Milestone Pharmaceuticals Reports First Quarter 2021 Financial Results and Provides Clinical, Regulatory, and Corporate Update

May 17, 2021

MONTREAL and CHARLOTTE, N.C., May 17, 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 first quarter ended March 31, 2021 and provided a clinical, regulatory, and corporate update.

"We continue to work closely with our existing clinical trial sites, as well as add new sites, to address the impact that the COVID-19 pandemic has had on patient enrollment in the pivotal Phase 3 RAPID trial of etripamil in patients with PSVT. While we are encouraged by recent improvements in enrollment rates, we now expect to report topline data from the RAPID trial in the second half of 2022," said Joseph Oliveto, President and Chief Executive Officer of Milestone Pharmaceuticals. "We are also pleased to announce that following FDA's review of the etripamil program's interim safety data, including that from the initial repeat dose experience from the RAPID trial, we will be adding the higher exposure, repeat dose regimen into the ongoing NODE-303 open-label safety study. We continue to believe etripamil has the potential to serve as an important new option for patients with PSVT, and we are committed to ensuring it is able to realize its full potential."

Mr. Oliveto added, "Earlier today, we were excited to announce that we have entered into an exclusive license agreement with Ji Xing Pharmaceuticals to develop and, if approved, commercialize the investigational drug etripamil for PSVT in greater China. This agreement strengthens both our balance sheet and our executional capabilities, and we look forward to working with the Ji Xing team to expand the potential reach of etripamil to patients in the greater China region."

Recent Updates

- **Announced Exclusive License Agreement with Ji Xing Pharmaceuticals to Develop and Commercialize Etripamil for PSVT in Greater China.** Milestone today announced that it has entered an exclusive license and collaboration agreement with Ji Xing Pharmaceuticals (Ji Xing), a biotechnology company headquartered in Shanghai and backed by RTW Investments, LP (RTW) focused on advancing innovative medicines in China, to develop and, if approved, commercialize the investigational drug etripamil in patients with paroxysmal supraventricular tachycardia (PSVT) and additional cardiovascular conditions in Greater China. Milestone will receive an upfront cash payment consisting of $15 million and a $5 million equity investment by RTW Investments. In addition, Milestone is eligible to receive up to $107.5 million in milestone payments and royalties on future sales of etripamil in Greater China. Milestone will supply etripamil and delivery devices to Ji Xing. Ji Xing will be responsible for development and commercialization costs in Greater China.
- **Company Expects to Report Topline Data from Pivotal Phase 3 RAPID Trial in 2H22.** Enrollment remains ongoing in the pivotal Phase 3 RAPID trial of etripamil nasal spray in patients with PSVT. The ongoing COVID-19 pandemic has restricted access to many medical centers, reduced visits to physician offices, and caused patients to delay medical care. The Company continues to work diligently with investigators to identify potential site-specific solutions to mitigate these COVID-related delays, and has also increased the number of participating centers. Milestone now expects to report topline data in the second half of 2022. The Company believes its current cash resources, including the upfront payment from Ji Xing and proceeds from the equity investment from RTW, will be sufficient to support operations beyond the data readout into mid-2023.
  The RAPID trial, which is targeting a total of 180 adjudicated paroxysmal supraventricular tachycardia (PSVT) events, is expected to randomize approximately 500 patients 1:1 to receive either etripamil nasal spray or placebo. As previously announced, to maximize the potential treatment effect of etripamil, patients will be directed to administer a second 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 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.
- **NODE-303 Open-Label Safety Study Amended to Include Repeat Dose of Etripamil.** Following an interim safety data analysis of the RAPID study, the Company requested and the U.S. Food and Drug Administration (FDA) agreed to amend the ongoing NODE-303 study to allow a repeat dose of etripamil if symptoms persist for 10 minutes after the first dose. NODE-303 is a global open-label study which primarily evaluates the safety of etripamil when self-administered without medical supervision during single or multiple SVT episodes. Important secondary measures include efficacy, patient quality of life, and pharmacoeconomic assessments.
- **Data from NODE-301 Trial Featured During Oral Presentation at the American College of Cardiology 70th Annual Scientific Session and Expo (ACC.21).** An oral presentation titled, "Etripamil Nasal Spray Relieves Symptoms And Reduces Emergency Room Interventions In Patients With Paroxysmal Supraventricular Tachycardia (PSVT): Analysis Of

Clinical Outcomes In The NODE-301 Trial" (#403-13), was featured at the recent ACC.21 virtual meeting. The presentation was delivered by Bruce Stambler, MD, FHRS, Piedmont Heart Institute, Atlanta, GA, and investigator in the NODE-301 trial.

