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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 20549

FORM 10-Q

(Mark One)

☒ **QUARTERLY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the quarterly period ended June 30, 2022

OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the transition period from to

Commission File Number: 001-38899

Milestone Pharmaceuticals Inc.

(Exact Name of Registrant as Specified in its Charter)

Québec	**Not applicable**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)

1111 Dr. Frederik-Philips Boulevard, Suite 420
Montréal, Québec CA H4M 2X6
(514) 336-0444
(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Shares	MIST	The Nasdaq Stock Market LLC

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☒ No ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	☐	Accelerated filer	☐
Non-accelerated filer	☒	Smaller reporting company	☒
Emerging growth company	☒		

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☒

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ☐ No ☒

As of August 10th, 2022, the registrant had 30,010,873 common shares, no par value per share, outstanding.

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“Milestone Pharmaceuticals” and the Milestone logo appearing in this Quarterly Report on Form 10-Q are unregistered trademarks of Milestone Pharmaceuticals Inc. All other trademarks, trade names and service marks appearing in this Quarterly Report on Form 10-Q are the property of their respective owners. Solely for convenience, the trademarks and trade names in this Quarterly Report on Form 10-Q may be referred to without the ® and ™ symbols, but such references should not be construed as any indicator that their respective owners will not assert their rights thereto.

This Quarterly Report on Form 10-Q contains references to United States dollars and Canadian dollars. All dollar amounts referenced, unless otherwise indicated, are expressed in United States dollars. References to “$” are to United States dollars and references to “C$” are to Canadian dollars.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Quarterly Report on Form 10-Q contains forward-looking statements about us and our industry that involve substantial risks and uncertainties. All statements other than statements of historical facts contained in this Quarterly Report on Form 10-Q, including statements regarding our strategy, future financial condition, future operations, projected costs, prospects, plans, objectives of management and expected market growth, are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as "aim," "anticipate," "assume," "believe," "contemplate," "continue," "could," "design," "due," "estimate," "expect," "goal," "intend," "may," "objective," "plan," "predict," "positioned," "potential," "seek," "should," "target," "will," "would" and other similar expressions that are predictions of or indicate future events and future trends, or the negative of these terms or other comparable terminology.

We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our financial condition, results of operations, business strategy and financial needs. These forward-looking statements are subject to a number of known and unknown risks, uncertainties and assumptions, including risks described in the section titled "Risk Factors" and elsewhere in this Quarterly Report on Form 10-Q, regarding, among other things:

- the initiation, timing, progress and results of our current and future clinical trials of etripamil, including our Phase 3 clinical trials of etripamil for the treatment of paroxysmal supraventricular tachycardia, our Phase 2 clinical trial of etripamil for the treatment of atrial fibrillation with rapid ventricular rate, and of our research and development programs;
- uncertain impacts that the COVID-19 pandemic may have on our business, strategy, clinical trial progress and research and development efforts;
- our plans to develop and commercialize etripamil and any future product candidates;
- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing;
- our ability to develop and, if approved by regulatory authorities, commercialize etripamil in China and Taiwan through our license agreement with Ji Xing Pharmaceuticals;
- our ability to establish collaborations or obtain additional funding;
- our ability to obtain regulatory approval of our current and future product candidates;
- our expectations regarding the potential market size and the rate and degree of market acceptance of etripamil and any future product candidates;
- our ability to fund our working capital requirements and expectations regarding the sufficiency of our capital resources;

- the implementation of our business model and strategic plans for our business, etripamil and any future product candidates;
- our intellectual property position and the duration of our patent rights;
- developments or disputes concerning our intellectual property or other proprietary rights;
- our expectations regarding government and third-party payer coverage and reimbursement;
- our ability to compete in the markets we serve;
- the impact of government laws and regulations;
- developments relating to our competitors and our industry; and
- other factors that may impact our financial results.

The foregoing list of risks is not exhaustive. Other sections of this Quarterly Report on Form 10-Q and the section titled "Risk Factors" previously disclosed in Part I, Item 1A. in our Annual Report on Form 10-K may include additional factors that could harm our business and financial performance. Moreover, we operate in a very competitive and rapidly changing environment. New risk factors emerge from time to time, and it is not possible for our management to predict all risk factors nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in, or implied by, any forward-looking statements.

In light of the significant uncertainties in these forward-looking statements, you should not rely upon forward-looking statements as predictions of future events. Although we believe that we have a reasonable basis for each forward-looking statement contained in this Quarterly Report on Form 10-Q, we cannot guarantee that the future results, levels of activity, performance or events and circumstances reflected in the forward-looking statements will be achieved or occur at all. You should refer to the section titled "Risk Factors" previously disclosed in Part I, Item 1A. in our Annual Report on Form 10-K, filed with the SEC and under Milestone’s SEDAR profile at www.sedar.com on March 24, 2022, for a discussion of important factors that may cause our actual results to differ materially from those expressed or implied by our forward-looking statements. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. Except as required by law, we undertake no obligation to publicly update any forward-looking statements, whether as a result of new information, future events or otherwise.

PART I—FINANCIAL INFORMATION

Item 1. Financial Statements.

Milestone Pharmaceuticals Inc.
Condensed Consolidated Balance Sheets (Unaudited)
(in thousands of US dollars, except share data)

	June 30, 2022	December 31, 2021
Assets		
Current assets		
Cash and cash equivalents	$ 63,237	$ 114,141
Short-term investments	23,000	—
Research and development tax credits receivable	539	356
Prepaid expenses	3,465	4,299
Other receivables	261	127
Total current assets	90,502	118,923
Operating lease assets	570	711
Property and equipment	227	215
Total assets	$ 91,299	$ 119,849
Liabilities, and Shareholders' Equity		
Current liabilities		
Accounts payable and accrued liabilities	$ 4,087	$ 6,551
Operating lease liabilities	169	224
Total current liabilities	4,256	6,775
Operating lease liabilities (net of current portion)	384	474
Total liabilities	4,640	7,249
Shareholders' Equity		
Common shares, no par value, unlimited shares authorized 30,005,884 shares issued and outstanding as of June 30, 2022, 29,897,559 shares issued and outstanding as of December 31, 2021	252,236	251,901
Pre-funded warrants - 12,327,780 issued and outstanding as of June 30, 2022 and 12,327,780 as of December 31, 2021	52,941	52,941
Additional paid-in capital	20,090	15,711
Cumulative translation adjustment	(1,634)	(1,634)
Accumulated deficit	(236,974)	(206,319)
Total shareholders' equity	86,659	112,600
Total liabilities and shareholders' equity	$ 91,299	$ 119,849

The accompanying notes are an integral part of these interim condensed consolidated financial statements.

Milestone Pharmaceuticals Inc.
Condensed Consolidated Statements of Earnings (Loss) (Unaudited)
(in thousands of US dollars, except share and per share data)

	Three months ended June 30,		Six months ended June 30,	
	2022	2021	2022	2021
Revenue	$ —	$ 15,000	$ —	$ 15,000
Operating expenses				
Research and development, net of tax credits	10,657	9,427	19,425	18,022
General and administrative	3,918	3,018	7,561	5,651
Commercial	2,231	1,843	3,867	3,209
Earnings (loss) from operations	(16,806)	712	(30,853)	(11,882)
Interest income, net	158	58	198	138
Net earnings (loss)	$ (16,648)	$ 770	$ (30,655)	$ (11,744)
Weighted average number of shares and pre-funded warrants outstanding, basic	42,278,563	41,673,370	42,260,682	41,465,961
Net earnings (loss) per share, basic	$ (0.39)	$ 0.02	$ (0.73)	$ (0.28)
Weighted average number of shares and pre-funded warrants outstanding, diluted	42,278,563	44,530,121	42,260,682	41,465,961
Net earnings (loss) per share, diluted	$ (0.39)	$ 0.02	$ (0.73)	$ (0.28)

The accompanying notes are an integral part of these interim condensed consolidated financial statements.

