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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 20549

FORM 10-Q

(Mark One)

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

For the quarterly period ended June 30, 2019

OR

o 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)

Quebec	**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 x No o

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 x No o

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	o	Accelerated filer	o
Non-accelerated filer	x	Smaller reporting company	x
Emerging growth company	x		

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. x

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

As of August 7, 2019, the registrant had 24,490,742 common shares, no par value per share, outstanding.

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Quarterly Report on Form 10-Q contains forward-looking statements. In some cases, you can identify these statements by forward-looking words 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,” or similar expressions, or the negative or plural of these words or expressions. These forward-looking statements include statements concerning the following:

- 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 PSVT, and of our research and development programs;
- 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 successfully acquire or in-license additional product candidates on reasonable terms;
- 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 payor 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
- the factors that may impact our financial results.

These statements are only current predictions and are subject to known and unknown risks, uncertainties and other factors that may cause our or our industry’s actual results, levels of activity, performance or achievements to be materially different from those anticipated by the forward-looking statements. We discuss many of these risks in greater detail under the heading “Risk Factors” and elsewhere in this report. 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 the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee future results, levels of activity, performance or achievements. Except as required by law, we are under no duty to update or revise any of the forward-looking statements in this report, whether as a result of new information, future events or otherwise, after the date of this report.

Unless the context otherwise requires, the terms “Milestone,” “Milestone Pharmaceuticals,” “the company,” “we,” “us,” “our” and similar references in this Quarterly Report on Form 10-Q refer to Milestone Pharmaceuticals Inc. and its consolidated subsidiary. 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.

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, 2019	December 31, 2018
Assets		
Current assets		
Cash and cash equivalents	$ 110,824	$ 85,947
Short-term investments (note 3)	35,000	29
Research and development tax credits receivable	357	290
Prepaid expenses	5,032	1,398
Other receivables	338	387
Total current assets	151,551	88,051
Operating lease right-of-use asset (note 2)	243	—
Property and equipment	43	30
Total assets	$ 151,837	$ 88,081
Liabilities		
Current liabilities		
Accounts payable and accrued liabilities (note 4)	$ 6,288	$ 4,477
Current portion of operating lease liabilities (note 2)	175	—
Income taxes payable	—	56
Total current liabilities	6,463	4,533
Operating lease liabilities (note 2)	61	—
Total liabilities	6,524	4,533
Convertible Preferred Shares (note 1 and 5)		
Class A-1 preferred shares, no par value, unlimited shares authorized, 372,211 shares issued	—	2,027
Class A-2 preferred shares, no par value, unlimited shares authorized, 2,443,914 shares issued	—	12,643
Class B preferred shares, no par value, unlimited shares authorized, 2,830,907 shares issued	—	17,198
Class C preferred shares, no par value, unlimited shares authorized, 3,786,878 shares issued	—	27,236
Class D1 preferred shares, no par value, unlimited shares authorized, 6,893,236 shares issued	—	64,719
Class D2 preferred shares, no par value, unlimited shares authorized, 1,223,656 shares issued	—	14,935
Total convertible preferred shares	—	138,758
Shareholders' Equity (Deficit) (note 1 and 5)		
Share capital		
Common shares, no par value, unlimited shares authorized, 24,490,742 shares issued and outstanding as of June 30, 2019 596,787 shares issued and outstanding as of December 31, 2018	226,211	2,039
Additional paid-in capital	3,116	2,655
Cumulative translation adjustment	(1,634)	(1,634)
Accumulated deficit	(82,380)	(58,270)
Total shareholders' equity (deficit)	145,313	(55,210)
Total liabilities, convertible preferred shares and shareholders' equity	$ 151,837	$ 88,081

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

Milestone Pharmaceuticals Inc.
Condensed Consolidated Statements of Loss and Comprehensive Loss
(Unaudited)

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

	Three months ended June 30,		Six months ended June 30,	
	2019	2018	2019	2018
Operating expenses				
Research and development, net of tax credits (note 7)	$ 10,527	$ 2,551	$ 18,292	$ 5,642
General and administrative	1,641	750	2,620	1,189
Commercial	2,166	375	4,352	1,100
Loss from operations	$ (14,334)	$ (3,676)	$ (25,264)	$ (7,931)
Interest income, net of bank charges	672	89	1,172	180
Loss and comprehensive loss before income taxes	(13,662)	(3,587)	(24,092)	(7,751)
Income tax (recovery) expense	(4)	2	18	18
Net loss and comprehensive loss for the period	$ (13,658)	$ (3,589)	$ (24,110)	$ (7,769)
Weighted average number of shares outstanding, basic and diluted (note 1)	13,190,638	282,322	6,931,611	275,450
Net loss per share, basic and diluted (note 8)	$ (1.04)	$ (12.71)	$ (3.48)	$ (28.20)

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

Milestone Pharmaceuticals Inc.
Condensed Consolidated Statements of Shareholders' Equity (Deficit) and Convertible Preferred Shares
(Unaudited)

(thousands of US dollars, except per share data)

	Common Shares		Convertible Preferred Shares														
			Class A1		Class A2		Class B		Class C		Class D1		Class D2				
	Number of shares	Amount	Number of shares	Amount	Number of shares	Amount	Number of shares	Amount	Number of shares	Amount	Number of shares	Amount	Number of shares	Amount	Additional paid-in capital	Cumulative translation adjustment	Accumulated deficit	Total
Balance at December 31, 2017	239,990	$ 1,228	372,211	$ 2,027	2,443,914	$ 12,643	2,830,907	$ 17,198	3,786,878	$ 27,236	—	—	—	—	$ 2,372	$ (1,634)	$ (35,085)	$ 25,985
Transactions in three-month period ended March 31, 2018																		
Net loss and comprehensive loss	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	(4,181)	(4,181)
Exercise of stock options (note 5)	37,675	55		—	—	—	—	—	—	—	—	—	—	—	(25)	—	—	30
Share-based compensation (note 5)	—	—	—	—	—	—	—	—	—	—	—	—	—	—	125	—	—	125
Balance at March 31, 2018	277,665	$ 1,283	372,211	$ 2,027	2,443,914	$ 12,643	2,830,907	$ 17,198	3,786,878	$ 27,236	—	—	—	—	$ 2,472	$ (1,634)	$ (39,266)	$ 21,959
Transactions in three-month period ended June 30, 2018																		
Net loss and comprehensive loss	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	(3,589)	(3,589)
Exercise of stock options (note 5)	5,106	14		—	—	—	—	—	—	—	—	—	—	—	(7)	—	—	7
Share-based compensation (note 5)	—	—	—	—	—	—	—	—	—	—	—	—	—	—	79	—	—	79
Balance at June 30, 2018	282,771	$ 1,297	372,211	$ 2,027	2,443,914	$ 12,643	2,830,907	$ 17,198	3,786,878	$ 27,236	—	—	—	—	$ 2,544	$ (1,634)	$ (42,855)	$ 18,456
Balance at December 31, 2018	596,787	2,039	372,211	2,027	2,443,914	12,643	2,830,907	17,198	3,786,878	27,236	6,893,236	64,719	1,223,656	14,935	2,655	(1,634)	(58,270)	83,548
Transactions in three-month period ended March 31, 2019																		
Net loss and comprehensive loss	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	(10,452)	(10,452)
Exercise of stock options (note 5)	18,153	51	—	—	—	—	—	—	—	—	—	—	—	—	(26)	—	—	25
Share-based compensation (note 5)	—	—	—	—	—	—	—	—	—	—	—	—	—	—	211	—	—	211
Balance at March 31, 2019	614,940	$ 2,090	372,211	$ 2,027	2,443,914	$ 12,643	2,830,907	$ 17,198	3,786,878	$ 27,236	6,893,236	64,719	1,223,656	14,935	$ 2,840	$ (1,634)	$ (68,722)	$ 73,332
Transactions in three-month period ended June 30,2019																		
Net loss and comprehensive loss	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	(13,658)	(13,658)
Exercise of stock options (note 5)	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Share-based compensation (note 5)	—	—	—	—	—	—	—	—	—	—	—	—	—	—	276	—	—	276
Initial public offering (note 5)	6,325,000	85,363	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	85,363
Preferred share conversion (note 5)	17,550,802	138,758	(372,211)	(2,027)	(2,443,914)	(12,643)	(2,830,907)	(17,198)	(3,786,878)	(27,236)	(6,893,236)	(64,719)	(1,223,656)	(14,935)	—	—	—	—
Balance at June 30, 2019	24,490,742	$ 226,211	—	—	—	—	—	—	—	—	—	—	—	—	$ 3,116	$ (1,634)	$ (82,380)	$ 145,313

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

Milestone Pharmaceuticals Inc.
Condensed Consolidated Statements of Cash Flows
(Unaudited)

(thousands of US dollars)

	Six months ended June 30,	
	2019	**2018**
Cash flows from:		
Operating activities		
Net loss for the period	$ (24,110)	$ (7,769)
Adjustments to reconcile net loss to net cash used in operating activities:		
Amortization of property and equipment	5	5
Share-based compensation expense (note 5)	487	204
Changes in operating assets and liabilities:		
Other receivables	49	(69)
Research and development tax credits receivable	(67)	247
Prepaid expenses	(3,634)	(343)
Operating lease, net	(7)	—
Accounts payable and accrued liabilities	1,082	(415)
Income taxes payable	(56)	(4)
Net cash used in operating activities	(26,251)	(8,144)
Investing activities		
Acquisition of property and equipment	(18)	(5)
Acquisition of short-term investments	(35,000)	—
Redemption of short-term investments	29	15,035
Net cash (used) provided by investing activities	(34,989)	15,030
Financing activities		
Net proceeds from issuance of common shares in Initial Public Offering (note 5)	86,092	—
Issuance of common shares on exercise of share options (note 5)	25	37
Net cash provided by financing activities	86,117	37
Net increase in cash and cash equivalents during the period	24,877	6,923
Cash and cash equivalents — Beginning of period	85,947	10,880
Cash and cash equivalents — End of period	$ 110,824	$ 17,803

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

Milestone Pharmaceuticals Inc.
Notes to Condensed Consolidated Financial Statements
(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 Phase 3 clinical-stage biopharmaceutical company incorporated under the Business Corporations Act of Quebec. Milestone is dedicated to developing and commercializing etripamil for the treatment of cardiovascular indications. 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 the patient to terminate episodes of paroxysmal supraventricular tachycardia as they occur.

Reverse stock split

On April 26, 2019, the Company's Board of Directors approved an amendment to the Company's articles of incorporation to effect a 1-for-5.3193 reverse stock split of the Company's common shares, convertible preferred shares and the share options of the Company. Accordingly, all common shares, convertible preferred shares, share options and per share amounts in these unaudited interim consolidated financial statements have been retroactively adjusted for all periods presented to give effect to the reverse stock split. The reverse stock split was effected on April 26, 2019.

On May 13, 2019, the Company completed its initial public offering ("IPO"), whereby the Company issued 5,500,000 common shares at a public offering price of $15.00 per share. The shares began trading on The Nasdaq Global Select Market on May 9, 2019. On May 15, 2019, the underwriters fully exercised their option to purchase an additional 825,000 common shares at the public offering price of $15.00 per share. The gross proceeds received by the Company from the offering were $94.9 million, before deducting underwriting discounts and commissions and other estimated offering expenses payable by the Company. Upon the closing of the IPO, all outstanding shares of Class A1, A2, B, C, D1 and D2 preferred shares converted into 17,550,802 common shares.

2 Summary of significant accounting policies

a) Basis of consolidation

The unaudited interim condensed consolidated financial statements include the accounts of the Company and its wholly-owned subsidiary, Milestone Pharmaceuticals USA, Inc. Milestone Pharmaceuticals USA, Inc. began its operations on March 3, 2017. All intercompany transactions and balances have been eliminated.

b) Basis of presentation and use of accounting estimates

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, except for the adoption of ASC 842 "Leases" described in c) below. 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, 2018.

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 financial position as of June 30, 2019, and its results of operations for the three and six months ended June 30, 2019 and 2018.

Milestone Pharmaceuticals Inc.
Notes to Condensed Consolidated Financial Statements
(Unaudited)

(in thousands of US dollars, except where noted and for share and per share data)

2 Summary of significant accounting policies (Cont'd)

b) Basis of presentation and use of accounting estimates (Cont'd)

The condensed consolidated balance sheet as of December 31, 2018, was derived from audited annual consolidated financial statements, but does not contain all of 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 unaudited interim condensed 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, research and development tax credits recoverable, research and development expenses, and share-based compensation. Accordingly, actual results may differ from those estimates and such differences may be material.

c) Adoption of New Accounting Standards

Effective January 1, 2019, the Company adopted Accounting Standards Update (ASU) No. 2016-02, "Leases". This ASU requires substantially all leases to be recorded on the balance sheet as right-of-use asset and lease obligations. The Company elected the package of practical expedients permitted under the transition guidance and applied the modified retrospective approach which allowed the Company to carry forward the historical lease classification. Adoption of this standard resulted in the recording of an operating lease right-of-use asset and corresponding operating lease liabilities of $0.3 million. The Company's condensed consolidated balance sheets for reporting periods beginning on January 1, 2019 are presented under the new guidance, while prior period amounts were not adjusted and continue to be reported in accordance with previous guidance.

The Company does not record an operating lease right-of-use asset and corresponding lease liability for leases with an initial term of twelve months or less and recognizes lease expense for these leases as incurred over the lease term. Upon adoption date, the Company had only one operating lease with a remaining term of less than 12 months for its offices located in Charlotte, NC, which had a termination date of July 31, 2019, and for which the Company was not reasonably certain of renewing the lease. In the second quarter ended June 30, 2019, the lease was extended for an additional month to end on August 31, 2019. The remaining operating lease payments are $12 as of June 30, 2019.

Operating lease right-of-use asset and operating lease liabilities are recognized upon the adoption date based on the present value of lease payments over the remaining lease term. The Company does not have a public credit rating and carries no debt. As such, several factors were considered in the determination of its incremental borrowing rate used in determining the present value of lease payments. The Company examined the Bloomberg credit ratings for similar companies; assumed equivalency between the Canadian and US markets for collateralized debt; factored in the cumulative dividend rate on convertible preferred shares; and used short-term rates for the remaining lease term of 23 months. This resulted in an incremental borrowing rate of 8%. Lease expense is recognized on a straight-line basis over the lease term, which is accomplished by increasing the amortization of the right-of-use asset as interest expense on the lease liability declines over the lease term. The Company's lease arrangement does not have lease and non-lease components which are accounted for separately. The adoption of the accounting standard did not

Milestone Pharmaceuticals Inc.
Notes to Condensed Consolidated Financial Statements
(Unaudited)

(in thousands of US dollars, except where noted and for share and per share data)

2 Summary of significant accounting policies (Cont'd)

c) Adoption of New Accounting Standards (Cont'd)

materially impact the Company's consolidated statement of operations or its consolidated statement of cash flows for the six months ended June 30, 2019.

The Company's only one-operating lease right-of-use asset is as follows as at June 30, 2019:

Right-of-use adoption date of January 1, 2019	$ 321
Amortization of right-of-use asset during the six-month period ending June 30, 2019	(78)
	$ 243

Operating lease expenses of $78 are included in general and administrative operating expenses in the consolidated statement loss and comprehensive loss, and within operating activities in the statement of cash flows for the six-month period ended June 30, 2019.

The following table summarizes the future minimum lease payments of right-of-use assets operating lease as at June 30, 2019:

July 1, 2019 to June 30, 2020	$ 187
July 1, 2020 to November 30, 2020	62
	249
Less interest	(13)
	$ 236

As at December 31, 2018, the Company had a lease commitment for its headquarters located in Ville Saint-Laurent, Quebec, expiring on November 30, 2020 with an option to renew for an additional three years and a commitment for its office located in Charlotte, North Carolina, expiring on July 30, 2019. The minimum lease payments as at December 31, 2018 were as follows:

	Lease operating expenses	Lease base rent expenses	Total lease commitment
2019	$ 86	$ 130	$ 216
2020	79	85	164
	$ 165	$ 215	$ 380

Total rental expense under operating leases for the year ended December 31, 2018 was $232.

On June 3, 2019, the Company entered into a new lease arrangement for a three-year term for its office located in Charlotte, NC. The Company will recognize the operating lease right-of-use asset and operating lease liabilities at the lease expected commencement date on September 1, 2019. A security deposit of $19 was recorded in prepaid expenses as at June 30, 2019 related to the new lease arrangement.

Milestone Pharmaceuticals Inc.
Notes to Condensed Consolidated Financial Statements
(Unaudited)

(in thousands of US dollars, except where noted and for share and per share data)

3 Short-term investments

Short-term investments are comprised of term deposits issued in US currency, earning interest ranging from 2.47% to 2.48%, maturing between September 30, 2019 and October 25, 2019.

4 Accounts payable and accrued liabilities

Accounts payable and accrued liabilities comprised the following:

	June 30, 2019	December 31, 2018
Trade accounts payable	$ 3,228	$ 2,603
Accrued research & development liabilities	1,691	1,012
Other accrued liabilities	645	164
Accrued compensation and benefits payable	724	698
	$ 6,288	$ 4,477

5 Shareholders' equity (deficit)

Authorized share capital

An unlimited number of common shares, voting and participating, without par value.

In May 2019, the Company completed its initial public offering ("IPO"), whereby the Company issued in total 6,325,000 common shares at a public offering price of $15.00 per share *(note 1)*. The gross proceeds received by the Company from the offering were $94.9 million. Upon the closing of the IPO, all outstanding shares of Class A1, A2, B, C, D1 and D2 preferred shares converted into 17,550,802 common shares.

The Company's board of directors adopted and its shareholders approved the 2019 Employee Share Purchase Plan ("ESPP") in April 2019, which became effective on May 8, 2019. The number of common shares initially reserved for issuance under the ESPP was 278,734 common shares. The number of shares reserved for issuance will automatically increase on January 1 of each calendar year, beginning on January 1, 2020 through January 1, 2029, by the lesser of (1) 1% of the total number of shares of the Company's share capital outstanding on the last day of the calendar month before the date of the automatic increase and (2) 487,837 shares; provided that before the date of any such increase, the Company's board of directors may determine that such increase will be less than the amount set forth in clauses (1) and (2). As of June 30, 2019, no common shares have been issued under the ESPP. The first offering period has not yet been decided by the Company's board of directors.