- **Enrollment Continues in ReVeRA Phase 2 Proof-of-Concept Trial Evaluating Etripamil in Patients with Atrial Fibrillation and Rapid Ventricular Rate (AFib-RVR).** In March 2021, Milestone announced that the first patient was enrolled in ReVeRA, its Phase 2 proof-of-concept study of etripamil nasal spray in patients experiencing AFib-RVR. Patient enrollment is ongoing, with the trial expected to enroll approximately 50 patients randomized 1:1 to receive either 70 mg of etripamil nasal spray or placebo. The Phase 2 double blind, placebo controlled, proof-of-concept study is designed to assess the safety and efficacy of etripamil nasal spray to reduce ventricular rate in patients with AFib-RVR experiencing an episode of elevated heart rate requiring treatment. The trial will be 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.

First Quarter 2021 Financial Results

- As of March 31, 2021, Milestone had cash, cash equivalents, and short-term investments of $129.9 million and 29.8 million common shares and 11.4 million common shares issuable upon exercise of pre-funded warrants outstanding.
- Research and development expense for the first quarter of 2021 was $8.6 million compared with $11.9 million for the prior year period. The COVID-19 pandemic contributed to delays in new clinical site initiation and patient enrollment, which translated into lower than expected research and development spending in the quarter ended March 31, 2021.
- General and administrative expense for the first quarter of 2021 was $2.6 million compared with $2.7 million for the prior year period.
- Commercial expense for the first quarter of 2021 was $1.4 million compared with $2.2 million for the prior year period. The decrease of commercial expense in the quarter ended March 31, 2021 reflects efforts in reducing operating expenses affecting primarily pre-commercialization activities as Milestone focused its efforts on an optimized clinical development pathway for etripamil.
- For the first quarter of 2021, operating loss was $12.6 million compared to $16.8 million for the prior year period.

About Paroxysmal Supraventricular Tachycardia

Paroxysmal supraventricular tachycardia (PSVT) is a rapid heart rate condition characterized by intermittent episodes of supraventricular tachycardia (SVT) that start and stop suddenly and without warning which affects approximately two million Americans. Episodes of SVT are often associated with symptoms including palpitations, sweating, chest pressure or pain, shortness of breath, sudden onset of fatigue, lightheadedness or dizziness, fainting, and anxiety. Certain calcium channel blockers have long been approved for the treatment of PSVT as well as other cardiac conditions. However, calcium channel blockers approved for the termination of SVT episodes must be administered intravenously under medical supervision, usually in an emergency department or other acute care setting.

About Atrial Fibrillation and 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 and 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 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 approximately 40% of patients with AFib experience one or more symptomatic episodes of AFib-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 "may," "will," "expect," "plan," "anticipate," "estimate," "potential," "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 the potential of etripamil 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 plans to study etripamil in atrial fibrillation patients, the sufficiency of Milestone's current cash resources to support its operations, Milestone's and Ji Xing's intention and ability to develop and commercialize etripamil in China 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 COVID-19, 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 COMPRENHENSIVE LOSS

(Unaudited, in thousands of US dollars, except share and per share data)

	Three months ended March 31,	
	2021	2020
	$	$
Operating expenses		
Research and development, net of tax credits	**8,595**	11,872
General and administrative	**2,633**	2,703
Commercial	**1,366**	2,183
Loss from operations	**(12,594)**	(16,758)
Interest income, net of bank charges	**80**	415
Net loss and comprehensive loss for the period	**(12,514)**	(16,343)
Weighted average number of shares and pre-funded warrants outstanding, basic and diluted	**41,256,248**	24,548,777
Net loss per share, basic and diluted	**(0.30)**	(0.67)

INTERIM CONDENSED CONSOLIDATED BALANCE SHEETS

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

	March 31, 2021	December 31, 2020
	$	$
ASSETS		
Current Assets		
Cash, cash equivalents and short-term investments	**129,859**	142,310
Prepaid expenses and other current assets	**7,385**	6,376
Total current assets	**137,244**	148,686
Operating lease right-of-use asset	**914**	980
Property and equipment	**285**	308
Total assets	**138,443**	149,974
LIABILITIES		
Current liabilities		
Accounts payable and accrued liabilities	**5,564**	5,914
Current portion of operating lease liabilities	**252**	245
Total current liabilities	**5,816**	6,159
Operating lease liabilities	**635**	696
Total liabilities	**6,451**	6,855
Shareholders' Equity		

Share capital		
Common shares, no par value, unlimited shares authorized 29,846,000 shares issued and outstanding as of March 31, 2021, 29,827,997 shares issued and outstanding as of December 31, 2020	**251,716**	251,682
Pre-funded warrants - 11,417,034 issued and outstanding as of March 31, 2021 and as of December 31, 2020	**48,007**	48,007
Additional paid in capital	**9,883**	8,530
Cumulative translation adjustment	**(1,634)**	(1,634)
Accumulated deficit	**(175,980)**	(163,466)
Total shareholders' equity	**131,992**	143,119
Total liabilities and shareholders' equity	**138,443**	149,974

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