Milestone Pharmaceuticals Inc.
Condensed Consolidated Statements of Shareholders' Equity (Unaudited)
(in thousands of US dollars, except share data)

	Common Shares		Pre-funded warrants					
	Number of shares	Amount	Number of warrants	Amount	Additional paid-in capital	Cumulative translation adjustment	Accumulated deficit	Total
Balance as of March 31, 2021	29,846,000	$ 251,716	11,417,034	$ 48,007	$ 9,883	$ (1,634)	$ (175,980)	$ 131,992
Transactions in three-month period ended June 30, 2021								
Net earnings	—	—	—	—	—	—	770	770
Exercise of stock options	—	—	—	—	—	—	—	—
Private Placement	—	—	910,746	4,920	—	—	—	4,920
Share-based compensation	—	—	—	—	1,912	—	—	1,912
Balance as of June 30, 2021	29,846,000	$ 251,716	12,327,780	$ 52,927	$ 11,795	$ (1,634)	$ (175,210)	$ 139,594
Balance as of March 31, 2022	29,917,326	$ 251,990	12,327,780	$ 52,941	$ 17,785	$ (1,634)	$ (220,326)	**$** 100,756
Transactions in three-month period ended June 30, 2022								
Net loss	—	—	—	—	—	—	(16,648)	(16,648)
Exercise of stock options	88,558	246	—	—	(106)	—	—	140
Private Placement	—	—	—	—	—	—	—	—
Share-based compensation	—	—	—	—	2,411	—	—	2,411
Balance as of June 30, 2022	30,005,884	$ 252,236	12,327,780	$ 52,941	$ 20,090	$ (1,634)	$ (236,974)	$ 86,659
Balance as of December 31, 2020	29,827,997	$ 251,682	11,417,034	$ 48,007	$ 8,530	$ (1,634)	$ (163,466)	$ 143,119
Transactions in six-month period ended June 30, 2021								
Net loss	—	—	—	—	—	—	(11,744)	(11,744)
Exercise of stock options	18,003	34	—	—	(15)	—	—	19
Private Placement	—	—	910,746	4,920	—	—	—	4,920
Share-based compensation	—	—	—	—	3,280	—	—	3,280
Balance as of June 30, 2021	29,846,000	$ 251,716	12,327,780	$ 52,927	$ 11,795	$ (1,634)	$ (175,210)	$ 139,594
Balance as of December 31, 2021	29,897,559	$ 251,901	12,327,780	$ 52,941	$ 15,711	$ (1,634)	$ (206,319)	**$** 112,600
Transactions in six-month period ended June 30, 2022								
Net loss	—	—	—	—	—	—	(30,655)	(30,655)
Exercise of stock options	108,325	335	—	—	(146)	—	—	189
Share-based compensation	—	—	—	—	4,525	—	—	4,525
Balance as of June 30, 2022	30,005,884	$ 252,236	12,327,780	$ 52,941	$ 20,090	$ (1,634)	$ (236,974)	$ 86,659

The accompanying notes are an integral part of these interim condensed consolidated financial statements.

Milestone Pharmaceuticals Inc.
Condensed Consolidated Statements of Cash Flows (Unaudited)
(in thousands of US dollars)

	Six months ended June 30,	
	2022	**2021**
Cash flows used in operating activities		
Net loss	$ (30,655)	$ (11,744)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation of property and equipment	47	46
Share-based compensation expense	4,525	3,280
Changes in operating assets and liabilities:		
Other receivables	(134)	(19)
Research and development tax credits receivable	(183)	(178)
Prepaid expenses	834	(2,019)
Operating lease assets and liabilities	(4)	24
Accounts payable and accrued liabilities	(2,464)	(845)
Net cash used in operating activities	(28,034)	(11,455)
Cash provided by (used in) investing activities		
Acquisition of property and equipment	(59)	—
Acquisition of short-term investments	(23,000)	—
Redemption of short-term investments	—	32,000
Net cash provided by (used in) investing activities	(23,059)	32,000
Cash provided by financing activities		
Proceeds from exercise of options	189	19
Net Proceeds from issuance of pre-funded warrants in a private placement	—	4,920
Cash provided by financing activities	189	4,939
Net decrease in cash and cash equivalents	(50,904)	25,484
Cash and cash equivalents – Beginning of period	114,141	72,310
Cash and cash equivalents – End of period	$ 63,237	$ 97,794

The accompanying notes are an integral part of these interim condensed consolidated financial statements.

Milestone Pharmaceuticals Inc.
Notes to Condensed Consolidated Financial Statements
For The Six Months Ended June 30, 2022 and 2021 (Unaudited)
(in thousands of US dollars, except where noted and for share and per share data)

1 Organization and Nature of Operations

Milestone Pharmaceuticals Inc. (Milestone or the Company) is a biopharmaceutical company incorporated under the *Business Corporations Act* (Québec). Milestone is focused on the development and commercialization of cardiovascular medicines. Milestone's lead product candidate, etripamil, is a novel, potent short-acting calcium channel blocker that the Company designed and is developing as a rapid-onset nasal spray to be administered by patients. The Company is developing etripamil to treat paroxysmal supraventricular tachycardia, atrial fibrillation, and other cardiovascular indications.

2 Summary of Significant Accounting Policies

a) Basis of Consolidation

The consolidated financial statements include the accounts of the Company and Milestone Pharmaceuticals USA, Inc. All intercompany transactions and balances have been eliminated.

b) Basis of presentation and use of accounting estimates and significant accounting policies

These unaudited interim condensed consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America (US GAAP) and on a basis consistent with those accounting principles followed by the Company and disclosed in Note 2 of its most recent annual consolidated financial statements. Certain information, in particular the accompanying notes normally included in the annual financial statements prepared in accordance with US GAAP have been omitted or condensed. Accordingly, the unaudited interim condensed consolidated financial statements do not include all the information required for full annual financial statements, and therefore, should be read in conjunction with the annual consolidated financial statements and the notes thereto for the year ended December 31, 2021.

In the opinion of the Company's management, the accompanying unaudited interim condensed consolidated financial statements contain all adjustments, consisting of only normal recurring adjustments, necessary for a fair statement of its balance sheet as of June 30, 2022, and its statements of earnings (loss), shareholders' equity for the three and six months ended June 30, 2022 and 2021 and its statement of cash flows for the six months ended June 30, 2022 and 2021.

The condensed consolidated balance sheet as of December 31, 2021, was derived from audited annual consolidated financial statements, but does not contain all the footnote disclosures required by accounting principles generally accepted in the United States of America.

These unaudited interim condensed consolidated financial statements are presented in US dollars, which is the Company's functional currency.

The preparation of unaudited interim condensed consolidated financial statements in conformity with US GAAP requires the Company to make estimates and judgments that affect certain reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the consolidated financial statements and the reported amounts of revenue and expenses during the period. The Company bases its estimates and assumptions on current facts, historical experience and various other factors that it believes are reasonable under the circumstances, to determine the carrying values of assets and liabilities that are not readily apparent from other sources. Significant estimates and judgments include, but are not limited to,

- Estimates of the percentage of work completed of the total work over the life of an individual clinical trial in accordance with agreements established with contracted research organizations ("CRO"), contracted

manufacturing organizations ("CMO") and clinical trial sites which in turn impact the research & development expenses.

- Estimate of the grant date fair value share options granted to employees, consultants and directors, and the resulting share-based compensation expense, using the Black-Scholes option-pricing model.

c) Significant Risks and Uncertainties

The ongoing COVID-19 pandemic has had an impact on the Company's business, operations and clinical development timelines. The pandemic has resulted in many state, local and foreign governments implementing, and making adjustments to, various orders and restrictions in order to control the spread of the disease, which have impacted patient recruitment, enrollment and follow-up visits at clinical sites The Company will continue to evaluate the COVID-19 pandemic impact on the development timelines of its clinical programs. Estimates and assumptions about future events and their effects cannot be determined with certainty and therefore require the exercise of judgment. As of the date of issuance of these consolidated financial statements, the Company is not aware of any specific event or circumstance that would require the Company to update its estimates, assumptions and judgments. These estimates may change as new events occur and additional information is obtained and are recognized in the consolidated financial statements as soon as they become known. Actual results could differ from those estimates and any such differences may be material to the Company's unaudited interim condensed consolidated financial statements.

In addition, the Company is subject to other challenges and risks specific to its business and its ability to execute on its strategy, as well as risks and uncertainties common to companies in the pharmaceutical industry, including, without limitation, risks and uncertainties associated with: obtaining regulatory approval of its product candidate; delays or problems in the supply of its study drug or failure to comply with manufacturing regulations; identifying, acquiring or in-licensing product candidates; pharmaceutical product development and the inherent uncertainty of clinical success; and the challenges of protecting and enhancing its intellectual property rights; and complying with applicable regulatory requirements.

d) Recent Accounting Pronouncements

The Company has considered recent accounting pronouncements and concluded that they are either not applicable to the business or that the effect is not expected to be material to the unaudited condensed consolidated financial statements as a result of future adoption.

e) Sources of Liquidity and Funding Requirements

The Company incurred operating losses and has experienced negative operating cash flows since its inception and anticipates to continue to incur losses for at least the next several years. As of June 30, 2022, the Company had cash, cash equivalents and short-term investments of $86.2 million and an accumulated deficit of $237.0 million. Management has evaluated the Company's current operating plan against our existing cash and cash equivalents and access to potential financing sources and determined that we expect to be able to support our ongoing operations for at least the next twelve months from the date of issuance of this quarterly report on Form 10-Q.