During the six-month period ended June 30, 2019, the Company issued a total of 18,153 common shares [2018 — 42,781] for a total cash consideration of $25 [2018 - $37] pursuant to the exercise of 18,153 stock options [2018 — 42,781] at an average exercise price of US$1.3225 per option [2018 — US$0.8298]. As a result, an amount of $26 [2018 - $32] previously included in additional paid-in capital related to the exercised options has been credited to share capital and deducted from additional paid-in capital.

Milestone Pharmaceuticals Inc.
Notes to Condensed Consolidated Financial Statements
(Unaudited)

(in thousands of US dollars, except where noted and for share and per share data)

5 Shareholders' equity (deficit) (Cont'd)

Additional paid-in capital

	Three months ended June 30,		Six months ended June 30,	
	2019	2018	2019	2018
Opening balance	$ 2,840	$ 2,472	$ 2,655	$ 2,372
Share-based compensation expense	276	79	487	204
Exercise of stock options	—	(7)	(26)	(32)
Closing balance	$ 3,116	$ 2,544	$ 3,116	$ 2,544

Share-based compensation

The Company's board of directors adopted and its shareholders approved the 2019 Equity Incentive Plan (the "2019 Plan") in April 2019, which became effective on May 8, 2019 in connection with the IPO. Initially, the maximum number of the Company's common shares that may be issued under the 2019 Plan is 4,710,564 shares, which is the sum of (1) 1,923,501 new shares, plus (2) the number of shares (not to exceed 2,787,063 shares) (i) that remained available for the issuance of awards under the Company's Stock Option Plan (the "2011 Plan") at the time the 2019 Plan became effective, and (ii) any shares subject to outstanding options or other share awards that were granted under the 2011 Plan that terminate, expire or are otherwise forfeited, reacquired or withheld. In addition, the number of the Company's common shares reserved for issuance under the 2019 Plan will automatically increase on January 1 of each calendar year, starting on January 1, 2020 through January 1, 2029, in an amount equal to 4% of the total number of the Company's capital shares outstanding on the last day of the calendar month before the date of each automatic increase, or a lesser number of shares determined by the Company's board of directors. As of May 8, 2019, the Company's 2011 Plan was terminated and no further option grants will be made under the 2011 Plan.

On October 15, 2018, the Company amended for a third time and restated the 2011 Plan whereby options to purchase common shares of the Company's shares may be granted to directors, officers, employees, consultants and members of the scientific advisory board. The 2011 Plan was administered by the Board of Directors. The Board of Directors determined the number of options to be granted, the vesting period and the exercise price of new options. It was the Company's policy to establish the exercise price at an amount that approximated the fair value of the underlying shares on the date of grant as determined by the Board of Directors.

Under the 2011 Plan, unless otherwise decided by the Board of Directors, options vest and are exercisable as follows: 25% are exercisable from the first anniversary of grant date and 2.0833% become available at the end of each month after the first anniversary of grant date.

The 2011 Plan was terminated as of May 8, 2019 and a total of 2,393,631 options are still outstanding at June 30, 2019.

As of June 30, 2019, there were 2,322,573 options available for awards under the 2019 Plan, of which 46,998 were granted, leaving 2,275,575 available for future grants.

Milestone Pharmaceuticals Inc.
Notes to Condensed Consolidated Financial Statements
(Unaudited)

(in thousands of US dollars, except where noted and for share and per share data)

5 Shareholders' equity (deficit) (Cont'd)

Share-based compensation (Cont'd)

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

	2019		2018	
	Number of shares	Weighted average exercise price	Number of shares	Weighted average exercise price
Outstanding at beginning of period	2,295,045	$ 1.7714	968,782	$ 1.1330
Forfeited/cancelled	—	—	(12,198)	1.0958
Granted – 2011 Plan	116,739	9.4152	887,432	1.5400
Granted – 2019 Plan	46,998	15.0000	—	—
Exercised	(18,153)	1.3225	(42,781)	0.8298
Outstanding at end of period	2,440,629	$ 2.3963	1,801,235	$ 1.3405
Exercisable at end of period	771,478	$ 1.3777	563,565	$ 1.0266

As of June 30, 2019, the weighted average remaining contractual life was 8.3 years [2018 – 8.6 years]. The weighted average remaining contractual life was 6.6 years for vested options [2018 – 6.9 years]. There were no options forfeited for the six-month period ended June 30, 2019 (2018 –12,198).

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 (deficit). The weighted average fair values of options granted in the six-month period ended June 30, 2019 was $7.8518 per share [2018 - $1.1114]. Share-based compensation expense recognized for the six-month period ended June 30, 2019 was $487 [2018 - $204].

As of June 30, 2019, there was $3,434 [2018 - $1,360] of total unrecognized compensation cost, related to non-vested share options, which is expected to be recognized over a remaining weighted average vesting period of 2.9 years [2018 – 3.2 years].

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(in thousands of US dollars, except where noted and for share and per share data)

5 Shareholders' equity (deficit) (Cont'd)

Share-based compensation (Cont'd)

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

	2019		2018	
	Number of options	Weighted average fair value	Number of options	Weighted average fair value
Non-vested at beginning of period	1,706,303	$ 1.3458	451,113	$ 1.0266
Forfeited/cancelled	—	—	(12,198)	1.0639
Granted – 2011 Plan	116,739	6.6491	887,432	1.1114
Granted – 2019 Plan	46,998	10.7731	—	—
Vested, outstanding	(200,889)	1.1787	(88,600)	1.0958
Non-vested share options at end of period	1,669,151	$ 2.0041	1,237,747	$ 1.0798

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 was estimated using the Black-Scholes option pricing model, resulting in the following weighted average assumptions for the options granted for the three-month and six-month periods ended June 30:

	Three months ended June 30,		Six months ended June 30,	
	2019	2018	2019	2018
Exercise price	$ 12.05	$ 1.54	$ 11.02	$ 1.54
Share price	$ 12.05	$ 1.54	$ 11.02	$ 1.54
Volatility	82%	82%	81%	82%
Risk-free interest rate	2.36%	2.73%	2.41%	2.77%
Expected life	6.25 years	6.25 years	6.25 years	6.25 years
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 US 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 term. The simplified method

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5 Shareholders' equity (deficit) (Cont'd)

Share-based compensation (Cont'd)

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 for the three and six months ended June 30:

	Three months ended June 30,		Six months ended June 30,	
	2019	2018	2019	2018
Administration	$ 133	$ 21	$ 203	$ 50
Research and development	109	49	234	125
Commercial activities	34	10	50	29
	$ 276	$ 80	$ 487	$ 204

6 Net loss per share

Basic and diluted net loss per common share is determined by dividing net loss applicable to common shareholders by the weighted average number of common shares outstanding during the period. The outstanding convertible preferred shares and share-based compensation have been excluded from the calculation because their effects would be anti-dilutive. Therefore, the weighted average number of shares used to calculate both basic and diluted loss per share are the same.

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:

	2019	2018
Convertible preferred shares	—	9,433,910
Share options and unvested restricted share awards	2,440,629	1,801,235
	2,440,629	11,235,145

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

7 Government assistance

The Company incurred research and development expenditures that are eligible for investment tax credits. The investment tax credits recorded are based on management's estimates of amounts expected to be recovered and are subject to audit by the taxation authorities. These amounts have been recorded as a reduction of research and development expenditures for an amount of $171 for the six-month period ended June 30, 2019 [2018 - $148].

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(in thousands of US dollars, except where noted and for share and per share data)

8 Fair value of financial instruments

Pursuant to the accounting guidance for fair value measurement and its subsequent updates, fair value is defined as the price that would be received to sell an asset or paid to transfer a liability (i.e. the exit price) in an orderly transaction between market participants at the measurement date. The accounting guidance establishes a hierarchy for inputs used in measuring fair value that minimizes the use of unobservable inputs by requiring the use of observable market data when available. Observable inputs are inputs that market participants would use in pricing the asset or liability based on active market data. Unobservable inputs are inputs that reflect the assumptions market participants would use in pricing the asset or liability based on the best information available in the circumstances.

The fair value hierarchy is broken down into the three input levels summarized below:

Level 1 – Valuations are based on quoted prices in active markets for identical assets or liabilities and readily accessible by the Company at the reporting date.

Level 2 – Valuations based on inputs other than the quoted prices in active markets that are observable either directly or indirectly in active markets.

Level 3 – Valuations based on unobservable inputs in which there is little or no market data, which requires the Company to develop its own assumptions.

The Company has determined that the carrying values of its short-term financial assets and liabilities approximate their fair value given the short-term nature of these 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 financial information and the notes thereto included in this Quarterly Report on Form 10-Q and the audited financial information and the notes thereto included in our Prospectus that forms a part of our Registration Statement on Form S-1 (File No. 333-230846), which was filed with the Securities and Exchange Commission, or SEC, pursuant to Rule 424 on May 9, 2019, or the Prospectus.

Overview

We are a Phase 3 clinical-stage biopharmaceutical company dedicated to developing and commercializing etripamil for the treatment of cardiovascular indications. Etripamil is a novel, potent and short-acting calcium channel blocker that we designed and are developing as a rapid-onset nasal spray to be administered by the patient to terminate episodes of paroxysmal supraventricular tachycardia, or PSVT, as they occur. PSVT is a rapid heart rate condition that starts and stops without warning, often experienced by patients with symptoms 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. For episodes of PSVT, however, calcium channel blockers are administered intravenously under medical supervision, usually in the emergency department. Etripamil's combination of convenient delivery, rapid-onset and short duration of action has the potential to shift the current treatment paradigm 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 PSVT wherever and whenever they occur.

We completed our Phase 2 clinical trial of etripamil for the treatment of PSVT in the United States and Canada, with results published in the Journal of the American College of Cardiology. The study showed an 87% termination rate of induced PSVT within 15 minutes at the 70 mg dose versus a 35% termination rate for placebo. The 70 mg dose was selected for testing in Phase 3 and we are actively recruiting patients for our first Phase 3 clinical trial of etripamil, designated as NODE-301, which may serve as a single pivotal efficacy trial required for approval by the US Food and Drug Administration (FDA). We expect top-line data for NODE-301 in the first half of 2020. In addition to the pivotal efficacy trial, our Phase 3 clinical program for etripamil for PSVT includes two open-label safety studies, designated as NODE-302 which we initiated in December 2018, and NODE-303, which we expect to initiate before the end of the year.

We also recently announced positive regulatory updates from our recent interactions with the FDA. The FDA agreed to our request to increase the target number of PSVT events in NODE-301 trial to 150 events, up from 100 events. The upsized trial satisfies a regulatory request from the European Medicines Agency (EMA) to eliminate the use of un-blinded, third-party data reviews for purposes of handling potential randomization imbalances. The increased number of evaluable events adds potentially valuable sub-population analyses and pharmaco-economic assessments. The rate of events in NODE-301, which remains blinded, are tracking ahead of our initial projections, enabling us to maintain the expectation of topline data in the first half of 2020, even with the additional PSVT events. Further, after the NODE-301 trial reaches its target adjudicated PSVT events, collection of blinded data from randomized patients who have not yet experienced an event will continue. These data will be analyzed separately as a secondary data set, referred to as NODE-301B, and may contribute further to sub-population analyses and pharmaco-economic assessments.

Additionally, based on a review of etripamil safety data to date, we proposed and the FDA has agreed to allow patient enrollment in the NODE-303 study to begin without an in-office safety test dose that is currently utilized in the NODE-301 pivotal study and with a broad patient population consistent with ongoing studies, including the older patients and those patients taking concomitant beta-blockers and calcium channel blockers.

We plan to initiate a Phase 2 clinical trial in the fourth quarter of 2019 in atrial fibrillation, another supraventricular tachycardia in which some patients experience a rapid heart rate. We plan to subsequently initiate an additional Phase 2 etripamil clinical proof of concept trial in angina based on the utility of other calcium channel blockers.

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 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 six months ended June 30, 2019 and 2018, we recorded net losses of $24.1 million and $7.8 million, respectively. As of June 30, 2019, we had an accumulated deficit of $82.4 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 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 trial of etripamil for the treatment of PSVT;
- seek marketing approvals for etripamil for the treatment of PSVT and other cardiovascular indications;
- establish a sales, marketing, manufacturing and distribution capability to commercialize etripamil or any future product candidate for which we may obtain marketing approval;
- initiate preclinical studies and clinical trials for etripamil for any additional indications we may pursue, including the Phase 2 clinical trials for the treatment of atrial fibrillation and angina, and for any additional product candidates that we may pursue in the future;
- build a portfolio of product candidates through development, or the acquisition or in-license of drugs, product candidates or technologies and further develop and/or prepare to commercialize those product candidates;
- maintain, protect and expand our intellectual property portfolio;
- hire additional clinical, regulatory and scientific personnel; and
- add operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts.
- incur additional legal, accounting and other expenses associated with operating as a public company.

Initial Public Offering

On May 13, 2019, we completed our initial public offering, or IPO, whereby we issued 5,500,000 common shares at a public offering price of $15.00 per share. The shares began trading on The Nasdaq Global Select Market on May 9, 2019. On May 15, 2019, the underwriters fully exercised their option to purchase an additional 825,000 common shares at the public offering price of $15.00 per share. We received net proceeds from the IPO and the over-allotment exercise of $85.4 million, after deducting underwriting discounts and commissions and other offering expenses. Upon the closing of the IPO, all outstanding shares of our preferred shares converted into 17,550,802 common shares.

Reverse Stock Split

On April 26, 2019, our Board of Directors approved an amendment to our articles of incorporation to effect a 1-for-5.3193 reverse stock split of our common shares, convertible preferred shares and the share options of the Company. Accordingly, all common shares, convertible preferred shares, share options and per share amounts in the consolidated financial statements and MD&A have been retroactively adjusted for all periods presented to give effect to the reverse stock split. The reverse stock split was effected on April 26, 2019.

Components of Results of Operations

Research and Development Expenses

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. Historically, we have incurred research and development expenses that primarily relate to the development of etripamil for the treatment of PSVT. 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 and angina to increase for each of their respective Phase 2 clinical trials, we expect our research and development expenses related to the development of etripamil for PSVT to remain a large

majority of our total 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, 2019 and 2018.

	Three months ended June 30,		Six months ended June 30,	
(in thousands)	2019	2018	2019	2018
Clinical and pre-clinical	$ 8,463	$ 2,030	$ 15,212	$ 4,054
Drug manufacturing and formulation	1,638	336	2,268	1,155
Regulatory and other costs	519	250	982	581
Less: investment tax credits	(93)	(65)	(170)	(148)
Total research and development expenses	$ 10,527	$ 2,551	$ 18,292	$ 5,642

We expect our research and development expenses to increase substantially as we increase personnel costs, including share-based compensation, and as we continue the development of etripamil and pursue regulatory approval. The process of conducting the necessary clinical research to obtain regulatory approval is costly and time-consuming. 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 Expenses

General and administrative expenses include personnel and related compensation costs, expenses for outside professional services, lease 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 incur additional expenses as a public company, including expenses related to compliance with the rules and regulations of the Securities and Exchange Commission, 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. We also expect to increase our administrative headcount significantly to operate as public company and as we advance etripamil and any future product candidates through clinical development, which will also increase our general and administrative expenses.

Commercial Expenses

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, atrial fibrillation and angina. 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 payor; second, we want to understand and document the burden of disease posed by PSVT from an epidemiology, healthcare resource use, and cost perspective; and third, we want to engage our target patient, physician, and payor stakeholders with evidence-based and compliant educational materials that serve to increase the awareness and understanding of the impact of PSVT on patients and the overall healthcare system.

We expect our commercial expenses to remain relatively consistent until after we file our new drug application, or NDA with the FDA, at which time we anticipate they will increase substantially as we invest in the infrastructure and personnel required to launch our first product in the United States.

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, 2019 and 2018

The following table summarizes our results of operations and changes:

(in thousands)	Three months ended June 30, 2019	2018	$ Change	% Change
Operating expenses				
Research and development, net of tax credits	$ 10,527	$ 2,551	$ 7,976	313%
General and administrative	1,641	750	891	119%
Commercial	2,166	375	1,791	478%
Total operating expenses	14,334	3,676	10,658	290%
Loss from operations	(14,334)	(3,676)	(10,658)	290%
Interest income, net of bank charges	672	89	583	655%
Loss and comprehensive loss before income taxes	(13,662)	(3,587)	(10,075)	281%
Income tax expense	(4)	2	6	(300)%
Net loss and comprehensive loss	$ (13,658)	$ (3,589)	$ (10,069)	281%

(in thousands)	Six months ended June 30, 2019	2018	$ Change	% Change
Operating expenses				
Research and development, net of tax credits	$ 18,292	$ 5,642	$ 12,650	224%
General and administrative	2,620	1,189	1,431	120%
Commercial	4,352	1,100	3,252	296%
Total operating expenses	25,264	7,931	17,333	219%
Loss from operations	(25,264)	(7,931)	(17,333)	219%
Interest income, net of bank charges	1,172	180	992	551%
Loss and comprehensive loss before income taxes	(24,092)	(7,751)	(16,341)	210%
Income tax expense	18	18	—	—
Net loss and comprehensive loss	$ (24,110)	$ (7,769)	$ (16,341)	210%

Research and Development Expenses

Research and development, or R&D, expenses increased by $8.0 million, or 313%, for the three months ended June 30, 2019 compared to the three months ended June 30, 2018. Similarly, R&D expenses increased by $12.7 million, or 224% for the six months ended June 30, 2019 compared to the six months ended June 30, 2018. During the quarter ended June 30, 2019, we recorded $10.5 million in R&D expenses. During the six months ended June 30, 2019, we recorded $18.3 million in research and development expenses. Spending during both periods was primarily related to advancing our Phase 3 efficacy and safety trials in etripamil for the treatment of PSVT and increases in headcount related expenses to support the trials and activities important for regulatory approvals. We spent $7.2 million on these programs in the second quarter of 2019 and recorded personnel and related R&D costs of $3.4 million. During the same period of 2018, we recorded expenses of $2.6 million including $1.5 million related to the start-up costs for the efficacy trial in etripamil for the treatment of PSVT and recorded personnel and R&D related costs of $1.2 million. Additionally, we spent $12.5 million on these programs in the first six months of 2019 and recorded personnel and related R&D costs of $6.0 million. During the same period of 2018, we recorded expenses of $5.6 million including $2.8 million related to the start-up costs for the efficacy trial in etripamil for the treatment of PSVT and recorded personnel and R&D related costs of $3.0 million. We also recognized $0.1 million of R&D investment tax credits provided by the provincial government of Québec in the three-month periods ended June 30, 2019 and 2018 and $0.2 million of such tax credits in the six-month periods ended June 30, 2019 and 2018. Tax credits are recorded as a reduction of our R&D expenses.

