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

May 12, 2022

- *RAPID topline data readout remains on track for mid-second half 2022*
- *Results from NODE-302 study highlights etripamil safety and reduced need for ED interventions*

MONTREAL and CHARLOTTE, N.C., May 12, 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 first quarter ended March 31, 2022, and provided a clinical and corporate update.

"The beginning of 2022 has been a productive time for Milestone, marked by continued progress advancing our lead Phase 3 program, etripamil, for patients with PSVT," said Joseph Oliveto, President and Chief Executive Officer of Milestone Pharmaceuticals. "Of note, we were particularly excited by the recent presentation of NODE-302 at the Heart Rhythm Society's Heart Rhythm 2022 conference which highlighted data that continued to support the potential of etripamil as a self-treatment option for patients with PSVT, including those patients experiencing multiple episodes. We remain optimistic for the eventual safety profile of etripamil as clinical trial experience with the repeat dose regimen grows, and we look forward to reporting topline results from our Phase 3 RAPID trial in the middle of the second half of 2022."

Recent Updates

- **Company Remains on Track to Report Topline Data from RAPID Trial in Mid-Second Half 2022.** The RAPID trial, in which patients are randomized 1:1 to receive either etripamil or placebo, is targeting a total of 180 confirmed PSVT events. To maximize the potential treatment effect of etripamil, patients are directed to administer a repeat dose of study drug if they do not experience symptom relief within 10 minutes of the first dose. 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 submission for etripamil in patients with PSVT.
- **Data from Phase 3 NODE-302 Open-Label Extension Study of Etripamil for the Treatment of PSVT Presented at Heart Rhythm 2022.** In April 2022, new data from NODE-302, Milestone's Phase 3 open-label extension of the NODE-301 study evaluating a single, 70 mg dose of etripamil in patients with PSVT, were presented at the Heart Rhythm Society's Heart Rhythm 2022 conference. The data demonstrate the potential for patients to self-treat recurrent SVT episodes with etripamil. Of 188 positively-adjudicated episodes observed in the trial, the PSVT conversion rate at 30 minutes following etripamil administration was 60.2%, and the need for emergency department (ED) intervention to terminate a PSVT episode was low (13% of patients and 8.5% of positively adjudicated PSVT episodes). Etripamil was generally well-tolerated, with adverse events (AEs) consistent with those observed in previous trials and largely confined to local and brief nasal AEs at the administration site. A copy of the presentation is available in the Publications section of the Milestone Pharmaceuticals website.
- **Hosted Virtual KOL Event on Etripamil for the Treatment of PSVT.** In April 2022, Milestone hosted a virtual Key Opinion Leader (KOL) event focused on etripamil for the treatment of PSVT. Members of management were joined by Bruce Stambler, M.D., FHRS, Director of Cardiac Arrhythmia Research and Education, Piedmont Heart Institute, Atlanta, GA, and Sean Pokorney, M.D., MBA, Director of the Arrhythmia Core Laboratory, Duke Clinical Research Institute, Assistant Professor of Medicine, Duke University School of Medicine, Durham, NC. The event featured an overview of PSVT, including disease prevalence, the current treatment landscape, patient and healthcare system burdens, a review of the existing etripamil dataset in patients with PSVT, and a discussion of the potential commercial opportunity. A recording of the event is currently available under the News & Events of Milestone's website at www.milestonepharma.com.
- **New Clinical Analysis Evaluating the Drug Characteristics and Safety of Etripamil Presented at the American College of Cardiology (ACC) 71st Annual Scientific Session and Expo.** In April 2022, new analyses on the safety, tolerability, pharmacokinetics and pharmacodynamics of etripamil in healthy Japanese and non-Japanese adults was presented at the ACC 71st Annual Scientific Session and Expo. The data demonstrate a comparable safety and tolerability profile in both Japanese and non-Japanese male and female adults, indicating no ethnic differences, and treatment-related AEs consistent with the safety and tolerability profile of etripamil seen to date. A copy of the presentation is available in the Publications section of the Milestone Pharmaceuticals website.
- **Appointment of David Bharucha, M.D., Ph.D., as Chief Medical Officer.** In February 2022, Milestone announced the appointment of Dr. David Bharucha as Chief Medical Officer. Dr. Bharucha is a cardiac electrophysiologist who brings to

Milestone over thirty years of global drug development and clinical experience across a range of therapeutic areas, with a focus on cardiovascular medicine.