3 Revenues

For the quarter ended June 30, 2022, the Company has not recognized any revenue. During the quarter ended June 30, 2021, the Company recognized revenue of $15 million, in the form of a non-refundable upfront cash payment in connection with a license agreement

Milestone Pharmaceuticals Inc.
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For The Six Months Ended June 30, 2022 and 2021 (Unaudited)
(in thousands of US dollars, except where noted and for share and per share data)

4 Short-term Investments

Short term investments are classified as held-to-maturity, are initially recognized at fair value and are subsequently accounted for at amortized cost. They are comprised of guaranteed investment certificates with a maturity greater than 90 days but less than one year and, as such, are classified as current assets.

5 Accounts Payable and Accrued Liabilities

Accounts payable and accrued liabilities are comprised of the following:

	June 30, 2022	December 31, 2021
Trade accounts payable	$ 1,507	$ 4,384
Accrued compensation and benefits payable	527	1,458
Accrued research and development liabilities	964	272
Other accrued liabilities	1,089	437
Total	$ 4,087	$ 6,551

6 Shareholders' equity

Authorized Share Capital

The Company has authorized and issued common shares, voting and participating, without par value, of which unlimited shares were authorized and 30,005,884 shares were issued and outstanding as of June 30, 2022.

As of June 30, 2022, there were 1,121,076 common shares available for issuance under the Employee Stock Purchase Plans and no common shares have been issued under such plan.

Additional Paid-in Capital

The additional paid-in capital balances were as follows:

	Three months ended June 30,		Six months ended June 30,	
	2022	2021	2022	2021
Opening balance	$ 17,785	$ 9,883	$ 15,711	$ 8,530
Share-based compensation expense	2,411	1,912	4,525	3,280
Exercise of stock options	(106)	—	(146)	(15)
Closing balance	$ 20,090	$ 11,795	$ 20,090	$ 11,795

7 Share Based Compensation

Under the Company's 2019 Equity Incentive Plan (the 2019 Plan) and the Company's Stock Option Plan (the 2011 Plan), unless otherwise decided by the Board of Directors, options vest and are exercisable as follows: 25% vest and are exercisable on the one year anniversary of the grant date and one thirty-sixth ($1/36^{th}$) of the remaining options vest and are exercisable each month thereafter, such that options are vested in full on four-year anniversary of the grant date.

On January 1, 2022, the number of the Company's common shares reserved for issuance under the 2019 Plan increased by 1,195,902 common shares. In addition, 125,127 options have been forfeited under the 2011 Plan since the adoption of

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the 2019 Plan and have become available for issuance under the 2019 Plan. As of June 30, 2022, there were 5,811,310 shares available for issuance under the 2019 Plan, of which 660,669 shares were available for future grants.

On November 10, 2021, the Company established a 2021 Inducement Plan through the granting of awards. This 2021 Inducement Plan is intended to help the Company provide an inducement material for certain individuals to enter into employment with the Company, incentives for such persons to exert maximum efforts for the success of the Company and provide a means by which employees may benefit from increases in value of the common shares. There were 523,000 options granted and outstanding under the 2021 Inducement Plan during the six month period ended June 30, 2022. The options were granted at a weighted average exercise price of $6.37.

Beginning July 15, 2022, the Company will begin to offer an ESPP (“Employee Stock Purchase Plan”), in which participation will be available to substantially all of our employees in the United States and Canada who meet certain service eligibility requirements. As of June 30, 2022, the Company has 1,121,076 shares available under the ESPP with no shares issued under this plan.

Milestone Pharmaceuticals Inc.
Notes to Condensed Consolidated Financial Statements
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(in thousands of US dollars, except where noted and for share and per share data)

The total outstanding and exercisable options from the 2011 Plan, 2019 Plan and Inducement Plan as of June 30 were as follows:

	2022				
	Number of shares				Weighted average exercise price
	2019 Plan	Inducement Plan	2011 Plan	Total	
Outstanding at beginning of year - 2011 Plan	$ —	—	$ 1,995,971	1,995,971	$ 2.07
Outstanding at beginning of year - 2019 Plan	3,759,834	—	—	3,759,834	9.51
Granted - 2019 Plan	1,385,700	—	—	1,385,700	5.47
Granted - Inducement Plan	—	523,000	—	523,000	6.37
Expired - 2011 Plan	—	—	(1,121)	(1,121)	0.96
Exercised - 2011 Plan	—	—	(94,225)	(94,225)	1.43
Exercised - 2019 Plan	(14,100)	—	—	(14,100)	3.76
Cancelled - 2011 Plan	—	—	(19,387)	(19,387)	9.42
Cancelled - 2019 Plan	(13,893)	—	—	(13,893)	13.36
Outstanding at end of period	$ 5,117,541	523,000	1,881,238	7,521,779	$ 6.68
Outstanding at end of period - Weighted average exercise price	$ 8.42	6.37	$ 2.03		
Exercisable at end of period	2,017,527	—	1,796,396	3,813,923	$ 6.09
Exercisable at end of period - Weighted average exercise price	$ 9.74	—	$ 1.99		

	2021				
	Number of shares				Weighted average exercise price
	2019 Plan	Inducement Plan	2011 Plan	Total	
Outstanding at beginning of year - 2011 Plan	$ —	—	$ 2,080,097	2,080,097	$ 2.15
Outstanding at beginning of year - 2019 Plan	1,706,190	—	—	1,706,190	13.55
Granted - 2019 Plan	1,863,950	—	—	1,863,950	6.31
Exercised - 2011 Plan	—	—	(16,753)	(16,753)	0.88
Exercised - 2019 Plan	(1,250)	—	—	(1,250)	3.74
Outstanding at end of period	3,568,890	—	2,063,344	5,632,234	$ 6.99
Outstanding at end of period - Weighted average exercise price	$ 9.77	—	$ 2.16		
Exercisable at end of period	591,885	—	1,613,229	2,205,114	$ 4.86
Exercisable at end of period - Weighted average exercise price	$ 12.55	—	$ 2.05		

The weighted average remaining contractual life was 8.1 and 8.3 years for outstanding options as of June 30, 2022 and 2021, respectively. The weighted average remaining contractual life was 6.9 and 7.0 years for vested options, as of June 30, 2022 and 2021, respectively.

There was $19.0 million and $19.4 million total unrecognized compensation cost related to non-vested share options as of June 30, 2022 and 2021, respectively. The share options are expected to be recognized over a remaining weighted average vesting period of 2.7 years and 2.8 years as of June 30, 2022 and 2021, respectively.

Options granted are valued using the Black-Scholes option pricing model. Amortization of the fair value of the options over vesting years has been expensed and credited to additional paid-in capital in shareholders' equity.

Milestone Pharmaceuticals Inc.
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For The Six Months Ended June 30, 2022 and 2021 (Unaudited)
(in thousands of US dollars, except where noted and for share and per share data)

The non-vested options as of June 30 were as follows:

	2022				
	Number of options				Weighted average fair value
	2019 Plan	Inducement Plan	2011 Plan	Total	
Non-vested share options at beginning of year - 2011 Plan	—	—	200,639	200,639	$ 1.86
Non-vested share options at beginning of year - 2019 Plan	2,665,518	—	—	2,665,518	6.39
Granted - 2019 Plan	1,385,700	—	—	1,385,700	4.13
Granted - Inducement Plan	—	523,000	—	523,000	4.81
Vested, outstanding 2011 Plan	—	—	(115,797)	(115,797)	1.75
Vested, outstanding 2019 Plan	(942,473)	—	—	(942,473)	5.63
Forfeited - 2019 Plan	(8,731)	—	—	(8,731)	6.27
Non-vested share options at end of period	3,100,014	523,000	84,842	3,707,856	$ 5.42
Non-vested share options at end of period - Weighted average fair value	$ 5.62	$ —	$ 2.01		

	2021				
	Number of options				Weighted average fair value
	2019 Plan	Inducement Plan	2011 Plan	Total	
Non-vested share options at beginning of year - 2011 Plan	—	—	543,192	543,192	$ 1.81
Non-vested share options at beginning of year - 2019 Plan	1,438,026	—	—	1,438,026	10.28
Granted - 2019 Plan	1,863,950	—	—	1,863,950	4.79
Vested, outstanding 2011 Plan	—	—	(93,087)	(93,087)	1.61
Vested, outstanding 2019 Plan	(324,971)	—	—	(324,971)	11.38
Non-vested share options at end of period	2,977,005	—	450,105	3,427,110	$ 6.08
Non-vested share options at end of period - Weighted average fair value	$ 6.72	$ —	$ 1.85		

There were 523,000 options granted, outstanding and non-vested under the 2021 Inducement Plan during the six month period ended June 30, 2022. The options were granted at a weighted average fair value price of $4.81.