General and Administrative Expenses

General and administrative expenses increased by $0.9 million, or 119% for the three months ended June 30, 2019 compared to the three months ended June 30, 2018 and increased by $1.4 million, or 120% for the six months ended June 30, 2019. During these three and six-month periods ended on June 30, 2019, we increased our administrative headcount and, as a result, compensation and related personnel costs increased when compared to the same periods in 2018. In addition, we incurred increased spending for consulting fees, recruiting fees and professional fees, including legal and accounting services incurred to support our IPO. Following the IPO, insurance costs increased in the second quarter of 2019 to support risk management activities as a public company.

Commercial Expenses

Commercial expenses increased by $1.8 million, or 478%, for the three months ended June 30, 2019 and by $3.3 million, or 296% for the six months ended June 30, 2019 when compared to the same periods in 2018. During these three and six-month periods, commercial expenses reflect increased commercial headcount and related costs, conduct of additional commercial and market research, increases in the scope of our patient advocacy activities, and costs of a medical affairs team focused on engaging key opinion leaders' and raising disease awareness.

Interest Income, Net

Interest income, net of bank charges was $0.7 million and $0.1 million for the three-month periods ended June 30, 2019 and 2018, respectively and $1.2 million and $0.2 million for the six months ended June 30, 2019 and 2018, respectively. The increase in the second quarter of 2019 and in the six months ended June 30, 2019 reflects increased earnings on cash, cash equivalents and short-term investments related to the proceeds from the October 2018 Series D preferred share financing and the net cash proceeds from the IPO and over-allotment exercised in May 2019.

Net Loss

For the foregoing reasons, we had net losses of $13.7 million and $3.6 million for the three months ended June 30, 2019 and 2018, and $24.1 million and $7.8 million for the six months ended June 30, 2019 and 2018, respectively.

Liquidity and Capital Resources

Sources of Liquidity

Prior to our IPO, we financed our operations primarily through sales of our convertible preferred shares to accredited investors generating net proceeds of $138.8 million. In May 2019, we received net proceeds of $85.4 million from our IPO.

We have incurred operating losses and experienced negative operating cash flows since our inception and anticipate that we will continue to incur losses for at least the next several years. As of June 30, 2019, we had cash, cash equivalents and short-term investments of $145.8 million and an accumulated deficit of $82.4 million.

Based on our current operating plan, we expect our existing cash, cash equivalents and short-term investments, together with the net proceeds from the IPO, will be sufficient to fund our operations into the third quarter of 2021. We have based this estimate on assumptions that may prove to be wrong, however, and we could use our capital resources sooner than we expect.

Funding Requirements

We use our cash primarily to fund research and development expenditures. We expect to incur an increase in research and development expenses as well as general and administrative expenses and commercial activities as our R&D progresses. 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 cannot forecast whether current or future product candidates may be subject to future collaborations, when such arrangements will be secured, if at all, and to what degree such arrangements would affect our development 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 of etripamil in PSVT 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 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;
- the extent to which we acquire or in-license other product candidates and technologies; and
- the costs of operating as a public company;

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 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. 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, results of operations and prospects.

Cash Flows

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

(in thousands)	Six months ended June 30, 2019	2018	$ Change	% Change
Net cash (used in) provided by:				
Operating activities	$ (26,251)	$ (8,144)	$ (18,107)	222%
Investing activities	(34,989)	15,030	(50,019)	(333)%
Financing activities	86,117	37	86,080	232,649%
Net increase (decrease) in cash and cash equivalents during the period	$ 24,877	$ 6,923	$ 17,954	

Operating Activities

In the six months ended June 30, 2019, we used $26.2 million of cash in operating activities, which consisted of a net loss of $24.1 million and a net change of $2.6 million in our net operating assets and non-cash charges of $0.5 million. The non-cash charges primarily consist of share-based compensation expense for grants to employees. The change in our net operating assets and liabilities was primarily due to an increase of $3.6 million for prepaid expenses in addition to an increase of $1.1 million for accounts payable and accrued liabilities offset by a net decrease of $0.1 million primarily related to other receivables, income tax payable and research and development tax credits receivable.

In the six months ended June 30, 2018, we used $8.1 million of cash in operating activities which consisted of a net loss of $7.8 million and a net change of $0.5 million in our net operating assets and non-cash charges of $0.2 million. The non-cash charges mainly consist of share-based compensation expense for grants to employees. The change in our net operating assets and liabilities was primarily due to an increase of $0.4 million for prepaid expenses offset by a decrease of $0.2 million in R&D tax credits receivable, a decrease of $0.4 million in accounts payable and accrued liabilities and a net decrease of $0.1million primarily related to other receivables and income tax payable.

Investing Activities

In the six months ended June 30, 2019, there was a net use of cash of $35.0 million for the acquisition of short-term investments compared to the same period in 2018 where the investing activities provided $15.0 million of cash due to the redemption of short-term investments that we had acquired during the year ended December 31, 2017.

Financing Activities

In the six months ended June 30, 2019, the IPO and the exercise by the underwriters of their option to purchase additional common shares provided a net cash consideration of $86.1 million. Financing fees amounting to $0.7 million were not paid at June 30, 2019 and are included in accounts payable and accrued liabilities. In the same period when compared to 2018, financing activities provided $25 thousand and $37 thousand, respectively, which consisted of the exercise of share options.

Off-Balance Sheet Arrangements

We have not entered into any off-balance sheet arrangements.

Contractual Obligations

During the six months ended June 30, 2019, 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 Prospectus.

Critical Accounting Policies and 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 at June 30, 2019, 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 and disclosed in note 2 of our most recent annual consolidated financial statements, except for the adoption of ASC 842 “Leases” described below. The preparation of these unaudited interim condensed 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, research and development tax credits recoverable, research and development expenses, and share-based compensation. 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.

There have been no significant changes to our critical accounting policies from those described in “Management’s Discussion and Analysis of Financial Condition and Results of Operations,” included in our Prospectus other than what is noted below.

Leases

Effective January 1, 2019, we adopted Accounting Standards Update (ASU) No. 2016-02, “Leases”. This ASU requires substantially all leases to be recorded on the balance sheet as right-of-use asset and lease obligations. We elected the package of practical expedients permitted under the transition guidance and applied the modified retrospective approach which allowed us to carry forward the historical lease classification. Adoption of this standard resulted in the recording of an operating lease right-of-use asset and corresponding operating lease liabilities of $0.3 million. Our condensed consolidated balance sheets for reporting periods beginning on January 1, 2019 are presented under the new guidance, while prior period amounts were not adjusted and continue to be reported in accordance with previous guidance.

We did not record an operating lease right-of-use asset and corresponding lease liability for leases with an initial term of 12 months or less. We recognize lease expense for these leases as incurred over the lease term. Upon adoption date, we had only one operating lease with a remaining term of less than 12 months for our offices located in Charlotte, NC, which had a termination date of July 31, 2019, and for which we were not reasonably certain of renewing the lease. In the second quarter ended June 30, 2019, the lease was extended for an additional month to end on August 31, 2019. The remaining operating lease payments are $12,000 at June 30, 2019.

Operating lease right-of-use asset and operating lease liabilities are recognized upon the adoption date based on the present value of lease payments over the remaining lease term. We do not have a public credit rating and carry no debt. As such, several factors were considered in the determination of our incremental borrowing rate used in determining the present value of lease payments. We examined the Bloomberg credit ratings for similar companies; assumed equivalency between the Canadian and US markets for collateralized debt; factored in the cumulative dividend rate on convertible preferred shares; and used short-term rates for the remaining lease term of 23 months. This resulted in an incremental borrowing rate of 8%. Lease expense is recognized on a straight-line basis over the lease term, which is accomplished by increasing the amortization of the right-of-use asset as interest expense on the lease liability declines over the lease term. Our lease arrangement does not have lease and non-lease components which are accounted for separately. The adoption of the accounting standard did not materially impact our consolidated statement of operations or our consolidated statement of cash flows for the six months ended June 30, 2019.

Our operating lease right-of-use asset is as follows as at June 30, 2019:

(in thousands)		
Adoption as at January 1, 2019	$	321
Recognition of right-of-use asset in the six-month period ending June 30, 2019		(78)
	$	243

Operating lease expenses of $78,000 are included in general and administrative operating expenses in the consolidated statement loss and comprehensive loss, and within operating activities in the statement of cash flows for the six-month period ended June 30, 2019.

The following table summarizes the future minimum lease payments of right-of-use assets operating lease as at June 30, 2019:

(in thousands)		
July 1, 2019 to June 30, 2020	$	187
July 1, 2020 to November 30, 2020		62
		249
Less interest		(13)
	$	236

Recent Accounting Pronouncements

Refer to Note 2, “Summary of Significant Accounting Policies,” for a discussion of recent accounting pronouncements in the accompanying notes to our audited consolidated financial statements as at December 31, 2018 appearing in the Prospectus, and in Note 2 of our unaudited interim consolidated financial statements as at June 30, 2019.

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 $145.8 million as of June 30, 2019, 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. At June 30, 2019, our net monetary assets denominated in Canadian dollars were equivalent to $0.4 million in U.S. dollars.

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 believe that inflation and changing prices had a significant impact on our results of operations for any periods presented herein. 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 Vice President, Finance, evaluated the effectiveness of our disclosure controls and procedures as of June 30, 2019. Based upon the evaluation, our Chief Executive Officer and Vice President, Finance 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.

Due to a transition period established by SEC rules applicable to newly public companies, our management is not required to evaluate the effectiveness of our internal control over financial reporting until after the filing of our Annual Report on Form 10-K for the year ended December 31, 2019. As a result, this Quarterly Report on Form 10-Q does not address whether there have been any changes in our internal control over financial reporting.

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.

An investment in shares of our common shares involves a high degree of risk. You should carefully consider the following information about these risks, together with the other information appearing elsewhere in this Quarterly Report on Form 10-Q, including our unaudited condensed consolidated financial statements and related notes hereto before deciding to invest in our common shares. The occurrence of any of the following risks could have a material adverse effect on our business, financial condition, results of operations and future growth prospects or cause our actual results to differ materially from those contained in forward-looking statements we have made in this report and those we may make from time to time. In these circumstances, the market price of our common shares could decline and you may lose all or part of your investment. We cannot assure you that any of the events discussed below will not occur.

Risks Related to Our Financial Position and Capital Needs

We have incurred significant operating losses since inception and anticipate that we will continue to incur substantial operating losses for the foreseeable future and may never achieve or maintain profitability.

Since inception in 2003, we have incurred significant operating losses. Our net loss was $8.1 million and $23.2 million for the years ended December 31, 2017 and 2018, respectively, and $24.1 million for the six months ended June 30, 2019. As of June 30, 2019, we had an accumulated deficit of $82.4 million. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. Since inception, we have devoted substantially all of our efforts to research and preclinical and clinical development of etripamil, as well as to expanding our management team and infrastructure. It could be several years, if ever, before

we have a commercialized drug. The net losses we incur may fluctuate significantly from quarter to quarter and year to year. We anticipate that our expenses will increase substantially if, and as, we:

- continue our ongoing and planned development of etripamil, including our Phase 3 clinical trials of etripamil for the treatment of paroxysmal supraventricular tachycardia, or PSVT;
- seek marketing approvals for etripamil for the treatment of PSVT and other cardiovascular indications and any future product candidates that successfully complete clinical trials;
- establish a sales, marketing, manufacturing and distribution capability 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 Phase 2 clinical trials for the treatment of atrial fibrillation and angina, and for any additional product candidates that we may pursue in the future;
- maintain, protect and expand our intellectual property portfolio;
- hire additional clinical, 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 and other expenses associated with operating as a public company.

To become and remain profitable, we must succeed in developing and eventually commercializing drugs that generate significant revenue. This will require us to be successful in a range of challenging activities, including completing clinical trials of etripamil and any future product candidates that way may pursue, obtaining regulatory approval, procuring commercial-scale manufacturing, marketing and selling etripamil and any future products for which we may obtain regulatory approval, as well as discovering or acquiring and then developing additional product candidates. We are only in the preliminary stages of some of these activities. We may never succeed in these activities and, even if we do, may never generate revenues that are significant enough to achieve profitability.

Because of the numerous risks and uncertainties associated with drug development, we are unable to accurately predict the timing or amount of expenses or when, or if, we will be able to achieve profitability.

Our expenses could increase beyond our expectations if we are required by the U.S. Food and Drug Administration, or FDA, the European Medicines Agency or other regulatory authorities to perform studies in addition to those we currently expect, or if there are any delays in the initiation and completion of our clinical trials or the development of etripamil or any future product candidates.

Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of our company and could impair our ability to raise capital, maintain our research and development efforts, expand our business or continue our operations. A decline in the value of our common shares could also cause you to lose all or part of your investment.

Our limited operating history may make it difficult for you to evaluate the success of our business to date and to assess our future viability.

We are a clinical-stage company founded in 2003, and our operations to date have been largely focused on raising capital, organizing and staffing our company, and undertaking preclinical studies and conducting clinical trials for etripamil. As an organization, we have not yet demonstrated an ability to successfully complete clinical development, obtain regulatory approvals, manufacture a commercial-scale product or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful commercialization. Consequently, any predictions about our future success or viability may not be as accurate as they could be if we had a longer operating history.

We may encounter unforeseen expenses, difficulties, complications, delays and other known or unknown factors in achieving our business objectives. We will need to transition at some point from a company with a research and development focus to a company capable of supporting commercial activities. We may not be successful in such a transition.

Additionally, we expect our financial condition and operating results to continue to fluctuate from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. Accordingly, you should not rely upon the results of any quarterly or annual periods as indications of future operating performance.

We will require substantial additional funding to finance our operations. If we are unable to raise capital when needed, we could be forced to delay, reduce or terminate our development of etripamil or other operations.

Based on our research and development plans, we expect that our existing cash, cash equivalents and short-term investments, will be sufficient to fund our operations into the third quarter of 2021. However, we will need to obtain substantial additional funding in connection with our continuing operations and planned activities. Our future capital requirements will depend on many factors, including:

- the timing, progress and results of our ongoing and planned clinical trials of etripamil in PSVT 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 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;
- the extent to which we acquire or in-license other product candidates and technologies; and
- the costs of operating as a public company.

Identifying potential product candidates and conducting preclinical testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain regulatory approval and achieve product sales. In addition, etripamil and any future product candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of drugs that we do not expect to be commercially available for several years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all. In addition, we may seek additional capital due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. If we are unable to raise capital when needed or on attractive terms, we could be forced to delay, reduce or altogether terminate our research and development programs or future commercialization efforts.

Raising additional capital may cause dilution to our shareholders, restrict our operations or require us to relinquish rights to our product candidates.

Until such time, if ever, as we can generate substantial product revenue, we expect to finance our cash needs through public or private equity or debt financings, third-party funding, marketing and distribution arrangements, as well as other collaborations, strategic alliances and licensing arrangements, or any combination of these approaches. We do not have any committed external source of funds. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest may be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a shareholder. Debt and equity financings, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as redeeming our shares, making investments, incurring additional debt, making capital expenditures, declaring dividends or placing limitations on our ability to acquire, sell or license intellectual property rights.

If we raise additional capital through future collaborations, strategic alliances or third-party licensing arrangements, we may have to relinquish valuable rights to our intellectual property, future revenue streams, research programs or product candidates, or grant licenses on terms that may not be favorable to us. If we are unable to raise additional capital when needed, we may be required to delay, limit, reduce or terminate our drug development or future commercialization efforts, or grant rights to develop and market product candidates that we would otherwise develop and market ourselves.

Our ability to use our non-capital loss carryforwards to offset future taxable income may be subject to certain limitations.

In general, where control of a corporation has been acquired by a person or group of persons, subsection 111(5) of the Income Tax Act (Canada), or the Canadian Tax Act, and equivalent provincial income tax legislation restrict the corporation’s ability to carry forward non-capital losses from preceding taxation years. We have not performed a detailed analysis to determine whether an acquisition of control for the purposes of subsection 111(5) of the Canadian Tax Act has occurred after each of our previous issuances of common shares or preferred shares. In addition, if we undergo an acquisition of control, our ability to utilize non-capital losses could be limited by subsection 111(5) of the Canadian Tax Act. As of December 31, 2018, we had Canadian federal and provincial non-capital loss carry forwards of $46.4 million and $45.7 million, respectively, which expire beginning in 2027 through 2038. In addition, we also have scientific research and experimental development expenditures of $5.8 million and $8.0 million, respectively, for Canadian federal and provincial income tax purposes, which have not been deducted. These expenditures are available to reduce future taxable income and have an unlimited carry-forward period. Research and development tax credits and expenditures are subject to verification by the tax authorities, and, accordingly, these amounts may vary. Future changes in our share ownership, some of which are outside of

our control, could result in an acquisition of control for the purposes of subsection 111(5) of the Canadian Tax Act. Furthermore, our ability to utilize non-capital losses (or U.S. equivalents) of companies that we may acquire in the future may be subject to limitations. As a result, even if we attain profitability, we may be unable to use a material portion of our non-capital losses and other tax attributes, which could negatively impact our future cash flows.

Risks Related to the Development of Our Product Candidates

We have only one product candidate, etripamil, for which we are currently pursuing clinical development. Our future success is substantially dependent on the successful clinical development and regulatory approval of etripamil. If we are not able to obtain required regulatory approvals for etripamil or any future product candidates, we will not be able to commercialize etripamil or any future product candidates and our ability to generate revenue will be adversely affected.

Etripamil is currently our only product candidate. We have not obtained regulatory approval for etripamil or any product candidate, and it is possible that neither etripamil nor any product candidates we may seek to develop in the future will ever obtain regulatory approval. Neither we nor any future collaborator is permitted to market any drug product candidates in the United States or other countries until we receive regulatory approval from the FDA or applicable foreign regulatory agency. The time required to obtain approval or other marketing authorizations by the FDA and comparable foreign regulatory authorities is unpredictable but typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. In addition, approval policies, regulations or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions.

