Milestone Pharmaceuticals Reports Fourth Quarter and Full Year 2021 Financial Results and Provides Clinical and Corporate Update

March 24, 2022

- *RAPID topline data readout expected mid-second half 2022*

MONTREAL and CHARLOTTE, N.C., March 24, 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 fourth quarter and year ended December 31, 2021 and provided a clinical and corporate update.

"2021 was a year of focused execution across our ongoing clinical programs which are evaluating etripamil in patients with PSVT and AFib-RVR," said Joseph Oliveto, President and Chief Executive Officer of Milestone Pharmaceuticals. "We are well-positioned for a transformative 2022, with topline data from the pivotal Phase 3 RAPID trial on track for the middle of the second half of the year. We are committed to unlocking the full potential of etripamil, if approved, to serve as a meaningful therapeutic option for patients with episodic cardiovascular conditions. We look forward to providing updates on our progress throughout the coming quarters."

Recent Updates

- **Company Expects to Report Topline Data in Mid-Second Half 2022.** The RAPID trial, which is targeting a total of 180 confirmed 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) submission for etripamil in patients with PSVT.

- **New Clinical Analysis Evaluating the Drug Characteristics and Safety of Etripamil to be Presented at the American College of Cardiology (ACC) 71st Annual Scientific Session and Expo.** New analyses on the safety, tolerability, pharmacokinetics and pharmacodynamics of etripamil will be presented at the upcoming ACC 71st Annual Scientific Session and Expo taking place from April 2-4, 2022, in Washington D.C. The presentation, titled "Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of Intranasal Etripamil in Healthy Japanese and Non-Japanese Adults", will be featured during a poster session on April 4, 2022 at 12:15 p.m. ET.

- **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.

- **Heart Rate Data from NODE-301 Study Presented at the American Heart Association (AHA) Scientific Sessions 2021.** In November 2021, new data from a post-hoc analysis of the Phase 3, randomized, double-blind, placebo-controlled NODE-301 trial were presented during an e-poster session at the AHA Scientific Sessions 2021 meeting. The data demonstrated that etripamil significantly decreased heart rate prior to conversion to sinus rhythm. A copy of the presentation, titled "Etripamil Nasal Spray Reduces Heart Rate in Patients with Paroxysmal Supraventricular Tachycardia Prior to Conversion to Sinus Rhythm", is available on the Publications page of the Milestone website.

- **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.

Fourth Quarter and Full Year 2021 Financial Results

- As of December 31, 2021, Milestone had cash, cash equivalents, and short-term investments of $114.1 million, compared to $142.3 million as of December 31, 2020, 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 fourth quarter of 2021 was $10.9 million, compared with $5.8 million for the prior year period. For the full year ended December 31, 2021, research and development expense was $38.7 million, compared with $34.5 million for the prior year. The increase of research and development expense is due to personnel-related costs, higher clinical consulting fees and CRO costs due to advancing RAPID Phase 3 efficacy and NODE-303 safety trials in etripamil for the treatment of PSVT along with an increase in non-cash compensation costs related to share-based compensation expense.

- General and administrative expense for the fourth quarter of 2021 was $3.8 million, compared with $1.7 million for the prior year period. For the full year ended December 31, 2021, general and administrative expense was $12.4 million, compared with $10.3 million for the prior year. The increase of general and administrative expense is due to an increase in share-based compensation expense.

- Commercial expense for the fourth quarter of 2021 was $2.2 million, compared with $1.3 million for the prior year period. For the full year ended December 31, 2021, commercial expense was $7.0 million, compared with $5.9 million for the prior year. The increase of commercial expense is due increase in personnel related costs and marketing activities.

- For the fourth quarter of 2021, operating loss was $16.9 million, compared to $8.8 million for the prior year period. For the full year ended December 31, 2021, Milestone's operating loss was $42.9 million, compared to $50.0 million for the prior year.

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 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, 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 December 31,		Year ended December 31,	
	2021	2020	2021	2020
Revenue	$ —	$ —	$ 15,000	$ —
Operating expenses				
Research and development, net of tax credits	10,916	5,766	38,671	34,488
General and administrative	3,787	1,674	12,399	10,285
Commercial	2,215	1,322	7,003	5,937
Loss from operations	(16,918)	(8,762)	(43,073)	(50,710)
Interest income, net	34	96	220	726
Loss before income taxes	(16,884)	(8,666)	(42,853)	(49,984)
Income tax benefit	—	—	—	17
Net loss	$ (16,884)	$ (8,666)	$ (42,853)	$ (49,967)
Weighted average number of shares and pre-funded warrants outstanding, basic & diluted	42,208,636	38,424,384	41,833,861	29,344,993
Net loss per share, basic and diluted	$ (0.40)	$ (0.23)	$ (1.02)	$ (1.70)

CONSOLIDATED BALANCE SHEETS

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

	December 31, 2021	December 31, 2020
Assets		
Current assets		
Cash and cash equivalents	$ 114,141	$ 72,310
Short-term investment	—	70,000
Research and development tax credits receivable	356	725
Prepaid expenses	4,299	5,428
Other receivables	127	223
Total current assets	118,923	148,686
Operating lease assets	711	980
Property and equipment	215	308
Total assets	$ 119,849	$ 149,974
Liabilities, and Shareholders' Equity		
Current liabilities		
Accounts payable and accrued liabilities	$ 6,551	$ 5,914
Operating lease liabilities	224	245
Total current liabilities	6,775	6,159
Operating lease liabilities (net of current portion)	474	696
Total liabilities	7,249	6,855
Shareholders' Equity		

Common shares, no par value, unlimited shares authorized 29,897,559 shares issued and outstanding as of December 31, 2021, 29,827,997 shares issued and outstanding as of December 31, 2020	251,901	251,682
Pre-funded warrants - 12,327,780 issued and outstanding as of December 31, 2021 and 11,417,034 as of December 31, 2020	52,941	48,007
Additional paid-in capital	15,711	8,530
Cumulative translation adjustment	(1,634)	(1,634)
Accumulated deficit	(206,319)	(163,466)
Total shareholders' equity	112,600	143,119
Total liabilities and shareholders' equity	$ 119,849	$ 149,974

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