The fair value of share-based payment transaction is measured using Black-Scholes valuation model. This model also requires assumptions, including expected option life, volatility, risk-free interest rate and dividend yield, which greatly affect the calculated values.

The fair value of options granted for the 2011 Plan, 2019 Plan and 2021 Inducement Plan were estimated using the Black-Scholes option pricing model, resulting in the following weighted average assumptions for the options granted:

	Three months ended June 30,		Six months ended June 30,	
	2022	2021	2022	2021
Exercise price	$ 6.21	$ 5.56	$ 5.72	$ 6.24
Share price	$ 6.21	$ 5.56	$ 5.72	$ 6.24
Volatility	91 %	92 %	91 %	94 %
Risk-free interest rate	2.72 %	0.86 %	2.31 %	1.04 %
Expected life	6.08	5.32	6.08	6.01
Dividend	0 %	0 %	0 %	0 %

Expected volatility is determined using comparable companies for which the information is publicly available. The risk-free interest rate is determined based on the U.S. sovereign rates benchmark in effect at the time of grant with a remaining term equal to the expected life of the option. Expected option life is determined based on the simplified method as the Company does not have sufficient historical exercise data to provide a reasonable basis upon which to estimate expected

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term. The simplified method is an average of the contractual term of the options and its ordinary vesting period. Dividend yield is based on the share option's exercise price and expected annual dividend rate at the time of grant.

The Company recognized share-based compensation expense as follows:

	Three months ended June 30,		Six months ended June 30,	
	2022	2021	2022	2021
Administration	$ 880	$ 750	$ 1,792	$ 1,323
Research and development	1,105	825	1,953	1,405
Commercial activities	426	337	780	552
Total	$ 2,411	$ 1,912	$ 4,525	$ 3,280

8 Net Loss Per Share

Basic net loss per common share is determined by dividing net loss applicable to common shareholders by the weighted average number of common shares and pre-funded warrants outstanding during the period.

For the six months ended June 30, 2022 and 2021, the Company was in a net loss position. Dilutive net loss per common share is determined by dividing net loss applicable to common shareholders by the weighted average number of common shares and shares issuable upon exercise of pre-funded warrants outstanding during the period. The following potentially dilutive securities have been excluded from the computation of diluted weighted average shares outstanding as of June 30, as they would be anti-dilutive:

	2022	2021
Share options	7,521,779	5,819,524

Amounts above reflect the common share equivalents of the noted instruments.

Item 2. Management's Discussion and Analysis of Financial Condition and Results of Operations.

The following information should be read in conjunction with the unaudited interim condensed consolidated statements and the notes thereto included in this Quarterly Report on Form 10-Q and the audited annual consolidated financial statements and the notes thereto included in our Annual Report on Form 10-K for the year ended December 31, 2021, which was filed with the Securities and Exchange Commission, or SEC, on March 24, 2022. Our actual results may differ materially from those anticipated in these forward-looking statements as a result of various factors, including those discussed in "Risk Factors" and in other parts of this Quarterly Report on Form 10-Q.

Overview

We are a biopharmaceutical company focused on the development and commercialization of innovative cardiovascular medicines. Our lead product candidate etripamil is a novel, potent and short-acting calcium channel blocker that we designed as a rapid-onset nasal spray to be self-administered by patients. We are developing etripamil for the treatment of specific arrhythmias with a lead indication to treat paroxysmal supraventricular tachycardia, or PSVT, with subsequent indications to treat atrial fibrillation and rapid ventricular rate, or AFib-RVR, and other indications.

Etripamil - Phase III Clinical Program in PSVT

PSVT is a rapid heart rate condition characterized by episodes of supraventricular tachycardia, or SVT, that start and stop without warning. Episodes of SVT are experienced by patients with symptoms often including palpitations, sweating, chest pressure or pain, shortness of breath, sudden onset of fatigue, lightheadedness or dizziness, fainting and anxiety. Calcium channel blockers have long been approved for the treatment of PSVT as well as other cardiac conditions. Calcium channel blockers available in oral form are frequently used prophylactically to control the frequency and duration of future episodes of SVT. For treatment of episodes of SVT, approved calcium channel blockers are administered intravenously under medical supervision, usually in the emergency department. The combination of convenient nasal-spray delivery, rapid-onset and short duration of action of etripamil has the potential to shift the current treatment paradigm for episodes of SVT away from the burdensome and costly emergency department setting. If approved, we believe that etripamil will be the first self-administered therapy for the rapid termination of episodes of SVT wherever and whenever they occur.

Our late-stage etripamil clinical program for the treatment of PSVT is currently executing on two ongoing Phase 3 safety and efficacy trials, RAPID and NODE-303. The RAPID study is our pivotal global randomized-controlled Phase 3 safety and efficacy trial. This study enrolled its first patient in October 2020 and in July 2022 reached its target of 180 confirmed PSVT events treated with double-blind study medication, marking the achievement of the event data required for the study's primary statistical efficacy analysis. The Company expects to report topline data from RAPID in mid-second half of 2022. NODE-303 is an open-label global safety trial enrolling patients to collect safety data that when combined with the safety data from the rest of the program will form the safety dataset to be evaluated by the FDA and other regulatory agencies to form the basis for marketing approval. We have also completed our first Phase 3 safety and efficacy trial of etripamil, NODE-301, and its open-label safety extension trial, NODE-302.

In March 2020, we reported topline results of the NODE-301 pivotal trial of etripamil for the treatment of PSVT, which is a placebo-controlled Phase 3 safety and efficacy trial. NODE-301, which enrolled a total of 431 patients across 65 sites in the United States and Canada, did not meet its primary endpoint of time to conversion of SVT to sinus rhythm compared to placebo over the five hour period in which patients wore a cardiac monitor following study drug administration.

In July 2020, we announced that we received guidance from the U.S. Food and Drug Administration, or FDA, on our proposal to alter the size and design of our ongoing NODE-301 trial (later renamed RAPID) as well as the overall program based on the data and learnings from the initial portion of the NODE-301 trial. The FDA indicated that the two trials, the proposed RAPID trial and the completed NODE-301 Part 1 trial, could potentially fulfill the efficacy requirement for our planned NDA for etripamil in patients with PSVT.

Under an updated analysis plan, the primary efficacy endpoint for both the RAPID and NODE-301 trials will be defined as time to conversion over the first 30 minutes, with a target p-value of less than 0.05 for each trial. This endpoint supports the desire of patients to rapidly address their PSVT symptoms during an episode and ideally avoid visiting the emergency department. Later and earlier time points will also be assessed as part of secondary analyses to fully characterize the efficacy profile of etripamil.

When employing the updated analysis retrospectively to the NODE-301 data, results in 54% of etripamil patients vs. 35% of placebo patients converted within 30 minutes (HR 1.87, p=0.02). Applying the same primary endpoint to the RAPID study, powering the study at 90% and using alpha of 0.05 to detect a 19% difference of etripamil versus placebo in 30 minute time to conversion that was observed in the NODE-301 study results in the size of 180 confirmed PSVT events.

The RAPID study was designed to be similar to NODE-301 however it introduced a new treatment regimen to the program. Based on discussions with the FDA regarding maximizing the treatment effect of etripamil, the RAPID trial allowed for repeat administration of study drug (either 70 mg of etripamil or placebo) for patients who had not experienced symptom relief within ten minutes of the first study drug administration. This repeat dose regimen, which is similar to current PSVT treatment practices in the emergency department setting, was tailored to the pharmacokinetic profile of etripamil to deliver increased exposure over approximately the first 30 minutes following initial administration. We believe that the repeat administration could benefit a broader group of patients, including those with more persistent episodes. For the primay efficacy analysis for RAPID, the FDA agreed that the single and repeat administrations of etripamil could be pooled and compared to placebo. In the NODE-301 study, 32% of etripamil patients and 14% of placebo patients converted to sinus rhythm within 10 minutes.