Prior to obtaining approval to commercialize etripamil and any other drug product candidate in the United States or elsewhere, we must demonstrate with substantial evidence from well controlled clinical trials, and to the satisfaction of the FDA or comparable foreign regulatory authorities, that such product candidates are safe and effective for their intended uses. Results from nonclinical studies and clinical trials can be interpreted in different ways. Even if we believe the nonclinical or clinical data for our product candidates are promising, such data may not be sufficient to support approval by the FDA and other regulatory authorities. The FDA may also require us to conduct additional nonclinical studies, including human factor studies, or clinical trials for our product candidates either prior to or post-approval, or it may object to elements of our clinical development program. Our current Phase 3 program involves only one efficacy trial, designed with a threshold p-value of $p<0.01$. This threshold was accepted by the FDA for our single efficacy trial to be used to support an NDA submission. While we believe that this is sufficient support for our NDA submission plan based on our end-of-Phase 2 meeting with the FDA, the standard FDA guidelines require two efficacy trials each with a threshold p-value of $p<0.05$ or a single trial with a threshold p-value of $p<0.00125$. Accordingly, there is a risk that additional clinical trials could be required. In addition, the FDA typically refers applications for novel drugs, like etripamil and potentially any future product candidates, to an advisory committee composed of outside experts. The FDA is not bound by the recommendation of the advisory committee, but it considers such recommendation when making its decision.

Of the large number of products in development, only a small percentage successfully complete the FDA or comparable foreign regulatory authorities' approval processes and are commercialized. The lengthy approval or marketing authorization process as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval or marketing authorization to market etripamil or any future product candidates, which would significantly harm our business, financial condition, results of operations and prospects.

We have invested a significant portion of our time and financial resources in the development of etripamil. Our business is dependent on our ability to successfully complete development of, obtain regulatory approval for, and, if approved, successfully commercialize etripamil and any future product candidates in a timely manner.

Even if we eventually complete clinical testing and receive approval of a new drug application, or NDA, or foreign marketing application for etripamil and any future product candidates, the FDA or the comparable foreign regulatory authorities may grant approval or other marketing authorization contingent on the performance of costly additional clinical trials, including post-market clinical trials. The FDA or the comparable foreign regulatory authorities also may approve or authorize for marketing a product candidate for a more limited indication or patient population that we originally request, and the FDA or comparable foreign regulatory authorities may not approve or authorize the labeling that we believe is necessary or desirable for the successful commercialization of a product candidate. Any delay in obtaining, or inability to obtain, applicable regulatory approval or other marketing authorization would delay or prevent commercialization of that product candidate and would materially adversely impact our business and prospects.

In addition, the FDA and comparable foreign regulatory authorities may change their policies, adopt additional regulations or revise existing regulations or take other actions, which may prevent or delay approval of our future products under development on a timely basis. Such policy or regulatory changes could impose additional requirements upon us that could delay our ability to obtain approvals, increase the costs of compliance or restrict our ability to maintain any marketing authorizations we may have obtained.

We may not be successful in our efforts to expand our pipeline of product candidates beyond etripamil for PSVT.

We intend to build a pipeline of product candidates beyond etripamil for PSVT and progress these product candidates through clinical development. We may not be able to expand the scope of cardiovascular indications for etripamil beyond PSVT, or leverage our expertise and experience with etripamil in PSVT to other product candidates. We may not be able to in-license, acquire or develop future product candidates that are safe and effective. Even if we are successful in continuing to expand etripamil to other indications and further build our pipeline, the potential product candidates that we identify may not be suitable for clinical development, including as a result of safety, tolerability, efficacy or other characteristics that indicate that they are unlikely to be drugs that will receive marketing approval, achieve market acceptance or obtain reimbursements from third-party payors. If we do not successfully execute on our strategy of expanding our product pipeline, it could significantly harm our financial position and adversely affect the trading price of our common shares.

The development of additional product candidates is risky and uncertain.

Efforts to identify, acquire or in-license, and then develop product candidates require substantial technical, financial and human resources, whether or not any product candidates are ultimately identified. Our efforts may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development, approved products or commercial revenues for many reasons, including the following:

- the methodology used may not be successful in identifying potential product candidates;
- competitors may develop alternatives that render any product candidates we develop obsolete;
- any product candidates we develop may nevertheless be covered by third parties' patents or other exclusive rights;
- a product candidate may be shown to have harmful side effects or other characteristics that indicate it is unlikely to be effective or otherwise does not meet applicable regulatory criteria;
- a product candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all; and
- a product candidate may not be accepted as safe and effective by physicians, patients, the medical community or third-party payors.

We have limited financial and management resources and, as a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater market potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial drugs or profitable market opportunities. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in circumstances under which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate. If we are unsuccessful in identifying and developing additional product candidates or are unable to do so, our business may be harmed.

Success in preclinical studies or earlier clinical trials may not be indicative of results in future clinical trials and we cannot assure you that any ongoing, planned or future clinical trials will lead to results sufficient for the necessary regulatory approvals.

Success in preclinical testing and earlier clinical trials does not ensure that later clinical trials will generate the same results or otherwise provide adequate data to demonstrate the efficacy and safety of a product candidate. Preclinical tests and Phase 1 and Phase 2 clinical trials are primarily designed to test safety, to study pharmacokinetics and pharmacodynamics and to understand the side effects of product candidates at various doses and schedules. Success in preclinical studies and earlier clinical trials does not ensure that later efficacy trials will be successful, nor does it predict final results. For example, our Phase 2 clinical trial of etripamil for PSVT was conducted in an electrophysiology lab, a controlled setting, in which PSVT episodes were induced and etripamil was administered by healthcare providers. Our Phase 3 clinical trials are and will be conducted in an outpatient setting with patients self-administering etripamil and monitoring their cardiac activity as episodes of PSVT occur. Additionally, in our Phase 2 clinical trial, four sprays of study drug were dispensed to patients using four separate FDA-approved single-spray devices. In our Phase 3 clinical trials, patients self-administer two sprays of study drug from an FDA-approved device that is capable of delivering two separate sprays. Accordingly, the results of our Phase 2 trial of etripamil may not be replicated in the outpatient setting of our Phase 3 clinical trials. In addition, until completion of our NODE-301 Phase 3 clinical trial, patients are in general only eligible to enroll in our open-label NODE-302 extension trial after successfully dosing in NODE-301. Etripamil and any future product candidates may fail to show the desired safety and efficacy in clinical development despite positive results in preclinical studies or having successfully advanced through earlier clinical trials.

In addition, the design of a clinical trial can determine whether its results will support approval of a product, and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced. Clinical trial design flaws are more likely in therapy areas, such as PSVT, where there are limited previous trials from which to learn and model clinical trials. As an organization, we have limited experience designing clinical trials and may be unable to design and execute a clinical trial to support regulatory approval. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials even after achieving promising results in preclinical testing and earlier clinical trials. Data obtained from preclinical and clinical activities

are subject to varying interpretations, which may delay, limit or prevent regulatory approval. In addition, we may experience regulatory delays or rejections as a result of many factors, including changes in regulatory policy during the period of our product candidate development. Any such delays could negatively impact our business, financial condition, results of operations and prospects.

We may encounter substantial delays or difficulties in our clinical trials.

We may not commercialize, market, promote or sell any product candidate without obtaining marketing approval from the FDA or comparable foreign regulatory authorities, and we may never receive such approvals. It is impossible to predict when or if any of our product candidates will prove effective or safe in humans and will receive regulatory approval. Before obtaining marketing approval from regulatory authorities for the sale of our product candidates, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. A failure of one or more clinical trials can occur at any stage of testing. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products.

We may experience numerous unforeseen events prior to, during, or as a result of, clinical trials that could delay or prevent our ability to receive marketing approval or commercialize etripamil and any future product candidates, including:

- delays in reaching a consensus with regulatory authorities on design or implementation of our clinical trials;
- regulators or institutional review boards, or IRBs, may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- delays in reaching agreement on acceptable terms with prospective clinical research organizations, or CROs, and clinical trial sites;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate, patients may drop out of these clinical trials at a higher rate than we anticipate or fail to return for post-treatment follow-up or we may fail to recruit suitable patients to participate in a trial;
- clinical trials of our product candidates may produce negative or inconclusive results;
- imposition of a clinical hold by regulatory authorities as a result of a serious adverse event, concerns with a class of product candidates or after an inspection of our clinical trial operations, trial sites or manufacturing facilities;
- occurrence of serious adverse events associated with the product candidate that are viewed to outweigh its potential benefits;
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols; or
- we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs.

Any inability to successfully complete preclinical and clinical development could result in additional costs to us or impair our ability to generate revenue from future drug sales or other sources. In addition, if we make manufacturing or formulation changes to our product candidates, we may need to conduct additional testing to bridge our modified product candidate to earlier versions. Clinical trial delays could also shorten any periods during which we may have the exclusive right to commercialize our product candidates, if approved, or allow our competitors to bring competing drugs to market before we do, which could impair our ability to successfully commercialize our product candidates and may harm our business, financial condition, results of operations and prospects.

Additionally, if the results of our clinical trials are inconclusive or if there are safety concerns or serious adverse events associated with our product candidates, we may:

- be delayed in obtaining marketing approval, if at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings;
- be subject to additional post-marketing testing requirements;
- be required to perform additional clinical trials to support approval or be subject to additional post-marketing testing requirements;
- have regulatory authorities withdraw, or suspend, their approval of the drug or impose restrictions on its distribution in the form of a modified risk evaluation and mitigation strategy, or REMS;
- be subject to the addition of labeling statements, such as warnings or contraindications;
- be sued; or
- experience damage to our reputation.

Our product development costs will also increase if we experience delays in testing or obtaining marketing approvals. We do not know whether any of our preclinical studies or clinical trials will begin as planned, need to be restructured or be completed on schedule, if at all.

Further, we, the FDA or an IRB may suspend our clinical trials at any time if it appears that we or our collaborators are failing to conduct a trial in accordance with regulatory requirements, including the FDA's current Good Clinical Practice, or GCP, regulations, that we are exposing participants to unacceptable health risks, or if the FDA finds deficiencies in our investigational new drug

applications, or INDs, or the conduct of these trials. Therefore, we cannot predict with any certainty the schedule for commencement and completion of future clinical trials. If we experience delays in the commencement or completion of our clinical trials, or if we terminate a clinical trial prior to completion, the commercial prospects of our product candidates could be negatively impacted, and our ability to generate revenues from our product candidates may be delayed.

Clinical trials are very expensive, time consuming and difficult to design and implement.

Our product candidates will require clinical testing before we are prepared to submit an NDA for regulatory approval. We cannot predict with any certainty if or when we might submit an NDA for regulatory approval for any of our product candidates or whether any such NDA will be approved by the FDA. Human clinical trials are very expensive and difficult to design and implement, in part because they are subject to rigorous regulatory requirements. For instance, the FDA may not agree with our proposed endpoints for any future clinical trial of our product candidates, which may delay the commencement of our clinical trials. In addition, we may not succeed in developing and validating disease-relevant clinical endpoints based on insights regarding biological pathways for the diseases we are studying. The clinical trial process is also time consuming. We estimate that the successful completion of clinical trials for etripamil and any future product candidates will take several years to complete. Furthermore, failure can occur at any stage, and we could encounter problems that cause us to abandon or repeat clinical trials.

Enrollment and retention of patients in clinical trials is an expensive and time-consuming process and could be delayed, made more difficult or rendered impossible by multiple factors outside our control.

Identifying and qualifying patients to participate in our clinical trials is critical to our success. If the actual number of patients with PSVT, or any other indications that we may pursue for etripamil or future product candidates, is smaller than we anticipate, we may encounter difficulties in enrolling patients in our clinical trials, thereby delaying or preventing development and approval of etripamil and any future product candidates. Even once enrolled we may be unable to retain a sufficient number of patients to complete any of our trials. Patient enrollment and retention in clinical trials depends on many factors, including the size of the patient population, the nature of the trial protocol, the existing body of safety and efficacy data, the number and nature of competing treatments and ongoing clinical trials of competing therapies for the same indication, the proximity of patients to clinical sites, the experience and capabilities of the clinical sites to recruit the correct patients, and the eligibility criteria for the trial. In our Phase 3 clinical trial, we are attempting to enroll higher risk elderly patients. We are doing this in order to obtain efficacy and safety data on patients representing the most vulnerable subset of our intended population. Such patients may be difficult to enroll in this trial, and the lack of data on these patients may negatively impact the approvability or labeling of etripamil.

In our Phase 2 clinical trial of etripamil for the treatment of PSVT, only 104 of 199 enrolled patients completed the trials, with 70 patients unable to induce or sustain PSVT during the trial period. The first Phase 3 trial of PSVT for etripamil will enroll up to 500 diagnosed PSVT patients meeting inclusion and exclusion criteria and based on recent FDA guidance, will be completed when a total of 150 adjudicated PSVT events are treated. PSVT is episodic and unpredictable, and our Phase 3 trial design depends on patients experiencing and recognizing an episode of PSVT, self-administering etripamil and monitoring their cardiac activity using a monitoring device. We cannot control the timing of these episodes or guarantee that patients will correctly recognize the episode, self-administer etripamil and use the cardiac monitor as directed. We also cannot predict with certainty the number or timing of any PSVT episodes for those patients that enroll in the trial. Conducting a Phase 3 clinical trial for a PSVT treatment in an outpatient setting is paradigm changing, and subject to a number of risks. There is limited, if any, meaningful precedent from which to inform our trial design and make assumptions about patient enrollment and compliance. Accordingly, our Phase 3 trial design is subject to significantly more risks than if there were numerous studies upon which we could model our protocols. Our efficacy and safety databases could take significantly longer to populate than projected, which would add cost to our development program and delay any potential approval of etripamil.

Furthermore, our efforts to build relationships with patient communities may not succeed, which could result in delays in patient enrollment in our clinical trials. In addition, any negative results we may report in clinical trials of etripamil and any future product candidate may make it difficult or impossible to recruit and retain patients in other clinical trials of that same product candidate. Delays or failures in planned patient enrollment or retention may result in increased costs, program delays or both, which could have a harmful effect on our ability to develop etripamil or any future product candidates or could render further development impossible. In addition, we expect to rely on CROs and clinical trial sites to ensure proper and timely conduct of our future clinical trials and, while we intend to enter into agreements governing their services, we will be limited in our ability to compel their actual performance. Similarly, our formulation of etripamil is designed to be self-administered as a nasal spray during a PSVT episode by patients enrolled in our Phase 3 trials. While we expect enrolled patients to adhere to the protocol, our ability to ensure patient compliance is limited.

Our product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit the commercial potential or result in significant negative consequences following any potential marketing approval.

During the conduct of clinical trials, patients report changes in their health, including illnesses, injuries and discomforts, to their doctor. Often, it is not possible to determine whether or not the product candidate being studied caused these conditions. Regulatory authorities

may draw different conclusions or require additional testing to confirm these determinations, if they occur. For example, in our Phase 2 clinical trial for PSVT, three serious adverse events, or SAEs, were considered possibly related to etripamil, including a second degree AV block that subsequently resolved. Calcium channel blockers have known side effects, such as slowing the heart rate below normal levels and hypotension, or low blood pressure. While we designed etripamil to have a short half-life to lower these risks, if etripamil is not quickly metabolized as designed, these known side effects may become more pronounced in patients who use etripamil.

In addition, it is possible that as we test etripamil or any future product candidates in larger, longer and more extensive clinical trials, such as our Phase 3 clinical trials, or as use of etripamil or any future product candidates becomes more widespread if they receive regulatory approval, illnesses, injuries, discomforts and other adverse events that were observed in earlier trials, as well as conditions that did not occur or went undetected in previous trials, will be reported by subjects or patients. Many times, side effects are only detectable after investigational drugs are tested in large-scale pivotal trials or, in some cases, after they are made available to patients on a commercial scale after approval. If additional clinical experience indicates that etripamil or any future product candidates have side effects or causes serious or life-threatening side effects, the development of the product candidate may fail or be delayed, or, if the product candidate has received regulatory approval, such approval may be revoked, which would harm our business, prospects, operating results and financial condition.

Interim, "top-line" and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may publish interim, "top-line" or preliminary data from our clinical trials. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Preliminary or "top-line" data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, interim and preliminary data should be viewed with caution until the final data are available. Differences between preliminary or interim data and final data could significantly harm our business prospects and may cause the trading price of our common shares to fluctuate significantly.

As an organization, we have never completed pivotal clinical trials, and we may be unable to do so for any product candidates we may develop, including our pivotal Phase 3 clinical trials for the treatment of PSVT.

We will need to successfully complete pivotal clinical trials in order to obtain the approval of the FDA and other regulatory agencies to market etripamil or any of our other product candidates. Carrying out later-stage clinical trials and the submission of a successful NDA is a complicated process. As an organization, we have not previously completed any later stage or pivotal clinical trials and have limited experience in preparing, submitting and prosecuting regulatory filings. Consequently, we may be unable to successfully and efficiently execute and complete necessary clinical trials in a way that leads to NDA submission and approval of etripamil for the treatment of PSVT. We may require more time and incur greater costs than our competitors and may not succeed in obtaining regulatory approvals of product candidates that we develop. Failure to commence or complete, or delays in, our planned clinical trials could prevent us from or delay us in commercializing etripamil for the treatment of PSVT.

Etripamil is intended to be used with a nasal spray device, which may result in additional supply and regulatory risks.

We currently obtain the nasal spray device for administration of Etripamil from a single source supplier. Our nasal spray device supplier relies on multiple suppliers for certain components of the device, some of whom are single source suppliers. There are a limited number of device suppliers that address our particular design requirements. While we intend to explore alternative nasal spray devices for the delivery of etripamil that are produced by other suppliers to have backup sources for future commercial needs, we may not identify other nasal device suppliers that meet our requirements, and such alternative devices may not be as effective at the delivery of etripamil as our current supplier's device. We do not currently have a formal supply agreement with our current sole nasal spray device supplier, and obtain such devices as needed. Even if we reach agreement for commercial supply, if we do not have additional nasal spray device suppliers, our sole supplier may be unable to meet our demands. Unpredictability of supply could have a material adverse effect on our commercialization plans for etripamil, if approved, and could have a material adverse effect on our business and financial condition.

