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

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MONTREAL and CHARLOTTE, N.C., Aug. 11, 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 second quarter ended June 30, 2021 and provided a clinical and corporate update.

"The second quarter of 2021 was marked by continued progress advancing our ongoing programs evaluating etripamil in patients with PSVT and AFib-RVR," said Joseph Oliveto, President and Chief Executive Officer of Milestone Pharmaceuticals. "With respect to the Phase 3 RAPID trial of etripamil in patients with PSVT, we are encouraged by continued improvements in study enrollment rates. We look forward to building on this momentum in the coming quarters and remain on track to report topline data in the second half of 2022."

Mr. Oliveto added, "Beyond PSVT, recent market research with cardiologists has strengthened our belief that etripamil has the potential to become a valuable treatment option for patients experiencing episodes of AFib-RVR."

Recent Updates

- **Entered Exclusive License Agreement with Ji Xing Pharmaceuticals to Develop and Commercialize Etripamil for PSVT in Greater China.** In May 2021, the Company announced that it 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. In connection with the agreement, Milestone received an upfront cash payment consisting of $15 million and a $5 million equity investment by RTW Investments. In addition, the Company could receive up to $107.5 million in total development and sales milestone payments as well as tiered royalty payments on all products sold in the Greater China territory. Milestone will supply etripamil and delivery devices to Ji Xing. Ji Xing will be responsible for development and commercialization costs in Greater China.

- **Company Remains on Track to Report Topline Data from Pivotal Phase 3 RAPID Trial in the Second Half of 2022.** Enrollment continues in the ongoing pivotal Phase 3 RAPID trial of etripamil nasal spray in patients with PSVT. As previously announced, the Company is working closely with study investigators to identify potential site-specific solutions to mitigate COVID-related enrollment and site initiation delays, and has also increased the number of participating centers. The Company continues to expect 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. 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.

- **Open-Label NODE-303 Safety Amended to Include Repeat Dosing of Etripamil.** In May 2021, the Company announced that the U.S. Food and Drug Administration agreed to allow future patients enrolled in the ongoing NODE-303 study to utilize a repeat dose of etripamil if symptoms persist for 10 minutes after the first dose. NODE-303 is Milestone's 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. The Company is in the process of implementing the repeat dose regimen in the study.

- **Data from Study of Prevalence and Incidence of Patients with PSVT in the U.S. Published in the Journal of Cardiovascular Electrophysiology.** In May 2021, findings from an observational retrospective longitudinal study using claims estimated the incidence and prevalence of PSVT in contemporary practice were published in the *Journal of Cardiovascular Electrophysiology*. The article, titled "Prevalence and incidence of patients with paroxysmal supraventricular tachycardia in the United States", estimated that 1.3 – 2.1 million people in the U.S. have PSVT, which includes patients

with potentially comorbid atrial fibrillation/atrial flutter.

- **Enrollment Continues in ReVeRA Phase 2 Proof-of-Concept Trial Evaluating Etripamil in Patients Experiencing Atrial Fibrillation with Rapid Ventricular Rate (AFib-RVR).** Enrollment is ongoing in ReVeRA, Milestone's Phase 2 proof-of-concept study of etripamil nasal spray in patients experiencing AFib-RVR, in which patients will be 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 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.

Second Quarter 2021 Financial Results

- As of June 30, 2021, Milestone had cash, cash equivalents, and short-term investments of $135.8 million and 29.8 million common shares issued and outstanding and 12.3 million common shares issuable upon exercise of pre-funded warrants outstanding.

- Revenue of $15 million was generated from the upfront payment under the License Agreement during the three months and six months ended June 30, 2021.

- Research and development expense for the second quarter of 2021 was $9.4 million compared with $8.6 million for the prior year period. The difference is due to an increase in clinical expense of $0.8 million. For the six months ended June 30, 2021, research and development expense was $18.0 million compared with $20.5 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 six months ended June 30, 2021.

- General and administrative expenses for the second quarter of 2021 and 2020 were $3.0 million. For both of the six month periods ended June 30, 2021 and 2020, respectively, general and administrative expense was $5.7 million.

- Commercial expense for the second quarter of 2021 was $1.8 million compared with $1.5 million for the prior year period. During the second quarter of 2020, the Company reduced commercial costs in order to focus its efforts on an optimized clinical development pathway for etripamil. During the three months ended June 30, 2021, the Company increased our investment in commercialization activities resulting in higher commercial expenses. For the six months ended June 30, 2021, commercial expense was $3.2 million compared with $3.7 million for the prior year period. The decrease of commercial expense in the six months ended June 30, 2021 reflects efforts reducing operating expenses from pre-commercialization activities.

- For the second quarter of 2021, operating income was $0.7 million compared to operating loss of $13.1 million in 2020. For the six months ended June 30, 2021, Milestone's operating loss was $11.9 million compared to $29.9 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 (SVT) that starts and stops suddenly and without warning that 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 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 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 "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 Greater 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 June 30,		Six months ended June 30,	
	2021	2020	**2021**	2020
	$	$	$	$
Collaboration Revenue	**15,000**	-	**15,000**	-
Operating expenses				
Research and development, net of tax credits	**9,427**	8,622	**18,022**	20,493
General and administrative	**3,018**	2,956	**5,651**	5,659
Commercial	**1,843**	1,527	**3,209**	3,710
Total Operating expenses	**14,288**	13,105	**26,882**	29,862
Income (Loss) from operations	**712**	(13,105)	**(11,882)**	(29,862)
Interest income, net of bank charges	**58**	126	**138**	540
Net income (loss) and comprehensive loss for the period	**770**	(12,979)	**(11,744)**	(29,322)
Weighted average number of shares and pre-funded warrants outstanding, basic and diluted	**41,673,370**	24,548,777	**41,465,961**	24,588,413
Net income (loss) per share, basic and diluted	0.02	(0.53)	(0.28)	(1.20)
Weighted average number of shares and pre-funded warrants outstanding, basic and diluted	**44,530,121**	24,548,777	**41,465,961**	24,588,413
Net income (loss) per share, basic and diluted	0.02	(0.53)	(0.28)	(1.20)

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

	June 30, 2021	December 31, 2020

	$	$
ASSETS		
Current Assets		
Cash, cash equivalents and short-term investments	**135,794**	142,310
Prepaid expenses and other current assets	**8,592**	6,376
Total current assets	**144,386**	148,686
Operating lease right-of-use asset	**847**	980
Property and equipment	**262**	308
Total assets	**145,495**	149,974
LIABILITIES		
Current liabilities		
Accounts payable and accrued liabilities	**5,069**	5,914
Current portion of operating lease liabilities	**259**	245
Total current liabilities	**5,328**	6,159
Operating lease liabilities	**573**	696
Total liabilities	**5,901**	6,855
Shareholders' Equity		
Share capital		
Common shares, no par value, unlimited shares authorized 29,846,000 shares issued and outstanding as of June 30, 2021, 29,827,997 shares issued and outstanding as of December 31, 2020	**251,716**	251,682
Pre-funded warrants - 12,327,780 issued and outstanding as of June 30, 2021 and 11,417,034 as of December 31, 2020	**52,927**	48,007
Additional paid in capital	**11,795**	8,530
Cumulative translation adjustment	**(1,634)**	(1,634)
Accumulated deficit	**(175,210)**	(163,466)
Total shareholders' equity	**139,594**	143,119
Total liabilities and shareholders' equity	**145,495**	149,974

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