NODE-302 was the Phase 3 open-label safety extension of the NODE-301 trial. Patients who completed NODE-301 enrolled in NODE-302 and could receive up to an additional 11 doses of etripamil. NODE-302 was a multi-center, open label study designed to evaluate the safety of etripamil nasal spray when self-administered by patients without medical supervision for spontaneous episodes of SVT in an outpatient setting. Efficacy assessments were also performed. Eligibility was contingent on satisfying all inclusion and exclusion criteria, including not experiencing a serious adverse event related to the study drug or the study procedure that precludes the self-administration of etripamil. We announced the top line data from the NODE-302 study which were presented at a late-breaking session of the Heart Rhythm Society's Heart Rhythm 2022 Annual conference. Of 198 eligible NODE-301 patients, 169 (85%) enrolled in NODE-302 and 105 (62%) experienced a perceived episode of PSVT, self-administered etripamil and were included in the safety population. Overall, the PSVT conversion rate at 30 minutes following etripamil administration was 60.2% with a median time to conversion of 15.5 minutes (95% CI, 11.3-22.1 minutes). Among 40 patients who self-treated two consecutive episodes, 21 of 26 (81%) who converted on their first episode were also successfully converted on their second. Moreover, 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 consistent with those observed in previous trials; the majority of adverse events related to treatment were localized to the nasopharynx administration site, and were mild and brief.

NODE-303 is a Phase 3, multi-center, open-label safety trial, evaluating the safety of etripamil when self-administered without medical supervision, and evaluating the treatment safety and efficacy of etripamil on multiple SVT episodes. The study initiated with the etripamil 70 mg single dose regimen and the 70 mg repeat dose regimen was introduced into the trial starting in the second half of 2021 following FDA acceptance of the protocol change. The trial is designed to add to the safety data from the remainder of the development program, including both the NODE-301 and RAPID trials, in order to fulfill the safety data set needed for NDA filing. Our plan is to ascertain the final sizing of the trial following future discussions with the FDA and other regulatory authorities.

We are conducting patient access programs to provide further access to etripamil to patients who have participated in the clinical development registration trials to treat future SVT episodes. These programs are tailored to meet the regulatory requirements in the territories in which the clinical sites are located.

Additionally, on July 1, 2022, our partner Ji Xing Pharmaceuticals Limited (JIXING), a clinical-stage biopharmaceutical company committed to bringing innovative medicines to underserved Chinese patients with serious and life-threatening diseases, announced the first patient enrollment at Nanfang Hospital of Southern Medical University in its phase 3 study

of etripamil in China for the treatment of paroxysmal supraventricular tachycardia (PSVT). The study is currently being carried out in more than 40 leading clinical centers across China. The study is designed to evaluate the efficacy and safety of self-administered etripamil nasal spray as treatment of PSVT and to provide clinical data to support a new drug application in China.

Etripamil: Atrial Fibrillation and Rapid Ventricular Rate

In addition to our PSVT clinical program, we began enrollment of patients in a Phase 2 proof-of-concept clinical trial in patients with atrial fibrillation titled ReVeRA in the first quarter of 2021 to evaluate the potential effectiveness of etripamil to reduce ventricular rate during AFib-RVR episodes. As with PSVT, calcium channel blockers are also approved for use in intravenous form for the treatment of some episodes of atrial fibrillation in which patients experience rapid ventricular rates. The Phase 2 double blind, placebo controlled, proof-of-concept, which is being conducted in Canada in collaboration with the Montreal Heart Institute and other research centers, is expected to enroll approximately 50 patients randomized 1:1 to receive either 70 mg of etripamil nasal spray or placebo. The primary endpoint will assess maximum reduction in ventricular rate, with key secondary endpoints including the time to achieve maximum reduction in ventricular rate and the duration of the effect. The trial is to be conducted in the hospital or emergency department setting under medical supervision.

Operations Overview

Since the commencement of our operations in 2003, we have devoted substantially all of our resources to performing research and development activities in support of our product development efforts, hiring personnel, raising capital to support and expand such activities, providing general and administrative support for these operations and, more recently preparing for commercialization. We operate our business using a significant outsourcing model. As such, our team is composed of a relatively smaller core of employees who direct a significantly larger number of team members who are outsourced in the forms of vendors and consultants to enable execution of our operational plans. We do not currently have any products approved for sale, and we continue to incur significant research and development and general administrative expenses related to our operations.

Since inception, we have incurred significant operating losses. For the three months ended June 30, 2022 and 2021 we recorded net loss of $16.6 million and we had net earnings of $0.8 million due to the receipt of a $15 million upfront payment under our License and Collaboration Agreement, or the License Agreement, with Ji Xing Pharmaceuticals, Limited, or Ji Xing, respectively. For the six months ended June 30, 2022 and 2021, we recorded net losses of $30.7 million and $11.7 million, respectively. As of June 30, 2022, we had an accumulated deficit of $237.0 million. We expect to continue to incur significant losses for the foreseeable future. We anticipate that a substantial portion of our capital resources and efforts in the foreseeable future will be focused on completing the necessary development activities required for obtaining regulatory approval and preparing for potential commercialization of our product candidates. We had $86.2 million of cash, cash equivalents and short-term investments at June 30, 2022.

We expect to continue to incur significant expenses and increasing operating losses for at least the next several years. Our net losses may fluctuate significantly from period to period, depending on the timing of our planned clinical trials and expenditures on other research and development activities. We expect our expenses will increase substantially over time as we:

- continue our ongoing and planned development of etripamil, including our Phase 3 clinical trials of etripamil for the treatment of PSVT and our Phase 2 clinical trial of etripamil for the treatment of AFib-RVR;
- seek marketing approvals for etripamil for the treatment of PSVT, AFib-RVR and other cardiovascular indications;

- establish a sales, marketing, manufacturing and distribution capability, either directly or indirectly through third parties, to commercialize etripamil or any future product candidate for which we may obtain marketing approval;
- build a portfolio of product candidates through development, or the acquisition or in-license of drugs, product candidates or technologies;
- initiate preclinical studies and clinical trials for etripamil for any additional indications we may pursue, including the clinical trials for the treatment of atrial fibrillation and rapid ventricular rate as well as other areas of unmet medical need, and for any additional product candidates that we may pursue in the future;
- maintain, protect and expand our intellectual property portfolio;
- hire additional clinical, commercial, regulatory and scientific personnel;
- add operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts; and
- incur additional legal, accounting, insurance and other expenses associated with operating as a public company.

COVID-19 Business Update

The periods of reduced global economic activity and volatility, the overall disruption of global healthcare systems and the other risks and uncertainties associated with the pandemic could have a material adverse effect on our business, financial condition, results of operations and growth prospectsWe continue to monitor the pandemic as we evolve our business continuity plans and response strategy.

Clinical Development

With respect to clinical development, we have taken measures to maintain patient safety and trial continuity and to preserve study integrity. While COVID-19 resurgences around the world impact different geographies and clinical sites to varying degrees and at different times, the PSVT clinical program average overall enrollment rate has stabilized, compared to 2020. Enrollment rates are still slower than expected as a result of COVID-19. During 2021 and 2020, the COVID-19 pandemic delayed the initiation of many proposed RAPID clinical trial sites as some health care institutions prioritized their resources for pandemic related activities with some precluding the initiation of new clinical trials or conduct of existing trials. It also delayed the initiation of clinical trial sites and the enrollment of patients into our ReVeRA trial of etripamil for AFib-RVR performed in the acute care hospital setting in Canada, due to closures of clinical sites as well as to the increased stress that COVID-19 places on Emergency Departments logistics and staff. Given the uncertainty and differing and evolving restrictions applicable to clinical trial sites and participants, additional disruptions and delays are possible. We will continue to monitor the impact of COVID-19 on our planned clinical sites and patient enrollment activities. We could also see an impact on the ability to supply study drug, report trial results, or interact with regulators, ethics committees or other important agencies due to limitations in regulatory authority employee resources or otherwise. In addition, we rely on contract research organizations or other third parties to assist us with clinical trials, and we cannot guarantee that they will continue to perform their contractual duties in a timely and satisfactory manner as a result of the COVID-19 pandemic. If the COVID-19 pandemic continues and persists for an extended period of time, we could experience further significant disruptions to our clinical development timelines, which would adversely affect our business, financial condition, results of operations and growth prospects.

Other Financial and Corporate Impacts

While we expect the COVID-19 pandemic to continue to affect our business operations and financial results, the extent of the impact on our clinical development and regulatory efforts, our corporate development objectives and the value of and market for our common shares, will depend on future developments that are highly uncertain and cannot be predicted with

confidence at this time, such as the ultimate duration of the pandemic, travel restrictions, business closure requirements in the United States, Canada, Europe and other countries, the timing and unpredictability of achieving widespread vaccination rates, the effectiveness of any vaccines against new variants, and the timing of the return of the global economy to pre-pandemic levels. In addition, we may be impacted by general economic, political, and market conditions, including deteriorating market conditions due to investor concerns regarding inflation and Russian hostilities in Ukraine and overall fluctuations in the financial markets in the United States and abroad.