Our finished drug product in the nasal delivery system will be regulated as a drug/device combination product. There are additional regulatory risks for drug/device combination products. We may experience delays in obtaining regulatory approval of etripamil given the increased complexity of the review process when approval of the product and a delivery device is sought under a single marketing application. In the United States, each component of a combination product is subject to the requirements established by the FDA for that type of component, whether a drug, biologic or device. The delivery system device will be subject to FDA device requirements regarding design, performance and validation as well as human factors testing, among other things. Delays in or failure of the studies conducted by us, or failure of our company, our collaborators, if any, or the third-party providers or suppliers to obtain or maintain regulatory approval could result in increased development costs, delays in or failure to obtain regulatory approval, and associated delays in etripamil reaching the market.

We may explore strategic collaborations that may never materialize, or we may be required to relinquish important rights to and control over the development of our product candidates to any future collaborators.

We intend to periodically explore a variety of possible strategic collaborations in an effort to gain access to additional product candidates or resources. At the current time, we cannot predict what form such a strategic collaboration might take. We are likely to face significant competition in seeking appropriate strategic collaborators, and strategic collaborations can be complicated and time consuming to negotiate and document. We may not be able to negotiate strategic collaborations on acceptable terms, or at all. We are unable to predict when, if ever, we will enter into any strategic collaborations because of the numerous risks and uncertainties associated with establishing them.

Future collaborations could subject us to a number of risks, including:

- we may be required to undertake the expenditure of substantial operational, financial and management resources;
- we may be required to issue equity securities that would dilute our shareholders' percentage ownership of our company;
- we may be required to assume substantial actual or contingent liabilities;
- we may not be able to control the amount and timing of resources that our strategic collaborators devote to the development or commercialization of our product candidates;
- strategic collaborators may select indications or design clinical trials in a way that may be less successful than if we were doing so;
- strategic collaborators may delay clinical trials, provide insufficient funding, terminate a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new version of a product candidate for clinical testing;
- strategic collaborators may not pursue further development of products resulting from the strategic collaboration arrangement or may elect to discontinue research and development programs;
- strategic collaborators may not commit adequate resources to the marketing and distribution of our product candidates, limiting our potential revenues from these products;
- disputes may arise between us and our strategic collaborators that result in the delay or termination of the research or development of our product candidates or that result in costly litigation or arbitration that diverts management's attention and consumes resources;
- strategic collaborators may experience financial difficulties;
- strategic collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in a manner that could jeopardize or invalidate our proprietary information or expose us to potential litigation;
- business combinations or significant changes in a strategic collaborator's business strategy may adversely affect a strategic collaborator's willingness or ability to complete its obligations under any arrangement;
- strategic collaborators could decide to move forward with a competing product candidate developed either independently or in collaboration with others, including our competitors; and
- strategic collaborators could terminate the arrangement or allow it to expire, which would delay the development and may increase the cost of developing our product candidates.

Risks Related to the Commercialization of Our Product Candidates

If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to market and sell etripamil or any future product candidates, we may not be successful in commercializing etripamil or any future product candidates, if and when they are approved.

To successfully commercialize etripamil or any future product candidate that may result from our development programs, we will need to build out our sales and marketing capabilities, either on our own or with others. The establishment and development of our own commercial team or the establishment of a contract field force to market any product candidate we may develop will be expensive and time-consuming and could delay any drug launch. Moreover, we cannot be certain that we will be able to successfully develop this capability. We may seek to enter into collaborations with other entities to use their established marketing and distribution capabilities, but we may be unable to enter into such agreements on favorable terms, if at all. If any current or future collaborators do not commit sufficient resources to commercialize our product candidates, or we are unable to develop the necessary capabilities on our own, we may be unable to generate sufficient revenue to sustain our business. We may compete with many companies that currently have extensive, experienced and well-funded marketing and sales operations to recruit, hire, train and retain marketing and sales personnel. We will likely also face competition if we seek third parties to assist us with the sales and marketing efforts of etripamil and any future product candidates. Without an internal team or the support of a third party to perform marketing and sales functions, we may be unable to compete successfully against these more established companies.

Even if etripamil or any future product candidates receive marketing approval, they may fail to achieve market acceptance by physicians, patients, third-party payors or others in the medical community necessary for commercial success.

Even if etripamil or any future product candidates receive marketing approval, they may fail to gain market acceptance by physicians, patients, third-party payors and others in the medical community. If such product candidates do not achieve an adequate level of

acceptance, we may not generate significant drug revenue and may not become profitable. The degree of market acceptance of etripamil or any future product candidates, if approved for commercial sale, will depend on a number of factors, including but not limited to:

- the convenience and ease of administration compared to alternative treatments and therapies;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the efficacy and potential advantages compared to alternative treatments and therapies;
- the effectiveness of sales and marketing efforts;
- the prevalence and severity of any side effects;
- the strength of our relationships with patient communities;
- the cost of treatment in relation to alternative treatments and therapies, including any similar generic treatments;
- our ability to offer such drug for sale at competitive prices;
- the strength of marketing and distribution support;
- the availability of third-party coverage and adequate reimbursement; any restrictions on the use of the drug together with other medications; and the awareness and support from key opinion leaders in cardiology.

Our efforts to educate physicians, patients, third-party payors and others in the medical community on the benefits of etripamil or any future product candidates may require significant resources and may never be successful. Such efforts may require more resources than are typically required due to the potential of etripamil to shift the treatment paradigm away from acute-care settings to self-administration. Because we expect sales of etripamil or any future product candidates, if approved, to generate substantially all of our revenues for the foreseeable future, the failure of these product candidates to find market acceptance would harm our business.

Even if we successfully obtain approval for etripamil, its success will be dependent on its proper use.

While we have designed etripamil to be self-administered, we cannot control the successful use of the product. While we have conducted, and intend in the future to conduct, human factors studies to determine how to optimize the instructions for use, the results in our clinical trials may not be replicated by users in the future. If we are not successful in promoting the proper use of etripamil, if approved, we may not be able to achieve market acceptance or effectively commercialize the drug. In addition, even in the event of proper use of etripamil, individual devices may fail. Increasing the scale of production inherently creates increased risk of manufacturing errors, and we may not be able to adequately inspect every device that is produced, and it is possible that individual devices may fail to perform as designed. Manufacturing errors could negatively impact market acceptance of any of our product candidates that receive approval, result in negative press coverage, or increase our liability.

If the market opportunities for etripamil and any future product candidates are smaller than we estimate, our business may suffer.

Our eligible patient population may differ significantly from the actual market addressable by our product candidates. Our projections of both the number of people who have these conditions, as well as the subset of people with these diseases who have the potential to benefit from treatment with our product candidates, are based on our beliefs and estimates. These estimates have been derived from a variety of sources, including the scientific literature, insurance claims databases or market research, and may prove to be incorrect. Further, new studies may change the estimated incidence or prevalence of these diseases. The number of patients may turn out to be lower than expected. Likewise, the potentially addressable patient population for each of our product candidates may be limited or may not be amenable to treatment with our product candidates, and new patients may become increasingly difficult to identify or access. If the market opportunities for our product candidates are smaller than we estimate, our business and results of operations could be adversely affected.

We may face substantial competition, which may result in others developing or commercializing drugs before or more successfully than us.

The development and commercialization of new drugs is highly competitive. We may face competition from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization.

More established companies may have a competitive advantage over us due to their greater size, resources and institutional experience. In particular, these companies have greater experience and expertise in securing reimbursement, government contracts and relationships with key opinion leaders, conducting testing and clinical trials, obtaining and maintaining regulatory approvals and distribution relationships to market products and marketing approved drugs. These companies also have significantly greater research and marketing capabilities than we do. If we are not able to compete effectively against existing and potential competitors, our business and financial condition may be harmed.

As a result of these factors, our competitors may obtain regulatory approval of their drugs before we are able to, which may limit our ability to develop or commercialize etripamil and any future product candidates. Our competitors may also develop therapies that are

safer, more effective, more widely accepted or less expensive than ours, and may also be more successful than we in manufacturing and marketing their drugs. These advantages could render our product candidates obsolete or non-competitive before we can recover the costs of such product candidates' development and commercialization.

Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller and early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific, management and commercial personnel, establishing clinical trial sites and subject registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

If we commercialize etripamil or any future product candidates outside of the United States, a variety of risks associated with international operations could harm our business.

We intend to seek approval to market etripamil outside of the United States, and may do so for future product candidates. If we market approved products outside of the United States, we expect that we will be subject to additional risks in commercialization including:

- different regulatory requirements for approval of therapies in foreign countries;
- reduced protection for intellectual property rights;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenues, and other obligations incident to doing business in another country;
- foreign reimbursement, pricing and insurance regimes;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geopolitical actions, including war and terrorism or natural disasters including earthquakes, typhoons, floods and fires.

We have no prior experience in these areas. In addition, there are complex regulatory, tax, labor and other legal requirements imposed by many of the individual countries in and outside of Europe with which we will need to comply. Many biopharmaceutical companies have found the process of marketing their own products in foreign countries to be very challenging.

Coverage and adequate reimbursement may not be available for etripamil or any future product candidates, which could make it difficult for us to gain market acceptance.

Market acceptance and sales of any product candidates that we commercialize, if approved, will depend in part on the extent to which reimbursement for these drugs and related treatments will be available from third-party payors, including government health administration authorities, managed care organizations and other private health insurers. Third-party payors decide for which therapies and establish reimbursement levels. While no uniform policy for coverage and reimbursement exists in the United States, third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own coverage and reimbursement policies. However, decisions regarding the extent of coverage and amount of reimbursement to be provided for any product candidates that we develop will be made on a payor-by-payor basis. Therefore, one payor's determination to provide coverage for a drug does not assure that other payors will also provide coverage, and adequate reimbursement, for the drug. Additionally, a third-party payor's decision to provide coverage for a therapy does not imply that an adequate reimbursement rate will be approved. Each payor determines whether or not it will provide coverage for a therapy, what amount it will pay the manufacturer for the therapy, and on what tier of its formulary it will be placed. The position on a payor's list of covered drugs, or formulary, generally determines the co-payment that a patient will need to make to obtain the therapy and can strongly influence the adoption of such therapy by patients and physicians. Patients who are prescribed treatments for their conditions and providers prescribing such services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Patients are unlikely to use our products unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our products.

Third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. We cannot be sure that coverage and reimbursement will be available for any drug that we commercialize and, if reimbursement is available, what the level of reimbursement will be. Inadequate coverage and reimbursement may impact the demand for, or the price of, any drug for which we obtain marketing approval. If coverage and adequate reimbursement are not available, or are available only to limited levels, we may not be able to successfully commercialize etripamil or any future product candidates that we develop.

Product liability lawsuits against us could cause us to incur substantial liabilities and could limit commercialization of any product candidates that we may develop.

We face an inherent risk of product liability exposure related to the testing of etripamil or any future product candidates in clinical trials and may face an even greater risk if we commercialize any product candidate that we may develop. If we cannot successfully defend ourselves against claims that any such product candidates caused injuries, we could incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any product candidate that we may develop;
- loss of revenue;
- substantial monetary awards to trial participants or patients;
- significant time and costs to defend the related litigation;
- withdrawal of clinical trial participants;
- increased insurance costs;
- the inability to commercialize any product candidate that we may develop; and injury to our reputation and significant negative media attention.

Although we maintain product liability insurance coverage with maximum coverage of C$10 million per incident and an aggregate loss limit of C$10 million, such insurance may not be adequate to cover all liabilities that we may incur. We anticipate that we will need to increase our insurance coverage each time we commence a clinical trial and if we successfully commercialize any product candidate. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

Risks Related to Regulatory Compliance

Even if we obtain and maintain approval for etripamil or any future product candidates from the FDA, we may never obtain approval of etripamil or any future product candidates outside of the United States, which would limit our market opportunities and could harm our business.

Approval of a product candidate in the United States by the FDA does not ensure approval of such product candidate by regulatory authorities in other countries or jurisdictions, and approval by one foreign regulatory authority does not ensure approval by regulatory authorities in other foreign countries or by the FDA. Sales of etripamil or any future product candidates outside of the United States will be subject to foreign regulatory requirements governing clinical trials and marketing approval. Even if the FDA grants marketing approval for a product candidate, comparable foreign regulatory authorities also must approve the manufacturing and marketing of the product candidate in those countries. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from, and more onerous than, those in the United States, including additional preclinical studies or clinical trials. In many countries outside the United States, a product candidate must be approved for reimbursement before it can be approved for sale in that country. In some cases, the price that we intend to charge for any product candidates, if approved, is also subject to approval. Obtaining approval for etripamil or any future product candidates in the European Union from the European Commission following the opinion of the European Medicines Agency, if we choose to submit a marketing authorization application there, would be a lengthy and expensive process. Even if a product candidate is approved, the FDA or the European Commission, as the case may be, may limit the indications for which the drug may be marketed, require extensive warnings on the drug labeling or require expensive and time-consuming additional clinical trials or reporting as conditions of approval. Obtaining foreign regulatory approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of etripamil or any future product candidates in certain countries.

Further, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries. Also, regulatory approval for our product candidates may be withdrawn. If we fail to comply with the regulatory requirements, our target market will be reduced and our ability to realize the full market potential of etripamil or any future product candidates will be harmed and our business, financial condition, results of operations and prospects could be harmed.

Even if we obtain regulatory approval for etripamil or any future product candidates, they will remain subject to ongoing regulatory oversight.

Even if we obtain regulatory approvals for etripamil or any future product candidates, such approvals will be subject to ongoing regulatory requirements for manufacturing, labeling, packaging, storage, advertising, promotion, sampling, record-keeping and submission of safety and other post-market information. Any regulatory approvals that we receive for etripamil or any future product candidates may also be subject to a REMS, limitations on the approved indicated uses for which the drug may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 trials, and surveillance to monitor the quality, safety and efficacy of the drug. Such regulatory requirements may differ from country to country depending on where we have received regulatory approval.

In addition, drug manufacturers and their facilities are subject to payment of user fees and continual review and periodic inspections by the FDA and other regulatory authorities for compliance with cGMP requirements and adherence to commitments made in the NDA or foreign marketing application. If we, or a regulatory authority, discover previously unknown problems with a drug, such as adverse

events of unanticipated severity or frequency, or problems with the facility where the drug is manufactured or if a regulatory authority disagrees with the promotion, marketing or labeling of that drug, a regulatory authority may impose restrictions relative to that drug, the manufacturing facility or us, including requesting a recall or requiring withdrawal of the drug from the market or suspension of manufacturing.

If we fail to comply with applicable regulatory requirements following approval of etripamil or any future product candidates, a regulatory authority may:

- issue an untitled letter or warning letter asserting that we are in violation of the law;
- seek an injunction or impose administrative, civil or criminal penalties or monetary fines;
- suspend or withdraw regulatory approval;
- suspend any ongoing clinical trials;
- refuse to approve a pending NDA or comparable foreign marketing application or any supplements thereto submitted by us or our partners;
- restrict the marketing or manufacturing of the drug;
- seize or detain the drug or otherwise require the withdrawal of the drug from the market;
- refuse to permit the import or export of product candidates; or
- refuse to allow us to enter into supply contracts, including government contracts.

Moreover, the FDA strictly regulates the promotional claims that may be made about drug products. In particular, a product may not be promoted for uses that are not approved by the FDA as reflected in the product's approved labeling. However, biopharmaceutical companies may share truthful and not misleading information that is otherwise consistent with the labeling. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant civil, criminal and administrative penalties.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. The occurrence of any event or penalty described above may inhibit our ability to commercialize etripamil or any future product candidates and harm our business, financial condition, results of operations and prospects.

The FDA's and other regulatory authorities' policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability, which would adversely affect our business, prospects, financial condition and results of operations.

In addition, we cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. For example, certain policies of the Trump administration may impact our business and industry. Namely, the Trump administration has taken several executive actions, including the issuance of a number of Executive Orders, that could impose significant burdens on, or otherwise materially delay, the FDA's ability to engage in routine regulatory and oversight activities such as implementing statutes through rulemaking, issuance of guidance, and review and approval of marketing applications. It is difficult to predict how these executive actions, including the Executive Orders, will be implemented and the extent to which they will affect the FDA's ability to exercise its regulatory authority. If these executive actions impose constraints on the FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted.

Our relationships with customers, physicians, and third-party payors are subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, false claims laws, health information privacy and security laws, and other healthcare laws and regulations. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties.

Healthcare providers, physicians and third-party payors in the United States and elsewhere will play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our current and future arrangements with healthcare professionals, principal investigators, consultants, customers and third-party payors subject us to various federal and state fraud and abuse laws, data privacy and security laws, transparency laws and other healthcare laws that may constrain the business or financial arrangements and relationships through which we research, sell, market, and distribute our products, if we obtain marketing approval. We will also be subject to healthcare regulation and enforcement by the U.S. federal government and the states and any other countries in which we conduct our business, including our research, and the sales, marketing and distribution of our product candidates and products once they have obtained marketing authorization.

Ensuring that our business arrangements with third parties comply with applicable healthcare laws and regulations will likely be costly. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil,

criminal and administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from participating in government funded healthcare programs, such as Medicare and Medicaid, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, contractual damages, reputational harm and the curtailment or restructuring of our operations.

If the physicians or other providers or entities with whom we expect to do business are found not to be in compliance with applicable laws, they may be subject to significant criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs. Even if resolved in our favor, litigation or other legal proceedings relating to healthcare laws and regulations may cause us to incur significant expenses and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common shares. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development, manufacturing, sales, marketing or distribution activities. Uncertainties resulting from the initiation and continuation of litigation or other proceedings relating to applicable healthcare laws and regulations could have a material adverse effect on our ability to compete in the marketplace.

Healthcare legislative reform measures may have a negative impact on our business and results of operations.

In the United States and some foreign jurisdictions, there have been, and continue to be, several legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of product candidates, restrict or regulate post-approval activities, and affect our ability to profitably sell any product candidates for which we obtain marketing approval. In particular, there have been and continue to be a number of initiatives at the U.S. federal and state levels that seek to reduce healthcare costs and improve the quality of healthcare. For example, in March 2010, the Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010, or, collectively, the PPACA, was passed, which substantially changed the way healthcare is financed by both governmental and private payors in the United States. Since the PPACA's enactment, there have been judicial and Congressional challenges to certain aspects of the PPACA, and we expect there will be additional challenges and amendments to the PPACA in the future. For example, the Tax Cuts and Jobs Act of 2017, or the Tax Act, was enacted, which includes a provision that repealed, effective January 1, 2019, the tax-based shared responsibility payment imposed by the PPACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." Since the enactment of the Tax Act, there have been additional amendments to certain provisions of the PPACA, and we expect the current Trump administration and Congress will likely continue to seek to modify, repeal, or otherwise invalidate the entirety, or certain provisions, of the PPACA. Additionally, on December 15, 2018, a Texas U.S. District Court Judge ruled that the PPACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress as part of the Tax Act. While the Texas U.S. District Court Judge, as well as the Trump administration and CMS, have stated that the ruling will have no immediate effect pending appeal of the decision, it is unclear how this decision, subsequent appeals, and other efforts to repeal and replace the PPACA will impact the PPACA and our business.

