Milestone Pharmaceuticals Reports Third Quarter 2021 Financial Results and Provides Clinical and Corporate Update

November 12, 2021

MONTREAL and CHARLOTTE, N.C., Nov. 12, 2021 /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, 2021 and provided a clinical and corporate update.

"We continue to make meaningful progress across our etripamil PSVT program. We've advanced our Phase 3 efficacy and safety studies and completed important patient research which enables a deeper understanding and characterization of the burden experienced by patients," said Joseph Oliveto, President and Chief Executive Officer of Milestone Pharmaceuticals. "Additionally, we look forward to presenting data from an analysis of heart rate in patients treated in the NODE-301 trial at the upcoming AHA Scientific Sessions 2021 meeting. We believe these data underscore the potential of etripamil to serve as an important intervention for patients with episodic cardiovascular conditions."

Recent Updates

- **Milestone Remains on Track to Report Topline Data from Pivotal Phase 3 RAPID Trial in the Second Half of 2022.** As previously announced, enrollment continues in the ongoing pivotal Phase 3 RAPID trial of etripamil nasal spray in patients with paroxysmal supraventricular tachycardia (PSVT). Milestone is working closely with study investigators to support patient enrollment and continues to activate new centers. The Company remains on track to report topline data in the second half of 2022.

  The RAPID trial, which is targeting a total of 180 adjudicated PSVT events, is expected to randomize approximately 500 patients 1:1 to receive either etripamil or placebo. To maximize the potential treatment effect of etripamil, patients will be directed to administer a repeat dose of study drug if they do not experience symptom relief within 10 minutes of the first study drug administration. The primary efficacy analysis for both the RAPID trial and the completed NODE-301 trial will be time to conversion of supraventricular tachycardia (SVT) over the first 30 minutes following initial study drug administration, with a target p-value of less than 0.05 for each trial. The RAPID and NODE-301 trials could potentially serve to fulfill the efficacy requirement for a future New Drug Application (NDA) for etripamil in patients with PSVT.

- **Heart Rate Data from NODE-301 Study to be Presented at the American Heart Association (AHA) Scientific Sessions 2021.** New analyses on the impact of etripamil on heart rate in patients with PSVT, from the NODE-301 Study, will be presented at the upcoming AHA Scientific Sessions 2021 meeting. The presentation, titled "Etripamil Nasal Spray Reduces Heart Rate in Patients with Paroxysmal Supraventricular Tachycardia Prior to Conversion to Sinus Rhythm", will be featured during an ePoster session on November 14, 2021 at 11:00 a.m. ET.

- **Analysis of Large Longitudinal Patient Reported Outcome Market Research Study Establishes Disease Burden in PSVT and Market Opportunity for Etripamil.** In the third quarter, Milestone completed an important patient reported outcomes (PRO) market research study in PSVT. The 247 patients who participated in the longitudinal portion of the study represent the broader PSVT population in terms of age, sex, medical history and time since diagnosis. Patients on average participated for 8.5 months and completed a survey every 12 days. In total, over 5,000 episodes were reported and characterized. Of these episodes, approximately 60% lasted longer than 10 minutes and 35% longer than 30 minutes.

  Patients who participated in the study demonstrated a wide range of annual SVT episode frequency (0 to >50), with a median frequency of 12-15 episodes per year. Based on internal analysis, Milestone estimates approximately 60% of patients experience multiple 10+ minute episodes each year characterized as moderate or severe in intensity. In addition, approximately 30% of patients experiencing episodes sought medical care for the episode, the majority of which were treated in the emergency department.

- **ReVeRA Phase 2 Proof-of-Concept Trial Continues Recruitment in Patients Experiencing Atrial Fibrillation with Rapid Ventricular Rate (AFib-RVR).** Recruitment is ongoing in ReVeRA, Milestone's Phase 2 proof-of-concept study of etripamil nasal spray in patients experiencing AFib-RVR. Patients are being randomized 1:1 to receive either 70 mg of etripamil or placebo. The Phase 2 double blind, placebo controlled, proof-of-concept in-patient study is designed to assess the safety and efficacy of etripamil nasal spray to reduce the ventricular rate in patients with AFib-RVR. The trial is being conducted in Canada in collaboration with the Montreal Heart Institute and other research centers. 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.

Third Quarter 2021 Financial Results

- As of September 30, 2021, Milestone had cash, cash equivalents, and short-term investments of $126.4 million and 29.9 million common shares issued and outstanding and 12.3 million common shares issuable upon exercise of pre-funded warrants outstanding.

- Research and development expense for the third quarter of 2021 was $9.7 million compared with $8.2 million for the prior year period. The increase reflects higher clinical consulting fees and contract research organization (CRO) costs due to advancing RAPID Phase 3 efficacy and safety trials in etripamil for the treatment of PSVT along with an increase in clinical personnel related costs. For the nine months ended September 30, 2021, research and development expense was $27.8 million compared with $28.7 million for the prior year period. The decrease was due to a reduction in clinical trial expenses of $2.3 million which was partially offset by an increase of $1.3 million in clinical personnel related costs which included a non-cash share-based compensation expense.