Components of Results of Operations

Revenues

We have not generated any revenues from product sales to date and we do not expect to generate revenues from product sales in the near future. Our revenues for the six months ended June 30, 2021 are from the license and collaboration agreement with Ji Xing and are comprised of upfront payments.

Research and Development

Research and development expenses consist primarily of salaries and fees paid to external service providers and also include personnel costs, including share-based compensation expense and other related compensation expenses. We expense research and development costs in the periods in which they are incurred. Costs for certain development activities are recognized based on an evaluation of the progress to completion of specific tasks using information and data provided to us by our vendors, collaborators and third-party service providers.

To date, substantially all of our research and development expenses have been related to the preclinical and clinical development of etripamil. As we advance etripamil or other product candidates for other indications, we expect to allocate our direct external research and development costs across each of the indications or product candidates. Further, while we expect our research and development costs for the development of etripamil in atrial fibrillation with rapid ventricular rate to increase for the ReVeRA clinical trial as we continue to expand this trial, we expect our research and development expenses related to the development of etripamil for PSVT to remain a very large majority of our total research and development expenses.

We expect our research and development expenses to increase as we continue the development of etripamil and prepare to pursue regulatory approval. The process of conducting the necessary clinical research to obtain regulatory approval is costly and time-consuming and is subject to uncertainties and delays, including as a result of the ongoing COVID-19 pandemic. COVID-19 has adversely affected enrollment rates. As a result of the uncertainties discussed above, we are unable to determine the duration and completion costs of our research and development projects or when and to what extent we will generate revenue from the commercialization and sale of our product candidates, if at all.

We recognize the benefit of Canadian research and development tax credits as a reduction of research and development costs for fully refundable investment tax credits.

General and Administrative

General and administrative expenses include personnel and related compensation costs, expenses for outside professional services, lease expense, insurance expense and other general administrative expenses. Personnel costs consist of salaries, bonuses, benefits, related payroll taxes and share-based compensation. Outside professional services consist of legal, accounting and audit services and other consulting fees.

We expect to continue to incur expenses as a public company, including expenses related to compliance with the rules and regulations of the Securities and Exchange Commission, or SEC, and those of any national securities exchange on which our securities are traded, additional insurance expenses, investor relations activities, and other administrative and professional services.

Commercial

Commercial expenses consist primarily of personnel and related compensation costs, market and health economic research, and market development activities for PSVT and, to a lesser extent, AFib-RVR. The focus of these expenses is three-fold: first, we want to leverage rigorous primary and secondary research to fully understand our target disease states from the perspective of the patient, healthcare provider, and payer; second, we want to understand and document the burden of disease posed by PSVT and AFib-RVR from an epidemiology, healthcare resource use, and cost perspective; and third, we want to engage our target patient, physician, and payer stakeholders with evidence-based and compliant educational materials that serve to increase the awareness and understanding of the impact of PSVT and AFib-RVR on patients and the overall healthcare system.

Starting approximately six months to one year before we file our new drug application, or NDA with the FDA, we anticipate our commercial expenses will increase substantially as we invest in the infrastructure, personnel, and operational expenses required to launch our first product in the United States, if approved.

Interest Income

Interest income primarily consists of interest income from our cash equivalents and short-term investments.

Results of Operations

Comparison of the Three and Six Months Ended June 30, 2022 and 2021

The following table summarizes our results of operations and changes:

	Three months ended June 30,			
(in thousands)	**2022**	**2021**	**$ Change**	**% Change**
Revenue	$ —	$ 15,000	$ (15,000)	100.0%
Operating expenses				
Research and development, net of tax credits	10,657	9,427	1,230	13.1%
General and administrative	3,918	3,018	900	29.8%
Commercial	2,231	1,843	388	21.1%
Total operating expenses	16,806	14,288	2,518	17.6%
Earnings (loss) from operations	(16,806)	712	(17,518)	(2460.4)%
Interest income, net	158	58	100	172.4%
Net earnings (loss)	$ (16,648)	$ 770	$ (17,418)	(2262.1)%

(in thousands)	Six months ended June 30, 2022	2021	$ Change	% Change
Revenue	$ —	$ 15,000	$ (15,000)	100.0%
Operating expenses				
Research and development, net of tax credits	19,425	18,022	1,403	7.8%
General and administrative	7,561	5,651	1,910	33.8%
Commercial	3,867	3,209	658	20.5%
Total operating expenses	30,853	26,882	3,971	14.8%
Loss from operations	(30,853)	(11,882)	(18,971)	159.7%
Interest income, net	198	138	60	43.5%
Net loss	$ (30,655)	$ (11,744)	$ (18,911)	161.0%

Revenue

We generated no revenue for the three months and six months ended June 30, 2022 compared to revenue of $15 million from upfront payments under the License Agreement during the three months and six months ended June 30, 2021.

Research and Development Expenses

The following table shows our research and development expenses by type of activity for the three and six months ended June 30, 2022 and 2021, respectively.

(in thousands)	Three months ended June 30, 2022	2021	$ Change	% Change	Six months ended June 30, 2022	2021	$ Change	% Change
Clinical	$ 9,118	$ 7,677	$ 1,441	18.8%	$ 15,818	$ 14,466	$ 1,352	9.4%
Drug manufacturing and formulation	1,123	1,237	(114)	(9.2)%	2,175	2,653	(478)	(18.0)%
Regulatory and other costs	543	600	(57)	(9.5)%	1,615	1,081	534	49.4%
Less: R&D tax credits	(127)	(87)	(40)	46.0%	(183)	(178)	(5)	2.8%
Total R&D expenses	$ 10,657	$ 9,427	$ 1,230	13.1%	$ 19,425	$ 18,022	$ 1,403	7.8%

Research and development expenses increased by $1.2 million, or 13.1%, for the three months ended June 30, 2022 compared to the three months ended June 30, 2021. The increase in clinical personnel related costs, clinical consulting fees and CRO costs due to advancing RAPID Phase 3 efficacy and safety trials in etripamil for the treatment of PSVT. These increases were offset by lower drug formulation and manufacturing costs.

Research and development expenses increased by $1.4 million, or 7.8% for the six months ended June 30, 2022 compared to the six months ended June 30, 2021. The increase in clinical personnel related costs, clinical consulting fees and CRO costs due to advancing RAPID Phase 3 efficacy and safety trials in etripamil for the treatment of PSVT. These increases were offset by lower drug formulation and manufacturing costs. Regulatory costs increased due to personal related costs.

We recognize the benefit of Canadian research and development tax credits as a reduction of research and development costs for fully refundable investment tax credits.

General and Administrative

General and administrative expenses increased by $0.9 million, or 29.8% for the three months ended June 30, 2022 compared to the three months ended June 30, 2021. The primary contributor was an increase of $0.8 million in personnel-related costs and consulting fees for general and administrative expenses.

General and administrative expenses increased by $1.9 million, or 33.8% for the six months ended June 30, 2022 compared to the six months ended June 30, 2021. The primary contributor was an increase of $1.7 million in personnel-related costs and consulting fees for general and administrative expenses.

Commercial

For the three months ended June 30, 2022, commercial expenses increased by $0.4 million, or 21.1%, compared to the three months ended June 30, 2021. The increase is due to consulting and marketing analytics.

Commercial expenses increased by $0.7 million, or 20.5%, for the six months ended June 30, 2022, compared the same period in 2021. The increase is due to personnel related costs.

Starting approximately six months to one year before we file our new drug application, or NDA with the FDA, we anticipate our commercial expenses will increase substantially as we invest in the infrastructure, personnel and operational expenses required to launch our first product in the United States, if approved.

Interest Income, net

Interest income, net, was $0.2 million and $0.1 million for the three months ended June 30, 2022 and 2021, respectively. Interest income, net of bank charges, was $0.2 million and $0.1 million for the six-month periods ended June 30, 2021 and 2020, respectively. The increase in interest income was due to higher interest rates earned on investments in 2022 when compared to 2021.

Liquidity and Capital Resources

Sources of Liquidity

We have incurred operating losses and experienced negative operating cash flows since our inception, and we anticipate continuing to incur losses for at least the next several years. As of June 30, 2022, we had cash, cash equivalents and short-term investments of $86.2 million and an accumulated deficit of $237.0 million.