Further, in the United States there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under government payor programs, and review the relationship between pricing and manufacturer patient programs. While some of the proposed measures will require additional authorization to become effective, U.S. Congress and the Trump administration have indicated that they will continue to seek new legislative and/or administrative measures to control drug costs. We expect that additional U.S. federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that the U.S. federal government will pay for healthcare products and services, which could result in reduced demand for etripamil or any future product candidates or additional pricing pressures.

We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action in the United States or any other jurisdiction. If we or any third parties we may engage are slow or unable to adapt to changes in existing or new requirements or policies, or if the we or such third parties are not able to maintain regulatory compliance, etripamil or any future product candidates we may develop may lose any regulatory approval that may have been obtained and we may not achieve or sustain profitability.

Our business involves the use of hazardous materials and we and our third-party manufacturers and suppliers must comply with environmental laws and regulations, which can be expensive and restrict how we do business.

Our research and development activities and our third-party manufacturers' and suppliers' activities involve the controlled storage, use and disposal of hazardous materials owned by us, including the components of etripamil and any future product candidates and other hazardous compounds. We and our manufacturers and suppliers are subject to laws and regulations governing the use, manufacture, storage, handling and disposal of these hazardous materials. In some cases, these hazardous materials and various wastes resulting from their use are stored at our and our manufacturers' facilities pending their use and disposal. We cannot eliminate the risk of

contamination, which could cause an interruption of our commercialization efforts, research and development efforts and business operations, environmental damage resulting in costly clean-up and liabilities under applicable laws and regulations governing the use, storage, handling and disposal of these materials and specified waste products. Although we believe that the safety procedures utilized by our third-party manufacturers for handling and disposing of these materials generally comply with the standards prescribed by these laws and regulations, we cannot guarantee that this is the case or eliminate the risk of accidental contamination or injury from these materials. In such an event, we may be held liable for any resulting damages and such liability could exceed our resources and state or federal or other applicable authorities may curtail our use of certain materials and/or interrupt our business operations. Furthermore, environmental laws and regulations are complex, change frequently and have tended to become more stringent. We cannot predict the impact of such changes and cannot be certain of our future compliance. We do not currently carry hazardous waste insurance coverage.

Risks Related to Our Dependence on Third Parties

We will rely on third parties to produce clinical and commercial supplies of etripamil and any future product candidates.

We do not own or operate facilities for drug manufacturing, storage and distribution, or testing. We are dependent on third parties to manufacture the clinical supplies of etripamil and any future product candidates. The facilities used by our contract manufacturers to manufacture etripamil and any future product candidates must be approved by the FDA pursuant to inspections that will be conducted after we submit our NDA to the FDA. We do not control the manufacturing process of, and are completely dependent on, our contract manufacturing partners for compliance with the regulatory requirements, known as cGMPs for manufacture of active drug substances, nasal spray device, and finished product candidates. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or others, we will not be able to secure and/or maintain regulatory approval for our product candidates. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. We intend to use multiple contract manufacturers for clinical and commercial supply of our drug product and drug substance. As such, we will need to demonstrate to the FDA that the drug product and drug substance from these contract manufacturers are comparable, which may include conducting additional equivalence studies. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our product candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our product candidates, if approved. Any significant delay in the supply of a product candidate, or the raw material components thereof, for an ongoing clinical trial due to the need to replace a third-party manufacturer could considerably delay completion of our clinical trials, product testing and potential regulatory approval of our product candidates.

Further, we also will rely on third-party manufacturers to supply us with sufficient quantities of etripamil and any future product candidates, if approved, for commercialization. We do not yet have a commercial supply agreement for commercial quantities of drug substance, drug product or nasal spray device. If we are not able to meet market demand for any approved product, it would negatively affect our ability to generate revenue, harm our reputation, and could have a material and adverse effect on our business and financial condition. Increasing the scale of production inherently creates increased risk of manufacturing errors, and we may not be able to adequately inspect every device that is produced, and it is possible that individual devices may fail to perform as designed. Manufacturing errors could negatively impact market acceptance of any of our product candidates that receive approval, result in negative press coverage, or increase our liability.

Further, our reliance on third-party manufacturers entails risks to which we would not be subject if we manufactured product candidates ourselves, including:

- inability to meet our product specifications and quality requirements consistently;
- delay or inability to procure or expand sufficient manufacturing capacity;
- issues related to scale-up of manufacturing;
- costs and validation of new equipment and facilities required for scale-up;
- our third-party manufacturers may not be able to execute our manufacturing procedures and other logistical support requirements appropriately;
- our third-party manufacturers may fail to comply with cGMP-compliance and other inspections by the FDA or other comparable regulatory authorities;
- our inability to negotiate manufacturing agreements with third parties under commercially reasonable terms, if at all;
- breach, termination or nonrenewal of manufacturing agreements with third parties in a manner or at a time that is costly or damaging to us;
- reliance on a single source for the nasal spray device;
- our third-party manufacturers may not devote sufficient resources to our product candidates;
- we may not own, or may have to share, the intellectual property rights to any improvements made by our third-party manufacturers in the manufacturing process for our product candidates;
- operations of our third-party manufacturers or suppliers could be disrupted by conditions unrelated to our business or operations, including the bankruptcy of the manufacturer or supplier; and carrier disruptions or increased costs that are beyond our control.

In addition, if we enter into a strategic collaboration with a third party for the commercialization of etripamil or any future product candidate, we will not be able to control the amount of time or resources that they devote to such efforts. If any strategic collaborator does not commit adequate resources to the marketing and distribution of etripamil or any future product candidate, it could limit our potential revenues.

Any of these events could lead to clinical trial delays, failure to obtain regulatory approval or affect our ability to successfully commercialize etripamil or any future product candidates once approved. Some of these events could be the basis for FDA action, including injunction, request for recall, seizure, or total or partial suspension of production.

We rely on third parties to conduct, supervise and monitor our preclinical studies and clinical trials, and if those third parties perform in an unsatisfactory manner, it may harm our business.

We have engaged CROs to conduct our Phase 3 clinical trials of etripamil for the treatment of PSVT, and we expect to engage a CRO for future clinical trials of etripamil and any future product candidates. We do not currently have the ability to independently conduct any clinical trials. We rely on CROs and clinical trial sites to ensure the proper and timely conduct of our preclinical studies and clinical trials, and we expect to have limited influence over their actual performance. We rely upon CROs to monitor and manage data for our clinical programs, as well as the execution of future nonclinical studies. We expect to control only certain aspects of our CROs' activities. Nevertheless, we will be responsible for ensuring that each of our preclinical studies and clinical trials is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards, and our reliance on the CROs does not relieve us of our regulatory responsibilities.

We and our CROs are required to comply with the good laboratory practices, or GLPs, and GCPs, which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities in the form of International Conference on Harmonization guidelines for any of our product candidates that are in preclinical and clinical development. The regulatory authorities enforce GCPs through periodic inspections of trial sponsors, principal investigators and clinical trial sites. Although we rely on CROs to conduct GCP-compliant clinical trials, we remain responsible for ensuring that each of our GLP preclinical studies and clinical trials is conducted in accordance with its investigational plan and protocol and applicable laws and regulations, and our reliance on the CROs does not relieve us of our regulatory responsibilities. If we or our CROs fail to comply with GCPs, the clinical data generated in our clinical trials may be deemed unreliable, and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. Accordingly, if our CROs fail to comply with these regulations or fail to recruit a sufficient number of subjects, we may be required to repeat clinical trials, which would delay the regulatory approval process.

Our reliance on third parties to conduct clinical trials will result in less direct control over the management of data developed through clinical trials than would be the case if we were relying entirely upon our own staff. Communicating with CROs and other third parties can be challenging, potentially leading to mistakes as well as difficulties in coordinating activities. Such parties may:

- have staffing difficulties;
- fail to comply with contractual obligations;
- experience regulatory compliance issues; or
- undergo changes in priorities or become financially distressed.

These factors may materially adversely affect the willingness or ability of third parties to conduct our clinical trials and may subject us to unexpected cost increases that are beyond our control. If our CROs do not successfully carry out their contractual duties or obligations, fail to meet expected deadlines, fail to comply with regulatory requirements, or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements or for any other reasons, our clinical trials may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for, or successfully commercialize, any product candidate that we develop. As a result, our financial results and the commercial prospects for any product candidate that we develop would be harmed, our costs could increase, and our ability to generate revenue could be delayed. While we will have agreements governing their activities, our CROs will not be our employees, and we will not control whether or not they devote sufficient time and resources to our future clinical and nonclinical programs. These CROs may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials, or other drug development activities that could harm our business. We face the risk of potential unauthorized disclosure or misappropriation of our intellectual property by CROs, which may reduce our trade secret protection and allow our potential competitors to access and exploit our proprietary technology.

If our relationship with any of these CROs terminates, we may not be able to enter into arrangements with alternative CROs or do so on commercially reasonable terms. Switching or adding additional CROs involves substantial cost and requires management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays occur, which can negatively affect our ability to meet our desired clinical development timelines. Though we intend to manage carefully our relationships with our CROs, there can be no assurance that we will not encounter challenges or delays in the future or that these delays or challenges will not have a negative impact on our business, financial condition and prospects.

In addition, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and receive compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to the FDA. The FDA may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected interpretation of the trial. The FDA may therefore question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the FDA and may ultimately lead to the denial of marketing approval of etripamil and any future product candidates.

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain patent protection for etripamil or any future product candidates, or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize drugs similar or identical to ours, and our ability to commercialize successfully our product candidates may be impaired.

Our success depends in large part on our ability to obtain and maintain patent protection in the United States and other countries with respect to etripamil and any future product candidates. We seek to protect our proprietary position by filing patent applications in the United States and abroad related to our product candidates. The patent application and prosecution process is expensive and time-consuming. We may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. We may also fail to identify patentable aspects of our research and development before it is too late to obtain patent protection. Therefore, these and any of our patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business. It is possible that defects of form in the preparation or filing of our patents or patent applications may exist, or may arise in the future, such as with respect to proper priority claims, inventorship, claim scope or patent term adjustments. If any future licensors or licensees are not fully cooperative or disagree with us as to the prosecution, maintenance or enforcement of any patent rights, such patent rights could be compromised and we might not be able to prevent third parties from making, using and selling competing products. If there are material defects in the form or preparation of our patents or patent applications, such patents or applications may be invalid and unenforceable. Moreover, our competitors may independently develop equivalent knowledge, methods and know-how. Any of these outcomes could impair our ability to prevent competition from third parties.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the United States. No consistent policy regarding the breadth of claims allowed in biotechnology and pharmaceutical patents has emerged to date in the United States or in many foreign jurisdictions. In addition, the determination of patent rights with respect to pharmaceutical compounds and technologies commonly involves complex legal and factual questions, which has in recent years been the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Furthermore, recent changes in patent laws in the United States, including the America Invents Act of 2011, may affect the scope, strength and enforceability of our patent rights or the nature of proceedings that may be brought by us related to our patent rights.

We may not be aware of all third-party intellectual property rights potentially relating to etripamil or any future product candidates. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. For example, U.S. applications filed before November 28, 2000 and certain U.S. applications filed after that date that will not be filed outside the United States remain confidential until a patent issue. Therefore, we cannot be certain that we were the first to make the inventions claimed in our patents or pending patent applications, or that we were the first to file for patent protection of such inventions. Similarly, should we own any patents or patent applications in the future, we may not be certain that we were the first to file for patent protection for the inventions claimed in such patents or patent applications. As a result, the issuance, scope, validity and commercial value of our patent rights cannot be predicted with any certainty. Moreover, we may be subject to a third-party pre-issuance submission of prior art to the U.S. Patent and Trademark Office, or USPTO, or become involved in opposition, derivation, reexamination, inter parties review, post grant review, or interference proceedings, in the United States or elsewhere, challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or product candidates and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights.

Our pending and future patent applications may not result in patents being issued that protect our technology or product candidates, in whole or in part, or which effectively prevent others from commercializing competitive technologies and products. Even if our patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection against competing products or processes sufficient to achieve our business objectives, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Our competitors may be able to circumvent our owned or licensed patents by developing similar or alternative technologies or products in a non-infringing manner. Our competitors may seek to market generic versions of any approved products by submitting abbreviated new drug applications to the FDA in which they claim that patents owned or licensed by

us are invalid, unenforceable and/or not infringed. Alternatively, our competitors may seek approval to market their own products similar to or otherwise competitive with our products. In these circumstances, we may need to defend and/or assert our patents, including by filing lawsuits alleging patent infringement. In any of these types of proceedings, a court or other agency with jurisdiction may find our patents invalid and/or unenforceable.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products. In addition, given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by government patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. In addition, periodic maintenance fees, renewal fees, annuity fees and various other government fees on patents and/or applications will have to be paid to the USPTO and various government patent agencies outside of the United States over the lifetime of our owned patents and/or applications and any patent rights we may own or license in the future. We rely on our outside counsel to pay these fees due to non-U.S. patent agencies. The USPTO and various non-U.S. government patent agencies require compliance with several procedural, documentary, fee payment and other similar provisions during the patent application process. We employ reputable law firms and other professionals to help us comply.

Non-compliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. If we fail to maintain the patents and patent applications covering our products or technologies, we may not be able to stop a competitor from marketing products that are the same as or similar to etripamil or any future product candidates, which would have a material adverse effect on our business. In many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. There are situations, however, in which non-compliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, potential competitors might be able to enter the market and this circumstance could harm our business.

Patent terms may be inadequate to protect our competitive position on our product candidates for an adequate amount of time.

Given the amount of time required for the development, testing and regulatory review of new product candidates, such as etripamil, patents protecting such candidates might expire before or shortly after such candidates are commercialized. We expect to seek extensions of patent terms in the United States and, if available, in other countries where we are prosecuting patents. In the United States, the Drug Price Competition and Patent Term Restoration Act of 1984 permits a patent term extension of up to five years beyond the normal expiration of the patent, which is limited to the approved indication (or any additional indications approved during the period of extension). However, the applicable authorities, including the FDA and the USPTO in the United States, and any equivalent regulatory authority in other countries, may not agree with our assessment of whether such extensions are available, and may refuse to grant extensions to our patents, or may grant more limited extensions than we request. If this occurs, our competitors may be able to take advantage of our investment in development and clinical trials by referencing our clinical and preclinical data and launch their drug earlier than might otherwise be the case.

Intellectual property rights do not necessarily address all potential threats to our business.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations and may not adequately protect our business. The following examples are illustrative:

- others may be able to make compounds or formulations that are similar to etripamil or formulations of etripamil or our future product candidates but that are not covered by the claims of any patents, should they issue, that we own or control;
- we or any strategic partners might not have been the first to make the inventions covered by the issued patents or pending patent applications that we own or control;
- we might not have been the first to file patent applications covering certain of our inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- it is possible that our pending patent applications will not lead to issued patents;
- issued patents that we own or control may not provide us with any competitive advantages, or may be held invalid or unenforceable as a result of legal challenges;

- our competitors might conduct research and development activities in the United States and other countries that provide a safe harbor from patent infringement claims for certain research and development activities, as well as in countries where we do not have patent rights and then use the information learned from such activities to develop competitive drugs for sale in our major commercial markets;
- we may not develop additional proprietary technologies that are patentable; and the patents of others may have an adverse effect on our business.

Should any of these events occur, they could have a material adverse effect on our business, financial condition, results of operations and prospects.

We may become involved in lawsuits to protect or enforce our patents or other intellectual property rights, which could be expensive, time consuming and unsuccessful.

Competitors may infringe our issued patents, future trademarks, copyrights or other intellectual property. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming and divert the time and attention of our management and scientific personnel. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents, trademarks, copyrights or other intellectual property. In addition, in a patent infringement proceeding, there is a risk that a court will decide that a patent of ours is invalid or unenforceable, in whole or in part, and that we do not have the right to stop the other party from using the invention at issue. There is also a risk that, even if the validity of such patents is upheld, the court will construe the patent's claims narrowly or decide that we do not have the right to stop the other party from using the invention at issue on the grounds that our patents do not cover the invention. An adverse outcome in a litigation or proceeding involving our patents could limit our ability to assert our patents against those parties or other competitors, and may curtail or preclude our ability to exclude third parties from making and selling similar or competitive products. Similarly, if we assert trademark infringement claims, a court may determine that the marks we have asserted are invalid or unenforceable, or that the party against whom we have asserted trademark infringement has superior rights to the marks in question. In this case, we could ultimately be forced to cease use of such trademarks.

In any infringement litigation, any award of monetary damages we receive may not be commercially valuable. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during litigation. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common shares. Moreover, there can be no assurance that we will have sufficient financial or other resources to file and pursue such infringement claims, which typically last for years before they are concluded. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Even if we ultimately prevail in such claims, the monetary cost of such litigation and the diversion of the attention of our management and scientific personnel could outweigh any benefit we receive as a result of the proceedings. Accordingly, despite our efforts, we may not be able to prevent third parties from infringing, misappropriating or successfully challenging our intellectual property rights. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a negative impact on our ability to compete in the marketplace.

Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain and could have a negative impact on the success of our business.

Our commercial success depends, in part, upon our ability and the ability of future collaborators, if any, to develop, manufacture, market and sell etripamil and any future product candidates and use our proprietary technologies without infringing the proprietary rights and intellectual property of third parties. The biotechnology and pharmaceutical industries are characterized by extensive and complex litigation regarding patents and other intellectual property rights. We may in the future become party to, or be threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to etripamil and any future product candidates and technology, including interference proceedings, post grant review and inter partes review before the USPTO. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future, regardless of their merit. There is a risk that third parties may choose to engage in litigation with us to enforce or to otherwise assert their patent rights against us. Even if we believe such claims are without merit, a court of competent jurisdiction could hold that these third-party patents are valid, enforceable and infringed, which could have a negative impact on our ability to commercialize our current and any future product candidates. In order to successfully challenge the validity of any such U.S. patent in federal court, we would need to overcome a presumption of validity. As this burden is a high one requiring us to present clear and convincing evidence as to the invalidity of any such U.S. patent claim, there is no assurance that a court of competent jurisdiction would invalidate the claims of any such U.S. patent. If we are found to infringe a third party's valid and enforceable intellectual property rights, we could be required to obtain a license from such third party to continue developing, manufacturing and marketing our product candidate(s) and technology. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors and other third parties access to the same technologies licensed to us, and it could require us to make substantial licensing and royalty payments. We could be forced, including by court order, to cease developing,

manufacturing and commercializing the infringing technology or product candidate. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees, if we are found to have willfully infringed a patent or other intellectual property right. A finding of infringement could prevent us from manufacturing and commercializing etripamil or any future product candidates or force us to cease some or all of our business operations, which could materially harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business, financial condition, results of operations and prospects. See the section herein titled "Legal Proceedings" for additional information.