- General and administrative expenses for the third quarter of 2021 and 2020 were $3.0 million. For both of the nine month periods ended September 30, 2021 and 2020, respectively, general and administrative expense was $8.6 million.

- Commercial expense for the third quarter of 2021 was $1.6 million compared with $0.9 million for the prior year period. The increase is attributable to investment in commercial activities during the three months ended September 30, 2021 in contrast to the three months ended September 30, 2020, a period during which Milestone reduced commercial spending in order to focus efforts on an optimized clinical development pathway for etripamil after issuing topline results of the first part of the NODE-301 in March 2020. For the nine months ended September 30, 2021, commercial expense was $4.8 million compared with $4.6 million for the prior year period. This change was due to an increased investment in commercialization activities.

- For the third quarter of 2021, operating loss was $14.3 million compared to $12.1 million in 2020. For the nine months ended September 30, 2021, Milestone's operating loss was $26.2 million compared to $41.9 million in the prior year period.

About Paroxysmal Supraventricular Tachycardia

Paroxysmal supraventricular tachycardia (PSVT) is a condition characterized by intermittent episodes of rapid heart beat that starts and stops suddenly and without warning that affects approximately two million Americans. Episodes of supraventricular tachycardia (SVT) are often associated with palpitations, sweating, chest pressure or pain, shortness of breath, sudden onset of fatigue, lightheadedness or dizziness, fainting, and anxiety. Adenosine and certain calcium channel blockers have long been approved for the treatment of PSVT. However, these medications must be administered intravenously 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 in which patients with AFib experience 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 manage the heart rate in this condition. When episodes do occur, the corresponding symptoms often cause patients to seek care in the acute care setting such as the emergency department, where standard of care procedures include intravenous administration of calcium channel blockers or beta blockers under medical supervision. Milestone's initial qualitative market research indicates that approximately 40% of patients with AFib experience one or more symptomatic episodes of RVR per year that require treatment, suggesting a target addressable market for etripamil in patients with AFib of approximately two million patients.

About Etripamil

Etripamil, Milestone's lead investigational product, 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 the at-home setting. Milestone is conducting a comprehensive development program for etripamil, with Phase 3 trials ongoing in paroxysmal supraventricular tachycardia (PSVT) and now a Phase 2 proof-of-concept trial underway in patients with atrial fibrillation and 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 and rapid ventricular rate (AFib-RVR). Milestone Pharmaceuticals operates in Canada and the United States. For more information, visit www.milestonepharma.com and follow the Company 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," "will," "expect," "continue," "estimate," "potential," "progress" 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 and ReVeRA trials; Milestone's ability to execute on the remainder of the PSVT program, 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, 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, 2020, under the caption "Risk Factors." 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.

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

	Three months ended September 30,		Nine months ended September 30,	
	2021	**2020**	**2021**	**2020**
Collaboration revenue	$ —	$ —	$ 15,000	$ —
Operating expenses				
Research and development, net of tax credits	9,733	8,228	27,755	28,722
General and administrative	2,961	2,952	8,612	8,611
Commercial	1,579	905	4,788	4,615
Loss from operations	(14,273)	(12,085)	(26,155)	(41,948)
Interest income, net	48	89	186	630
Loss before income taxes	(14,225)	(11,996)	(25,969)	(41,318)
Income tax benefit	—	17	—	17
Net loss	$ (14,225)	$ (11,979)	$ (25,969)	$ (41,301)
Weighted average number of shares and pre-funded warrants outstanding, basic & diluted	42,182,887	29,774,065	41,707,563	26,329,581
Net loss per share, basic and diluted	$ (0.34)	$ (0.40)	$ (0.62)	$ (1.57)

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

	September 30, 2021	**December 31, 2020**
Assets		
Current assets		
Cash and cash equivalents	$ 111,426	$ 72,310
Short-term investment	15,000	70,000

Research and development tax credits receivable	275	725
Prepaid expenses	5,968	5,428
Other receivables	89	223
Total current assets	132,758	148,686
Operating lease assets	780	980
Property and equipment	238	308
Total assets	$ 133,776	$ 149,974
Liabilities, and Shareholders' Equity		
Current liabilities		
Accounts payable and accrued liabilities	$ 5,593	$ 5,914
Operating lease liabilities	254	245
Total current liabilities	5,847	6,159
Operating lease liabilities (net of current portion)	512	696
Total liabilities	6,359	6,855
Shareholders' Equity		
Common shares, no par value, unlimited shares authorized 29,869,785 shares issued and outstanding as of September 30, 2021, 29,827,997 shares issued and outstanding as of December 31, 2020	251,766	251,682
Pre-funded warrants - 12,327,780 issued and outstanding as of September 30, 2021 and 11,417,034 as of December 31, 2020	52,927	48,007
Additional paid-in capital	13,793	8,530
Cumulative translation adjustment	(1,634)	(1,634)
Accumulated deficit	(189,435)	(163,466)
Total shareholders' equity	127,417	143,119
Total liabilities and shareholders' equity	$ 133,776	$ 149,974

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