We have evaluated whether material uncertainties exist relating to clinical trials, the COVID-19 pandemic and the impact on market conditions. The COVID-19 pandemic has had an impact on our business, operations and clinical development timelines. Government orders and restrictions in order to control the spread of the disease have impacted patient recruitment, enrollment and follow-up visits at clinical sites. At the date of the publication of our quarterly report on form 10-Q, it is not possible to reliably estimate the length and severity of these developments. We expect that our current operating plan, existing cash and cash equivalents and access to financing sources to be sufficient to fund our operations and determined that there are no events or conditions that may cast substantial doubt on our ability to continue as a going concern for at least the next 12 months from the date of this filing. Based on our cash and cash equivalents as of June 30, 2022, we expect to be able to support our ongoing operations into second-half of 2023.

Funding Requirements

We use our cash primarily to fund research and development expenditures. We expect our total research and development expenses to increase as we continue the development of etripamil and prepare to pursue regulatory approval. We expect to incur an increase in general and administrative expenses, and a continued increase in expenses related to commercial activities in 2022 as we focus our efforts on the clinical pathway and potential commercialization of etripamil. We expect to incur increasing operating losses for the foreseeable future as we continue the clinical development of our product

candidate. At this time, due to the inherently unpredictable nature of clinical development, we cannot reasonably estimate the costs we will incur and the timelines that will be required to complete development, obtain marketing approval, and commercialize etripamil or any future product candidates, if at all. For the same reasons, we are also unable to predict when, if ever, we will generate revenue from product sales or whether, or when, if ever, we may achieve profitability. Clinical and preclinical development timelines, the probability of success, and development costs can differ materially from expectations.

In addition, we have exclusive development and commercialization rights for etripamil for all indications that we may pursue and as such have the potential to license development and or commercialization rights for etripamil to a potential partner. We plan to establish commercialization and marketing capabilities using a direct sales force to commercialize etripamil in the United States. Outside of the United States, we are considering commercialization strategies that may include collaborations with other companies.

For other new product candidates, our efforts are focused on licensing development and/or commercialization rights from potential partners. In the case of either in-licensing or out-licensing, we cannot forecast when such arrangements will be secured, if at all, and to what degree such arrangements would affect our development and commercialization plans and capital requirements.

The timing and amount of our operating expenditures will depend largely on:

- the timing, progress and results of our ongoing and planned clinical trials and other development activities of etripamil in PSVT, AFib-RVR and in other cardiovascular indications;
- the scope, progress, results and costs of preclinical development, laboratory testing and clinical trials of etripamil for additional indications or any future product candidates that we may pursue;
- our ability to establish collaborations on favorable terms, if at all;
- the ability of vendors and third-party service providers to accurately forecast expenses and deliver on expectations;
- the costs, timing and outcome of regulatory review of etripamil and any future product candidates;
- the costs and timing of future commercialization activities, including product manufacturing, marketing, sales and distribution, for etripamil and any future product candidates for which we receive marketing approval;
- the revenue, if any, received from commercial sales of etripamil and any future product candidates for which we receive marketing approval;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims; and
- the extent to which we acquire or in-license other product candidates and technologies.

Until such time, if ever, as we can generate substantial revenue from product sales, we expect to fund our operations and capital funding needs through equity and/or debt financing. We may also consider entering into collaboration arrangements, similar to the collaboration agreement entered into with Ji Xing, or selectively partnering for clinical development and commercialization. The sale of additional equity would result in additional dilution to our shareholders. The incurrence of debt financing would result in debt service obligations and the instruments governing such debt could provide for operating and financing covenants that restrict our operations or our ability to incur additional indebtedness or pay dividends, among other items. In addition, the COVID-19 pandemic, the Russian invasion of Ukraine and the implementation of a tightening monetary policy has contributed to periods of reduced global economic activity and

volatility. If these and other events contributes to future periods of disruption of the global financial markets, we could experience an inability to access additional capital, which could in the future negatively affect our operations. If we are not able to secure adequate additional funding, we may be forced to make reductions in spending, extend payment terms with suppliers, liquidate assets where possible, and/or suspend or curtail planned programs. Any of these actions could materially and adversely affect our business, financial condition and results of operations.

Discussion of Cash Flows

The following table summarizes our cash flows for the periods indicated:

	Six months ended June 30,			
(in thousands)	**2022**	**2021**	**$ Change**	**% Change**
Net cash (used in) provided by:				
Operating activities	$ (28,034)	$ (11,455)	(16,579)	144.7%
Investing activities	(23,059)	32,000	(55,059)	(172.1)%
Financing activities	189	4,939	(4,750)	(96.2)%
Net decrease in cash and cash equivalents during the period	$ (50,904)	$ 25,484	(76,388)	

Operating Activities

Net cash used in operating activities during the six months ended June 30, 2022 was $28.0 million, which consisted of a net loss of $30.7 million and a net change of $2.0 million in our operating assets and liabilities offset by non-cash charges of $4.6 million related to share-based compensation and depreciation expenses.

Net cash used in operating activities during the six months ended June 30, 2021 was $11.5 million, which consisted of a net loss of $11.7 million and a net change of $3.0 million in our operating assets and liabilities offset by non-cash charges of $3.3 million related to share-based compensation expense for grants to employees, board directors and consultants. The change in our net operating assets and liabilities was mainly due to a decrease of $0.8 million for accounts payable and accrued liabilities and an increase of $2.0 million for prepaid expenses.

Investing Activities

In the six months ended June 30, 2022 we acquired $23.0 million of short-term investments while we divested of $32.0 million during the same period in 2021.

Financing Activities

In the six months ended June 30, 2022, our financing activities provided a de minimis amount of proceeds from the exercise of share options. In the six months ended June 30, 2021, our financing activities provided $4.9 million, consisting of net proceeds from the Private Placement and a de minimis amount of proceeds from the exercise of share options.

We have not entered into off-balance sheet arrangements.

Contractual Obligations

During the six months ended June 30, 2022, there were no material changes to our contractual obligations and commitments described under "Management's Discussion and Analysis of Financial Condition and Results of Operations" in our Annual Report on Form 10-K, filed with the SEC on March 24, 2022.

Critical Accounting Estimates

Our management’s discussion and analysis of our financial condition and results of operations is based on our unaudited interim consolidated financial statements as of June 30, 2022, which have been prepared in accordance with United States

generally accepted accounting principles, or U.S. GAAP and on a basis consistent with those accounting principles followed by us. The preparation of these consolidated financial statements requires our management to make judgments and estimates that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements, as well as the reported revenue generated and expenses incurred during the reporting periods. Our estimates are based on our historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Significant estimates and judgments include, but are not limited to:

- Estimates of the percentage of work completed of the total work over the life of the individual trial in accordance with agreements established with CROs, CMOs and clinical trial sites which in turn impact the research & development expenses.

- Estimate of the grant date fair value share options granted to employees, consultants and direct, and the resulting share-based compensation expense, using the Black-Scholes option-pricing model.

Accordingly, actual results may differ from these judgments and estimates under different assumptions or conditions and any such differences may be material. We believe that the accounting policies discussed below are critical to understanding our historical and future performance, as these policies relate to the more significant areas involving management's judgments and estimates.

a) Research & Development Expenses — Accruals

Research and development costs are charged against income in the period of expenditure. Our research and development costs consist primarily of salaries and fees paid to CROs and to CMO.

Clinical trial expenses include direct costs associated with CROs, direct CMO costs for the formulation and packaging of clinical trial material, as well as investigator and patient-related costs at sites at which our trials are being conducted. Direct costs associated with our CROs and CMOs are generally payable on a time-and-materials basis, or when milestones are achieved. The invoicing from clinical trial sites can lag several months. We record expenses for our clinical trial activities performed by third parties based upon estimates of the percentage of work completed of the total work over the life of the individual trial in accordance with agreements established with CROs and clinical trial sites. We determine the estimates through discussions with internal clinical personnel, CROs and CMOs as to the progress or stage of completion of trials or services and the agreed-upon fee to be paid for such services based on facts and circumstances known to us as of each consolidated balance sheet date. The actual costs and timing of clinical trials are highly uncertain, subject to risks and may change depending upon a number of factors, including our clinical development plan. If the actual timing of the performance of services of the level of effort varies from the estimate, we will adjust the accrual accordingly. Adjustments to prior period estimates have not been material. We recognize the benefit of Canadian research and development tax credits as a reduction of research and development costs for fully refundable investment tax credits and as a reduction of income taxes for investment tax credits that can only be claimed against income taxes payable when there is reasonable assurance that the claim will be recovered.

b) Share-Based Compensation

We recognize compensation costs related to share options granted to employees, consultants and directors based on the estimated fair value of the awards on the date of grant. We estimate the grant date fair value, and the resulting share-based compensation expense, using the Black-Scholes option-pricing model. This Black-Scholes option pricing model uses various inputs to measure fair value, including estimated fair value of our underlying common shares at the grant date, expected term, estimated volatility, risk-free interest rate and expected dividend yields of our common shares. The estimated volatility creates a critical estimate because we have not been a public company long enough to demonstrate our own historical volatility. The grant date fair value of the share-based awards is recognized on a straight-line basis over the requisite service periods, which are generally the vesting period of the respective awards. Forfeitures are accounted for as they occur.