We may need to license intellectual property from third parties, and such licenses may not be available or may not be available on commercially reasonable terms.

A third party may hold intellectual property rights, including patent rights, that are important or necessary to the development of etripamil or any future product candidates. It may be necessary for us to use the patented or proprietary technology of third parties to commercialize our product candidates, in which case we would be required to obtain a license from these third parties. Such a license may not be available on commercially reasonable terms, or at all, and we could be forced to accept unfavorable contractual terms. If we are unable to obtain such licenses on commercially reasonable terms, our business could be harmed.

We may be subject to claims asserting that our employees, consultants or advisors have wrongfully used or disclosed alleged trade secrets of their current or former employers or claims asserting ownership of what we regard as our own intellectual property.

Many of our employees, consultants or advisors are currently, or were previously, employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees, consultants and advisors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that these individuals or we have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such individual's current or former employer. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

In addition, we may in the future be subject to claims by our former employees or consultants asserting an ownership right in our patents or patent applications, as a result of the work they performed on our behalf. Although it is our policy to require our employees and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own, and we cannot be certain that our agreements with such parties will be upheld in the face of a potential challenge or that they will not be breached, for which we may not have an adequate remedy. The assignment of intellectual property rights may not be self-executing or the assignment agreements may be breached, and we may be forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property.

Changes in U.S. patent law or the patent law of other countries or jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect etripamil and any future product candidates.

The United States has recently enacted and implemented wide ranging patent reform legislation. The U.S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on actions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could weaken our ability to obtain new patents or to enforce patents that we have licensed or that we might obtain in the future. Similarly, changes in patent law and regulations in other countries or jurisdictions, changes in the governmental bodies that enforce them or changes in how the relevant governmental authority enforces patent laws or regulations may weaken our ability to obtain new patents or to enforce patents that we have licensed or that we may obtain in the future.

We may not be able to protect our intellectual property rights throughout the world, which could negatively impact our business.

Filing, prosecuting and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States could be less extensive than those in the United States. In some cases, we may not be able to obtain patent protection for certain technology outside the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States, even in jurisdictions where we do pursue patent protection. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, even in jurisdictions where we do pursue patent protection or from selling or importing products made using our inventions in and into the United States or other jurisdictions.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents and other intellectual property protection, which could make it difficult for us to stop the infringement of our patents, if pursued and obtained, or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Reliance on third parties requires us to share our proprietary information, which increases the possibility that such information will be misappropriated or disclosed.

Because we rely on third parties to develop and manufacture etripamil and any future product candidates, or if we collaborate with third parties for the development or commercialization of etripamil or any future product candidates, we must, at times, share proprietary information with them. We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, material transfer agreements, consulting agreements or other similar agreements with our advisors, employees, third-party contractors and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information. Despite the contractual provisions employed when working with third parties, the need to share confidential information increases the risk that such information become known by our competitors, is inadvertently incorporated into the technology of others, or is disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how, a competitor’s discovery of our know-how or other unauthorized use or disclosure could have an adverse effect on our business and results of operations.

In addition, these agreements typically restrict the ability of our advisors, employees, third-party contractors and consultants to publish data potentially relating to our know-how. Despite our efforts to protect our know-how, we may not be able to prevent the unauthorized disclosure or use of our technical know-how by the parties to these agreements. Moreover, we cannot guarantee that we have entered into such agreements with each party that may have or have had access to our confidential information or proprietary technology and processes. Monitoring unauthorized uses and disclosures is difficult, and we do not know whether the steps we have taken to protect our proprietary technologies will be effective. If any of the collaborators, scientific advisors, employees, contractors and consultants who are parties to these agreements breaches or violates the terms of any of these agreements, we may not have adequate remedies for any such breach or violation. Moreover, if confidential information that is licensed or disclosed to us by our partners, collaborators, or others is inadvertently disclosed or subject to a breach or violation, we may be exposed to liability to the owner of that confidential information. Enforcing a claim that a third-party illegally obtained and is using our proprietary information, like patent litigation, is expensive and time consuming, and the outcome is unpredictable. In addition, courts outside the United States are sometimes less willing to protect proprietary information.

Any trademarks we may obtain may be infringed or successfully challenged, resulting in harm to our business.

We expect to rely on trademarks as one means to distinguish any of our product candidates that are approved for marketing from the products of our competitors. We have not yet selected trademarks for etripamil and have not yet begun the process of applying to register trademarks for etripamil or any other product candidate. Once we select trademarks and apply to register them, our trademark applications may not be approved. Third parties may oppose our trademark applications or otherwise challenge our use of the trademarks. In the event that our trademarks are successfully challenged, we could be forced to rebrand our products, which could result in loss of brand recognition and could require us to devote resources to advertising and marketing new brands. Our competitors may infringe our trademarks, and we may not have adequate resources to enforce our trademarks.

In addition, any proprietary name we propose to use with etripamil or any future product candidate in the United States must be approved by the FDA, regardless of whether we have registered it, or applied to register it, as a trademark. The FDA typically conducts a review of proposed product names, including an evaluation of the potential for confusion with other product names. If the FDA objects to any of our proposed proprietary product names, we may be required to expend significant additional resources in an effort to identify a suitable proprietary product name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA.

If we are unable to protect the confidentiality of our proprietary information, our business and competitive position would be harmed.

In addition to seeking patent and trademark protection for etripamil and any future product candidate, we also rely on unpatented know-how, technology and other proprietary information, to maintain our competitive position. We seek to protect our proprietary information, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. Despite

these efforts, any of these parties may breach the agreements and disclose our proprietary information. Monitoring unauthorized uses and disclosures of our intellectual property is difficult, and we do not know whether the steps we have taken to protect our intellectual property will be effective. In addition, we may not be able to obtain adequate remedies for any such breaches. Enforcing a claim that a party illegally disclosed or misappropriated proprietary information is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets.

Moreover, our competitors may independently develop knowledge, methods and know-how equivalent to our proprietary information. Competitors could purchase our products and replicate some or all of the competitive advantages we derive from our development efforts for technologies on which we do not have patent protection. If any of our proprietary information were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. If any of our proprietary information were to be disclosed to or independently developed by a competitor, our competitive position would be harmed.

We also seek to preserve the integrity and confidentiality of our data and other confidential information by maintaining physical security of our premises and physical and electronic security of our information technology systems. While we have confidence in these individuals, organizations and systems, agreements or security measures may be breached and detecting the disclosure or misappropriation of confidential information and enforcing a claim that a party illegally disclosed or misappropriated confidential information is difficult, expensive and time-consuming, and the outcome is unpredictable. Further, we may not be able to obtain adequate remedies for any breach. In addition, our confidential information may otherwise become known or be independently discovered by competitors, in which case we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us.

Risks Related to Our Business Operations, Employee Matters and Managing Growth

Our future success depends on our ability to retain key executives and to attract, retain and motivate qualified personnel.

We are highly dependent on our President and Chief Executive Officer, Joseph Oliveto, our founder and Chief Scientific Officer, Philippe Douville, our Chief Medical Officer, Francis Plat and our Chief Commercial Officer, Lorenz Muller. Each of them may currently terminate their employment with us at any time. The loss of the services of any of these persons could impede the achievement of our research, development and commercialization objectives. We do not currently maintain “key person” life insurance on the lives of our executives or any of our employees other than on our President and Chief Executive Officer, Joseph Oliveto.

Recruiting and retaining qualified scientific and clinical personnel and, if we progress the development of any of our product candidates, commercialization, manufacturing and sales and marketing personnel, will be critical to our success. The loss of the services of our executive officers or other key employees could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize our product candidates. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to continue to attract and retain high-quality personnel, our ability to pursue our growth strategy will be limited.

We expect to expand our organization, and we may experience difficulties in managing this growth, which could disrupt our operations.

As of June 30, 2019, we had 23 full-time employees. As the clinical development of etripamil progresses and as we expand our pipeline, we expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of research, drug development, regulatory affairs and, if etripamil or any future product candidates receives marketing approval, sales, marketing and distribution. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

Our internal computer systems, or those of our collaborators or other contractors or consultants, may fail or suffer security breaches, which could result in a significant disruption of our product development programs and our ability to operate our business effectively.

Our internal computer systems and those of our current and any future collaborators and other contractors or consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. Cyber attacks are increasing in their frequency, sophistication and intensity, and have become increasingly difficult to detect. Cyber attacks could include the deployment of harmful malware, ransomware, denial-of-service attacks, social engineering and other means to affect service reliability and threaten the confidentiality, integrity and availability of information. Cyber attacks also could include phishing attempts or e-mail fraud to cause payments or information to be transmitted to an unintended recipient.

While we have not experienced any significant system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a disruption of our development programs and our business operations, whether due to a loss of our trade secrets or other proprietary information or other similar disruptions. For example, the loss of clinical trial data from completed or future clinical trials by us or our CROs could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Additionally, any such event that leads to unauthorized access, use or disclosure of personal information, including personal information regarding our patients or employees, could harm our reputation, cause us not to comply with federal and/or state breach notification laws and foreign law equivalents and otherwise subject us to liability under laws and regulations that protect the privacy and security of personal information. Security breaches and other inappropriate access can be difficult to detect, and any delay in identifying them may lead to increased harm of the type described above. While we have implemented security measures to protect our information technology systems and infrastructure, such measures may not prevent service interruptions or security breaches that could adversely affect our business and to the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability, our competitive position could be harmed and the further development and commercialization of our product candidates could be delayed.

If we fail to comply with European data protection laws, including the new European Union General Data Protection Regulation 2016/679, or GDPR, when appropriate, and any other existing or future data protection regulations, our business, financial condition, results of operations and prospects may be materially adversely affected.

We anticipate seeking regulatory approval for, and commercialize, etripamil for the treatment of PSVT in Europe. We may also elect to do so for future product candidates. We intend to conduct clinical trial activities in Europe, which will subject us to European data protection laws, including GDPR. The GDPR, which came into effect on May 25, 2018, establishes new requirements applicable to the processing of personal data (i.e., data which identifies an individual or from which an individual is identifiable), affords new data protection rights to individuals (e.g., the right to erasure of personal data) and imposes penalties for serious breaches of up to 4% annual worldwide turnover or €20 million, whichever is greater. Individuals (e.g., study subjects) also have a right to compensation for financial or non-financial losses (e.g., distress). There may be circumstances under which a failure to comply with GDPR, or the exercise of individual rights under the GDPR, would limit our ability to utilize clinical trial data collected on certain subjects. The GDPR will likely impose additional responsibility and liability in relation to our processing of personal data. This may be onerous and materially adversely affect our business, financial condition, results of operations and prospects.

Our employees, principal investigators, consultants and commercial partners may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements and insider trading.

We are exposed to the risk of fraud or other misconduct by our employees, principal investigators, consultants and commercial partners. Misconduct by these parties could include intentional failures to comply with FDA regulations or the regulations applicable in other jurisdictions, provide accurate information to the FDA and other regulatory authorities, comply with healthcare fraud and abuse laws and regulations in the United States and abroad, report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Such misconduct also could involve the improper use of information obtained in the course of clinical trials or interactions with the FDA or other regulatory authorities, which could result in regulatory sanctions and cause serious harm to our reputation. It is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from government investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us and we are not successful in defending ourselves or asserting our rights, those actions could result in significant civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from participating in government funded healthcare programs, such as Medicare and Medicaid, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, contractual damages, reputational harm and

the curtailment or restructuring of our operations, any of which could have a negative impact on our business, financial condition, results of operations and prospects.

If we engage in future acquisitions or strategic collaborations, this may increase our capital requirements, dilute our shareholders, cause us to incur debt or assume contingent liabilities and subject us to other risks.

From time to time, we may evaluate various acquisitions and strategic collaborations, including licensing or acquiring complementary drugs, intellectual property rights, technologies or businesses, as deemed appropriate to carry out our business plan. Any potential acquisition or strategic partnership may entail numerous risks, including:

- increased operating expenses and cash requirements;
- the assumption of additional indebtedness or contingent liabilities;
- assimilation of operations, intellectual property and drugs of an acquired company, including difficulties associated with integrating new personnel;
- the diversion of our management's attention from our existing drug programs and initiatives in pursuing such a strategic partnership, merger or acquisition;
- retention of key employees, the loss of key personnel, and uncertainties in our ability to maintain key business relationships;
- risks and uncertainties associated with the other party to such a transaction, including the prospects of that party and their existing drugs or product candidates and regulatory approvals; and
- our inability to generate revenue from acquired technology and/or drugs sufficient to meet our objectives in undertaking the acquisition or even to offset the associated acquisition and maintenance costs.

In addition, if we engage in future acquisitions or strategic partnerships, we may issue dilutive securities, assume or incur debt obligations, incur large one-time expenses and acquire intangible assets that could result in significant future amortization expense. Moreover, we may not be able to locate suitable acquisition opportunities, and this inability could impair our ability to grow or obtain access to technology or drugs that may be important to the development of our business.

Risks Related to Ownership of Our Common Shares

The market price of our common shares may be volatile and fluctuate substantially, and you could lose all or part of your investment.

The market price of our common shares is likely to be volatile. The stock market in general and the market for biopharmaceutical and pharmaceutical companies in particular, has experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, you may not be able to sell your common shares at or above the price paid for the shares. In addition to the factors discussed in this "Risk Factors" section, the market price for our common shares may be influenced by the following:

- the commencement, enrollment or results of our planned or future clinical trials of etripamil and any future product candidates or those of our competitors;
- the success of competitive drugs or therapies;
- regulatory or legal developments in the United States and other countries;
- the success of competitive products or technologies;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to etripamil and any future product candidates or clinical development programs;
- the results of our efforts to discover, develop, acquire or in-license additional product candidates;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- our inability to obtain or delays in obtaining adequate drug supply for any approved drug or inability to do so at acceptable prices;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- significant lawsuits, including patent or shareholder litigation;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in the structure of healthcare payment systems, including coverage and adequate reimbursement for any approved drug;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, political, and market conditions and overall fluctuations in the financial markets in the United States and abroad; and
- investors' general perception of us and our business.

These and other market and industry factors may cause the market price and demand for our common shares to fluctuate substantially, regardless of our actual operating performance, which may limit or prevent investors from selling their shares at or above the price paid for the shares and may otherwise negatively affect the liquidity of our common shares. In addition, the stock market in general, and biopharmaceutical companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies.

Some companies that have experienced volatility in the trading price of their shares have been the subject of securities class action litigation. Any lawsuit to which we are a party, with or without merit, may result in an unfavorable judgment. We also may decide to settle lawsuits on unfavorable terms. Any such negative outcome could result in payments of substantial damages or fines, damage to our reputation or adverse changes to our business practices. Defending against litigation is costly and time-consuming, and could divert our management's attention and our resources. Furthermore, during the course of litigation, there could be negative public announcements of the results of hearings, motions or other interim proceedings or developments, which could have a negative effect on the market price of our common shares.

A public market may not develop or be liquid enough for you to sell your shares quickly or at market price.

Prior to our IPO in May 2019, there had not been a public market for our common shares. If an active trading market for our common shares does not develop, you may not be able to sell your shares quickly or at the market price. An inactive market may also impair our ability to raise capital to continue to fund operations by selling our common shares and may impair our ability to acquire other companies or technologies by using our common shares as consideration.

Concentration of ownership of our common shares among our existing executive officers, directors and principal shareholders may prevent new investors from influencing significant corporate decisions.

Based upon our common shares outstanding as of August 8, 2019, our executive officers, directors and shareholders who owned more than 5% of our outstanding common shares will, in the aggregate, beneficially own shares representing 73% of our outstanding common shares. If our executive officers, directors and shareholders who owned more than 5% of our outstanding common shares acted together, they may be able to significantly influence all matters requiring shareholder approval, including the election and removal of directors and approval of any merger, consolidation or sale of all or substantially all of our assets. The concentration of voting power and transfer restrictions could delay or prevent an acquisition of our company on terms that other shareholders may desire or result in the management of our company in ways with which other shareholders disagree.

If research analysts do not publish research or reports, or publish unfavorable research or reports, about us, our business or our market, our share price and trading volume could decline.

The trading market for our common shares will be influenced by the research and reports that industry or financial analysts publish about us or our business. Equity research analysts may discontinue research coverage of our common shares, and such lack of research coverage may adversely affect the market price of our common shares. We do not have any control over the analysts or the content and opinions included in their reports. The price of our shares could decline if one or more equity research analysts downgrade our shares or issue other unfavorable commentary or research about us. If one or more equity research analysts ceases coverage of us or fails to publish reports on us regularly, demand for our shares could decrease, which in turn could cause the trading price or trading volume of our common shares to decline.

Because we do not anticipate paying any cash dividends on our share capital in the foreseeable future, capital appreciation, if any, will be your sole source of gain.

You should not rely on an investment in our common shares to provide dividend income. We have never declared or paid cash dividends on our share capital. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. In addition, the terms of any future debt agreements or preferred equity may preclude us from paying dividends. As a result, capital appreciation, if any, of our common shares will be your sole source of gain for the foreseeable future.

We have broad discretion in the use of our cash, cash equivalents and short-term investments, and may use them in ways in which you do not agree or in ways that do not increase the value of your investment.

Our management will have broad discretion in the application of our cash, cash equivalents and short-term investments, and could spend the proceeds in ways that do not improve our results of operations or enhance the value of our common shares. The failure by our management to apply these funds effectively could result in financial losses that could have a negative impact on our business, cause the price of our common shares to decline and delay the development of our product candidates. Pending their use, we may invest our cash, cash equivalents and short-term investments, in a manner that does not produce income or that loses value.

