Interest income, net	474	48	672	186
Net loss	$ (14,556)	$ (14,225)	$ (45,211)	$ (25,969)
Weighted average number of shares and pre-funded warrants outstanding, basic & diluted	42,491,787	42,187,887	42,339,123	41,707,563
Net loss per share, basic and diluted	$ (0.34)	$ (0.34)	$ (1.07)	$ (0.62)

CONSOLIDATED BALANCE SHEETS
(Unaudited, in thousands of US dollars, except share data)

	September 30, 2022	December 31, 2021
Assets		
Current assets		
Cash and cash equivalents	$ 37,286	$ 114,141
Short-term investment	39,947	—
Research and development tax credits receivable	195	356
Prepaid expenses	5,058	4,299
Other receivables	435	127
Total current assets	82,921	118,923
Operating lease assets	2,545	711
Property and equipment	303	215
Total assets	$ 85,769	$ 119,849
Liabilities, and Shareholders' Equity		
Current liabilities		
Accounts payable and accrued liabilities	$ 6,035	$ 6,551
Operating lease liabilities	487	224
Total current liabilities	6,522	6,775
Operating lease liabilities (net of current portion)	2,092	474
Total liabilities	8,614	7,249
Shareholders' Equity		
Common shares, no par value, unlimited shares authorized 30,388,109 shares issued and outstanding as of September 30, 2022, 29,897,559 shares issued and outstanding as of December 31, 2021	254,937	251,901
Pre-funded warrants - 12,327,780 issued and outstanding as of September 30, 2022 and 12,327,780 as of December 31, 2021	52,941	52,941
Additional paid-in capital	22,441	15,711
Cumulative translation adjustment	(1,634)	(1,634)
Accumulated deficit	(251,530)	(206,319)
Total shareholders' equity	77,155	112,600
Total liabilities and shareholders' equity	$ 85,769	$ 119,849

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