Recent Accounting Pronouncements

Refer to Note 2, “Summary of Significant Accounting Policies”, for a discussion of recent accounting pronouncements and to the notes to our audited consolidated financial statements as of December 31, 2021 appearing in our Annual Report on Form 10-K, filed with the SEC on March 24, 2022.

Emerging Growth Company Status

The Jumpstart Our Business Startups Act of 2012 permits an “emerging growth company” such as us to take advantage of an extended transition period to comply with new or revised accounting standards applicable to public companies until those standards would otherwise apply to private companies. We have irrevocably elected to “opt out” of this provision and, as a result, we comply with new or revised accounting standards when they are required to be adopted by public companies that are not emerging growth companies.

Item 3. Quantitative and Qualitative Disclosures About Market Risk.

The primary objective of our investment activities is to preserve principal and liquidity while maximizing income without significantly increasing risk. We are exposed to market risks in the ordinary course of our business. These risks primarily relate to interest rate risks. We had cash, cash equivalents and short-term investments of $86.2 million as of June 30, 2022, which consist primarily of bank deposits and guaranteed investment certificates. We do not enter into investments for trading or speculative purposes. Due to the short-term nature of our investment portfolio, we do not believe an immediate 10% increase or decrease in interest rates would have a material effect on the fair market value of our portfolio, and accordingly we do not expect our operating results or cash flows to be materially affected by a sudden change in market interest rates.

We undertake certain transactions in Canadian dollars and as such are subject to risk due to fluctuations in exchange rates. Canadian dollar denominated payables are paid at the converted rate as due. We do not use derivative instruments to hedge exposure to foreign exchange rate risk due to the low volume of transactions denominated in foreign currencies. On June 30, 2022, our net monetary exposure denominated in Canadian dollars was $2.8 million.

Our operating results and financial position are reported in U.S. dollars in our consolidated financial statements. The fluctuation of the Canadian dollar in relation to the U.S. dollar might, consequently, have an impact upon our loss and may also affect the value of our assets and the amount of shareholders’ equity.

We do not have a formal hedging program with respect to foreign currency. A 10% increase or decrease in current exchange rates would not have a material effect on our consolidated financial results.

Item 4. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures.

We maintain “disclosure controls and procedures,” as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act, that are designed to ensure that information required to be disclosed in the reports that we file or submit under the Exchange Act is (1) recorded, processed, summarized and reported, within the time periods specified in the SEC’s rules and forms and (2) accumulated and communicated to our management, including our principal executive officer and principal financial officer, to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, evaluated the effectiveness of our disclosure controls and procedures as of June 30, 2022. Based upon the evaluation, our Chief Executive Officer and Chief Financial Officer concluded that, as of such date, our disclosure controls and procedures were effective at a reasonable assurance level.

Changes in Internal Control over Financial Reporting.

There were no changes in our internal control over financial reporting during the period covered by this Quarterly Report on Form 10-Q that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting. We have not experienced any material impact to our internal controls over financial reporting despite the fact that our employees have worked remotely due to the COVID-19 pandemic. We are continually monitoring and assessing the COVID-19 situation on our internal controls to minimize the impact on their design and operating effectiveness.

Inherent Limitations on Effectiveness of Controls.

Our management, including our Chief Executive Officer and Chief Financial Officer, believes that our disclosure controls and procedures and internal control over financial reporting are designed to provide reasonable assurance of achieving their objectives and are effective at the reasonable assurance level. However, our management does not expect that our disclosure controls and procedures or our internal control over financial reporting will prevent all errors and all fraud. A control system, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. Further, the design of a control system must reflect the fact that there are resource constraints, and the benefits of controls must be considered relative to their costs. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that all control issues and instances of fraud, if any, have been detected. These inherent limitations include the realities that judgments in decision making can be faulty, and that breakdowns can occur because of a simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by management override of the controls. The design of any system of controls also is based in part upon certain assumptions about the likelihood of future events, and there can be no assurance that any design will succeed in achieving its stated goals under all potential future conditions; over time, controls may become inadequate because of changes in conditions, or the degree of compliance with policies or procedures may deteriorate. Because of the inherent limitations in a cost-effective control system, misstatements due to error or fraud may occur and not be detected.

PART II—OTHER INFORMATION

Item 1. Legal Proceedings.

From time to time, we may become involved in legal proceedings arising in the ordinary course of our business. We are not currently a party to any material legal proceedings, and we are not aware of any pending or threatened legal proceeding against us that we believe could have an adverse effect on our business, operating results or financial condition.

Item 1A. Risk Factors

There have been no material changes from the risk factors previously disclosed in Part I, Item 1A. in our Annual Report on Form 10-K, filed with the SEC and under Milestone's SEDAR profile at www.sedar.com on March 24, 2022.

Item 2. Unregistered Sales of Equity Securities and Use of Proceeds.

Recent Sales of Unregistered Equity Securities

None

Item 3. Defaults Upon Senior Securities.

Not applicable

Item 4. Mine Safety Disclosures.

Not applicable

Item 5. Other Information.

Not applicable

Item 6. Exhibits.

Exhibit Number		Description
3.1		Amended Articles of Incorporation of the Company (incorporated herein by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K (File No. 001-38899), filed with the SEC on May 15, 2019).
3.2		Amended and Restated Bylaws of the Company (incorporated herein by reference to Exhibit 3.2 to the Company's Current Report on Form 8-K (File No. 001-38899), filed with the SEC on May 15, 2019).
31.1		Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
31.2		Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1*		Certification of Principal Executive Officer and Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101.INS		Inline XBRL Instance Document
101.SCH		Inline XBRL Taxonomy Extension Schema Document
101.CAL		Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF		Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB		Inline XBRL Taxonomy Extension Label Linkbase Document
101.PRE		Inline XBRL Taxonomy Extension Presentation Linkbase Document
104		The cover page from the Company's Quarterly Report on Form 10-Q for the quarter ended June 30, 2022, formatted in Inline XBRL.

* Furnished herewith and not deemed to be "filed" for purposes of Section 18 of the Exchange Act, and shall not be deemed to be incorporated by reference into any filing under the Securities Act of 1933, as amended, or the Exchange Act (whether made before or after the date of the Form 10-Q), irrespective of any general incorporation language contained in such filing.

\+ Certain portions of this exhibit have been omitted pursuant to Item 601(b)(10) of Regulation S-K. The Registrant hereby undertakes to furnish to the SEC, upon request, copies of any such instruments.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

MILESTONE PHARMACEUTICALS INC.

Date: August 10, 2022

By: /s/ Joseph Oliveto
Joseph Oliveto
President and Chief Executive Officer
(Principal Executive Officer)

Date: August 10, 2022

By: /s/ Amit Hasija
Amit Hasija
Chief Financial Officer
(Principal Financial Officer and Principal Accounting Officer)

Exhibit 31.1

CERTIFICATION PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Joseph Oliveto, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Milestone Pharmaceuticals Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: August 10, 2022

/s/ Joseph Oliveto
Joseph Oliveto
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Amit Hasija, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Milestone Pharmaceuticals Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: August 10, 2022

/s/ Amit Hasija
Amit Hasija
Chief Financial Officer
(Principal Financial Officer and Principal Accounting Officer)

Exhibit 32.1

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

Pursuant to the requirement set forth in Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended, (the "Exchange Act") and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. §1350), Joseph Oliveto, Chief Executive Officer of Milestone Pharmaceuticals Inc. (the "Company"), and Amit Hasija, Chief Financial Officer of the Company, each hereby certifies that, to the best of his or her knowledge:

1. The Company's Quarterly Report on Form 10-Q for the period ended June 30, 2022, to which this Certification is attached as Exhibit 32.1 (the "Periodic Report"), fully complies with the requirements of Section 13(a) or Section 15(d) of the Exchange Act; and

2. The information contained in the Periodic Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Dated: August 10, 2022

/s/ Joseph Oliveto	/s/ Amit Hasija
Joseph Oliveto Chief Executive Officer (Principal Executive Officer)	Amit Hasija Chief Financial Officer (Principal Financial Officer and Principal Accounting Officer)

This certification accompanies the Periodic Report to which it relates, is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of Milestone Pharmaceuticals Inc. under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended (whether made before or after the date of the Periodic Report), irrespective of any general incorporation language contained in such filing.