A significant portion of our total outstanding shares are restricted from immediate resale but may be sold into the market in the near future, which could cause the market price of our common shares to drop significantly, even if our business is performing well.

Sales of a substantial number of our common shares in the public market could occur at any time, subject to certain restrictions described below. These sales, or the perception in the market that holders of a large number of shares intend to sell shares, could reduce the market price of our common shares. We have outstanding 24,490,742 common shares as of August 8, 2019. This includes the shares that we sold in the IPO, which may be resold in the public market immediately without restriction, unless purchased by our affiliates. The remaining shares are currently restricted as a result of securities laws or lock-up agreements. Moreover, holders of an aggregate of 17,632,003 common shares will have rights, subject to some conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other shareholders. We intend to register all common shares that we may issue under our equity compensation plans. Once we register these shares, they can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates and the lock-up agreements.

If we are a passive foreign investment company, there could be adverse U.S. federal income tax consequences to U.S. Holders.

Based on our analysis of our income, assets, activities and market capitalization for our taxable year ending December 31, 2018, we believe that we may be classified as a passive foreign investment company, or PFIC, for our taxable year ending December 31, 2018. Based on the expected nature and composition of our income and assets for our taxable year ending December 31, 2019, we anticipate that we may be classified as a PFIC for our taxable year ending December 31, 2019. If we are a PFIC for our taxable year ending December 31, 2019, or any subsequent taxable years, we intend to annually furnish U.S. Holders, upon request, a "PFIC Annual Information Statement," with the information required to allow U.S. Holders to make a "qualified electing fund" election, or "QEF Election" for United States federal income tax purposes. No assurances regarding our PFIC status can be provided for any past, current or future taxable years. The determination of whether we are a PFIC is a fact-intensive determination made on an annual basis and the applicable law is subject to varying interpretation. In particular, the characterization of our assets as active or passive may depend in part on our current and intended future business plans, which are subject to change. In addition, for our current and future taxable years, the total value of our assets for PFIC testing purposes may be determined in part by reference to the market price of our common shares from time to time, which may fluctuate considerably. Under the income test, our status as a PFIC depends on the composition of our income which will depend on the transactions we enter into in the future and our corporate structure. The composition of our income and assets is also affected by how, and how quickly, we spend the cash we raise in any offering.

If we are a PFIC, U.S. Holders of our common shares will be subject to adverse U.S. federal income tax consequences, such as ineligibility for any preferential tax rates for individuals on capital gains or on actual or deemed dividends, interest charges on certain taxes treated as deferred, and additional reporting requirements under U.S. federal income tax laws and regulations.

If a United States person is treated as owning at least 10% of our common shares, such holder may be subject to adverse U.S. federal income tax consequences.

If a U.S. Holder is treated as owning (directly, indirectly or constructively) at least 10% of the value or voting power of our common shares, such U.S. Holder may be treated as a "United States shareholder" with respect to each "controlled foreign corporation" in our group (if any). Because our group includes at least one U.S. subsidiary (Milestone Pharmaceuticals USA Inc.), if we were to form or acquire any non-U.S. subsidiaries in the future, they may be treated as controlled foreign corporations. A United States shareholder of a controlled foreign corporation may be required to annually report and include in its U.S. taxable income its pro rata share of "Subpart F income," "global intangible low-taxed income" and investments in U.S. property by that controlled foreign corporation, regardless of whether that controlled foreign corporation, or we, make any distributions. An individual that is a United States shareholder with respect to a controlled foreign corporation generally would not be allowed certain tax deductions or foreign tax credits that would be allowed to a United States shareholder that is a U.S. corporation. We cannot provide any assurances that we will assist investors in determining whether any non-U.S. subsidiaries that we may form or acquire in the future will be treated as controlled foreign corporations or whether any such investor would be treated as a United States shareholder with respect to any of such controlled foreign corporations. Further, we cannot provide any assurances that we will furnish to any investor information that may be necessary to comply with the reporting and tax paying obligations discussed above. Failure to comply with these reporting obligations may subject a U.S. Holder to significant monetary penalties and may extend the statute of limitations with respect to its U.S. federal income tax return for the year for which reporting was due. U.S. Holders should consult their tax advisors regarding the potential application of these rules to their investment in our common shares.

Future changes to tax laws could materially adversely affect our company and reduce net returns to our shareholders.

Our tax treatment is subject to the enactment of, or changes in, tax laws, regulations and treaties, or the interpretation thereof, tax policy initiatives and reforms under consideration and the practices of tax authorities in jurisdictions in which we operate, including those related to the Organization for Economic Co-Operation and Development's, or OECD, Base Erosion and Profit Shifting, or BEPS, Project, the European Commission's state aid investigations and other initiatives. Such changes may include (but are not limited to) the taxation of operating income, investment income, dividends received or (in the specific context of withholding tax) dividends paid. We are unable to predict what tax reform may be proposed or enacted in the future or what effect such changes would have on our business, but such changes, to the extent they are brought into tax legislation, regulations, policies or practices, could affect our financial position and overall or effective tax rates in the future in countries where we have operations, reduce post-tax returns to our shareholders, and increase the complexity, burden and cost of tax compliance.

In addition, on December 22, 2017, the Tax Act was signed into law, which significantly revised the Internal Revenue Code of 1986, as amended. The overall impact of the Tax Act is uncertain and our business and financial condition could be adversely affected by it or as a result of interpretations thereof. In addition, it is uncertain if and to what extent various states will conform to the Tax Act. The impact of this tax reform on holders of our common shares is also uncertain and could be adverse. We urge you to consult with your legal and tax advisors with respect to this legislation and the potential tax consequences of investing in or holding our common shares.

Tax authorities may disagree with our positions and conclusions regarding certain tax positions, resulting in unanticipated costs, taxes or non-realization of expected benefits.

A tax authority may disagree with tax positions that we have taken, which could result in increased tax liabilities. For example, the Canadian Revenue Agency, the U.S. Internal Revenue Service or another tax authority could challenge our allocation of income by tax jurisdiction and the amounts paid between our affiliated companies pursuant to our intercompany arrangements and transfer pricing policies, including amounts paid with respect to our intellectual property development. Similarly, a tax authority could assert that we are subject to tax in a jurisdiction where we believe we have not established a taxable connection, often referred to as a "permanent establishment" under international tax treaties, and such an assertion, if successful, could increase our expected tax liability in one or more jurisdictions. A tax authority may take the position that material income tax liabilities, interest and penalties are payable by us, in which case, we expect that we might contest such assessment. Contesting such an assessment may be lengthy and costly and if we were unsuccessful in disputing the assessment, the result could increase our anticipated effective tax rate.

We are an "emerging growth company," and the reduced disclosure requirements applicable to emerging growth companies may make our common shares less attractive to investors.

We are an "emerging growth company," or EGC, as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, and we intend to take advantage of some of the exemptions from reporting requirements that are applicable to other public companies that are not emerging growth companies, including:

- not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting;
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;
- reduced disclosure obligations regarding executive compensation; and
- not being required to hold a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved.

We currently take advantage of some or all of these reporting exemptions and may continue to until we are no longer an EGC. We will remain an EGC until the earlier of (i) December 31, 2024, (ii) the last day of the fiscal year in which we have total annual gross revenue of at least $1.07 billion, (iii) the last day of the first fiscal year in which we are deemed to be a large accelerated filer, which means the market value of our common shares that is held by non-affiliates exceeds $700 million as of the prior June 30th, and (iv) the date on which we have issued more than $1.0 billion in non-convertible debt during the prior three-year period. We cannot predict whether investors will find our common shares less attractive because we will rely on these exemptions. If some investors find our common shares less attractive as a result, there may be a less active trading market for our common shares and our share price may be more volatile.

In addition, under Section 107(b) of the JOBS Act, EGCs can delay adopting new or revised accounting standards until such time as those standards apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards and, therefore, we will be subject to the same new or revised accounting standards as other public companies that are not EGCs.

We will incur increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives.

As a public company, and particularly after we are no longer an EGC, we will incur significant legal, accounting and other expenses that we did not incur as a private company. In addition, the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, and rules subsequently implemented by the SEC and The Nasdaq Stock Market LLC have imposed various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, we expect that these rules and regulations may make it more difficult and more expensive for us to obtain director and officer liability insurance.

Pursuant to Section 404 of the Sarbanes-Oxley Act, or Section 404, we will be required to furnish a report by our management on our internal control over financial reporting, including an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. However, while we remain an EGC, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that neither we nor our independent registered public accounting firm will be able to conclude within the prescribed timeframe that our internal control over financial reporting is effective as required by Section 404. This could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our consolidated financial statements.

Because we are a Canadian company, it may be difficult to serve legal process or enforce judgments against us.

We are a domestic filer in the United States; however, we are incorporated and have our corporate headquarters in Canada. In addition, while many of our directors and officers reside in the United States, several of them reside outside of the United States. Accordingly, service of process upon us may be difficult to obtain within the United States. Furthermore, because substantially all of our assets are located outside the United States, any judgment obtained in the United States against us, including one predicated on the civil liability provisions of the U.S. federal securities laws, may not be collectible within the United States. Therefore, it may not be possible to enforce those actions against us.

In addition, it may be difficult to assert U.S. securities law claims in original actions instituted in Canada. Canadian courts may refuse to hear a claim based on an alleged violation of U.S. securities laws against us or these persons on the grounds that Canada is not the most appropriate forum in which to bring such a claim. Even if a Canadian court agrees to hear a claim, it may determine that Canadian law and not

U.S. law is applicable to the claim. If U.S. law is found to be applicable, the content of applicable U.S. law must be proved as a fact, which can be a time-consuming and costly process. Certain matters of procedure will also be governed by Canadian law. Furthermore, it may not be possible to subject foreign persons or entities to the jurisdiction of the courts in Canada. Similarly, to the extent that our assets are located in Canada, investors may have difficulty collecting from us any judgments obtained in the U.S. courts and predicated on the civil liability provisions of U.S. securities provisions.

We are governed by the corporate laws of Quebec, which in some cases have a different effect on shareholders than the corporate laws of Delaware.

We are governed by the Business Corporations Act (Quebec), or the BCA, and other relevant laws, which may affect the rights of shareholders differently than those of a company governed by the laws of a U.S. jurisdiction, and may, together with our charter documents, have the effect of delaying, deferring or discouraging another party from acquiring control of us by means of a tender offer, a proxy contest or otherwise, or may affect the price an acquiring party would be willing to offer in such an instance. The material differences between the BCA and Delaware General Corporation Law, or the DGCL, that may have the greatest such effect include but are not limited to the following: (i) for material corporate transactions (such as mergers and amalgamations, other extraordinary corporate transactions or amendments to our articles), the BCA generally requires a two-thirds majority vote by shareholders, whereas the DGCL generally only requires a majority vote; and (ii) under the BCA, a holder of 5% or more of our common shares can requisition a special meeting of shareholders, whereas such right does not exist under the DGCL.

Our amended and restated bylaws and certain Canadian legislation contain provisions that may have the effect of delaying or preventing certain change in control transactions or shareholder proposals.

Certain provisions of our amended and restated bylaws and certain Canadian legislation, together or separately, could discourage or delay certain change in control transactions or shareholder proposals.

Our amended and restated bylaws contain provisions that establish certain advance notice procedures for nomination of candidates for election as directors at shareholders' meetings. The BCA requires that any shareholder proposal that includes nominations for the election of directors must be signed by one or more holders of shares representing in the aggregate not less than 5% of the shares or 5% of the shares of a class or series of shares of the corporation entitled to vote at the meeting to which the proposal is to be presented.

The *Investment Canada Act* requires that a non-Canadian must file an application for review with the Minister responsible for the *Investment Canada Act* and obtain approval of the Minister prior to acquiring control of a "Canadian business" within the meaning of the *Investment Canada Act*, where prescribed financial thresholds are exceeded. Furthermore, limitations on the ability to acquire and hold our common shares may be imposed by the *Competition Act* (Canada). This legislation permits the Commissioner of Competition, or Commissioner, to review any acquisition or establishment, directly or indirectly, including through the acquisition of shares, of

control over or of a significant interest in our company. Otherwise, there are no limitations either under the laws of Canada or Quebec, or in our articles on the rights of´ non-Canadians to hold or vote our common shares.

Any of these provisions may discourage a potential acquirer from proposing or completing a transaction that may have otherwise presented a premium to our shareholders.

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

Recent Sales of Unregistered Equity Securities

During the six months ended June 30, 2019, we granted to our employee's stock options to purchase an aggregate of 163,740 common shares at a weighted average exercise price of $11.02 per share pursuant to our Stock Option Plan, as amended and restated.

The offers, sales and issuances of the securities described in this section were exempt from registration either under Rule 701 promulgated under the Securities Act of 1933, as amended, or the Securities Act, in that the transactions were underwritten compensatory benefit plans and contracts relating to compensation. Appropriate legends were affixed to the securities issued in these transactions.

Use of Proceeds from the IPO

On May 13, 2019, we completed our IPO and issued 6,325,000 common shares at an initial offering price of $15.00 per share (inclusive of 825,000 common shares pursuant to the full exercise of an overallotment option granted to the underwriters in connection with the offering). We received net proceeds from the IPO of $85.4 million, after deducting underwriting discounts and commissions of $6.6 million, and estimated expenses of $2.9 million. None of the expenses associated with the IPO were paid to directors, officers, persons owning 10% or more of any class of equity securities, or to their associates. Jefferies LLC, Cowen and Company, LLC and Piper Jaffray & Co. acted as lead book-running managers. Oppenheimer & Co. Inc. acted as lead manager for the IPO.

Our common shares began trading on The Nasdaq Global Select Market on May 9, 2019. The offer and sale of the shares were registered under the Securities Act on Registration Statement on Form S-1 (Registration No. 333-230846), which was declared effective on May 8, 2019.

There has been no material change in the planned use of proceeds from our IPO as described in our Prospectus. We invested the funds received in cash equivalents and other short-term securities in accordance with our investment policy. We have not used any of the proceeds from the IPO.

Item 3. Defaults Upon Senior Securities.

Not applicable

Item 4. Mine Safety Disclosures.

Not applicable

Item 5. Other Information.

None.

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).
4.1	Form of Common Share Certificate of the Company (incorporated herein by reference to Exhibit 4.1 to the Company's Registration Statement on Form S-1/A (File No. 333-230846), filed with the SEC on April 29, 2019).
4.2	Third Amended and Restated Registration Rights Agreement, by and among the Company and certain of its shareholders, dated October 15, 2018 (incorporated herein by reference to Exhibit 4.2 to the Company's Registration Statement on Form S-1/A (File No. 333-230846), filed with the SEC on April 29, 2019).
10.1+	2019 Equity Incentive Plan (incorporated herein by reference to Exhibit 4.8 to the Company's Registration on Form S-8 (File No. 333-231347), filed with the SEC on May 9, 2019).
10.2+	Form of U.S. Stock Option Grant Notice and Stock Option Agreement under the 2019 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.4 to the Company's Registration Statement on Form S-1/A (File No. 333-230846), filed with the SEC on April 29, 2019).
10.3+	Form of U.S. Restricted Stock Unit Grant Notice and Restricted Stock Unit Award Agreement under the 2019 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.5 to the Company's Registration Statement on Form S-1/A (File No. 333-230846), filed with the SEC on April 29, 2019).
10.4+	Form of Canadian Stock Option Grant Notice and Option Agreement under the 2019 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.6 to the Company's Registration Statement on Form S-1/A (File No. 333-230846), filed with the SEC on April 29, 2019).
10.5+	Form of Canadian Restricted Stock Unit Grant Notice and Restricted Stock Unit Award Agreement under the 2019 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.7 to the Company's Registration Statement on Form S-1/A (File No. 333-230846), filed with the SEC on April 29, 2019).
10.6+	2019 Employee Share Purchase Plan (incorporated herein by reference to Exhibit 4.13 to the Company's Registration Statement on Form S-8 (File No. 333-231347), filed with the SEC on May 9, 2019).
10.7+	Amended and Restated Employment Agreement between Joseph Oliveto and Milestone Pharmaceuticals USA, Inc. (incorporated herein by reference to Exhibit 10.9 to the Company's Registration Statement on Form S-1/A (File No. 333-230846), filed with the SEC on April 29, 2019).
10.8+	Amended and Restated Employment Agreement between Philippe Douville and Milestone Pharmaceuticals Inc. (incorporated herein by reference to Exhibit 10.10 to the Company's Registration Statement on Form S-1/A (File No. 333-230846), filed with the SEC on April 29, 2019).
10.9+	Amended and Restated Employment Agreement between Francis Plat and Milestone Pharmaceuticals Inc. (incorporated herein by reference to Exhibit 10.11 to the Company's Registration Statement on Form S-1/A (File No. 333-230846), filed with the SEC on April 29, 2019).
10.10+	Amended and Restated Employment Agreement between Lorenz Muller and Milestone Pharmaceuticals USA, Inc. (incorporated herein by reference to Exhibit 10.12 to the Company's Registration Statement on Form S-1/A (File No. 333-230846), filed with the SEC on April 29, 2019).
10.11+	Employment Agreement between Timothy L. Maness and Milestone Pharmaceuticals USA, Inc. (incorporated herein by reference to Exhibit 10.13 to the Company's Registration Statement on Form S-1/A (File No. 333-230846), filed with the SEC on April 29, 2019).
10.12+	Form of Indemnity Agreement of the Company (incorporated herein by reference to Exhibit 10.14+ to the Company's Registration Statement on Form S-1/A (File No. 333-230846), filed with the SEC on April 29, 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	XBRL Instance Document
101.SCH	XBRL Taxonomy Extension Schema Document
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	XBRL Taxonomy Extension Label Linkbase Document
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document

* 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.

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 13, 2019

By: /s/ Joseph Oliveto

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

Date: August 13, 2019

By: /s/ Timothy L. Maness

Timothy L. Maness
Vice President, Finance
(Principal Financial and 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)) 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) 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

   (c) 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 13, 2019

/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, Timothy Maness, 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)) 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) 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

   (c) 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 13, 2019

/s/ Timothy Maness
Timothy Maness
Vice President, Finance
(Principal Financial and 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 Timothy Maness, Vice President, Finance 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, 2019, 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 13, 2019

/s/ Joseph Oliveto	/s/ Timothy Maness
Joseph Oliveto	Timothy Maness
Chief Executive Officer	Vice President, Finance
(Principal Executive Officer)	(Principal Financial and Accounting Officer)