- **Recruitment Continues in the ReVeRA Phase 2 Proof-of-Concept Trial in Patients Experiencing Atrial Fibrillation with Rapid Ventricular Rate (AFib-RVR).** Enrollment continues in ReVeRA, Milestone's Phase 2 double-blind, placebo-controlled, proof-of-concept in-patient study of etripamil nasal spray in patients experiencing AFib-RVR. The study, 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 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.

First Quarter 2022 Financial Results

- As of March 31, 2022, Milestone had cash, cash equivalents, and short-term investments of $100.2 million and 29.9 million common shares and 12.3 million common shares issuable upon exercise of pre-funded warrants outstanding.
- Research and development expense for the first quarter of 2022 was $8.8 million, compared with $8.6 million for the prior year period. The $0.2 million increase is the result of increased regulatory and regulatory personnel related costs offset by reduced clinical consulting fees and contracted research organization costs.
- General and administrative (G&A) expense for the first quarter of 2022 was $3.6 million, compared with $2.6 million for the prior year period. The $1.0 million increase in general and administrative expense is due to a $0.5 million increase in personnel related costs, $0.2 million increase in investment in business infrastructure, and $0.3 million increase in other miscellaneous G&A expenses.
- Commercial expense for the first quarter of 2022 was $1.6 million, compared with $1.4 million for the prior year period. The $0.3 million increase of commercial expense is the result of increased personnel related costs.
- For the first quarter of 2022, operating loss was $14.0 million, compared to $12.5 million for the prior year period. Included in this operating loss is a $0.7M increase in stock-based compensation, compared to the prior year period, noted above.

About Paroxysmal Supraventricular Tachycardia

Paroxysmal supraventricular tachycardia (PSVT) is a condition characterized by intermittent episodes of rapid heartbeat that starts and stops suddenly and without warning that affects approximately two million Americans. Episodes of supraventricular tachycardia (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 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 manage the heart rate in this condition. When AFib-RVR episodes occur, symptoms often cause patients to seek acute care in settings 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 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 in 2030 for etripamil in patients with AFib of approximately three to four 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 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 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 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 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," "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, 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 March 31,	
	2022	**2021**
Operating expenses		
Research and development, net of tax credits	$ 8,768	$ 8,595
General and administrative	3,643	2,633
Commercial	1,636	1,366
Loss from operations	(14,047)	(12,594)
Interest income, net	40	80
Net loss	$ (14,007)	$ (12,514)
Weighted average number of shares and pre-funded warrants outstanding, basic & diluted	42,243,021	41,256,248
Net loss per share, basic and diluted	$ (0.33)	$ (0.30)

CONSOLIDATED BALANCE SHEETS

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

	March 31, 2022	**December 31, 2021**
Assets		
Current assets		
Cash and cash equivalents	$ 92,241	$ 114,141
Short-term investment	8,000	—
Research and development tax credits receivable	412	356
Prepaid expenses	4,068	4,299
Other receivables	245	127
Total current assets	104,966	118,923
Operating lease assets	641	711
Property and equipment	192	215
Total assets	$ 105,799	$ 119,849
Liabilities, and Shareholders' Equity		
Current liabilities		
Accounts payable and accrued liabilities	$ 4,412	$ 6,551
Operating lease liabilities	198	224
Total current liabilities	4,610	6,775
Operating lease liabilities (net of current portion)	433	474
Total liabilities	$ 5,043	$ 7,249

Shareholders' Equity		
Common shares, no par value, unlimited shares authorized 29,917,326 shares issued and outstanding as of March 31, 2022, 29,897,559 shares issued and outstanding as of December 31, 2021	251,990	251,901
Pre-funded warrants - 12,327,780 issued and outstanding as of March 31, 2022 and 12,327,780 as of December 31, 2021	52,941	52,941
Additional paid-in capital	17,785	15,711
Cumulative translation adjustment	(1,634)	(1,634)
Accumulated deficit	(220,326)	(206,319)
Total shareholders' equity	100,756	112,600
Total liabilities and shareholders' equity	$ 105,799	$ 119,849

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