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Registration No. 333-230846
Registration No. 333-231304

PROSPECTUS

5,500,000 Common Shares

We are offering 5,500,000 common shares. This is our initial public offering and no public market currently exists for our common shares. The initial public offering price is $15.00 per common share. Our common stock has been approved for listing on The Nasdaq Global Select Market under the symbol "MIST."

We are an "emerging growth company" under the federal securities laws and will be subject to reduced public company reporting requirements for this prospectus and future filings.

Investing in our common shares involves a high degree of risk. See "Risk Factors" beginning on page 11 of this prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

	PER SHARE	TOTAL
Public Offering Price	$ 15.00	$ 82,500,000
Underwriting Discount and Commissions[(1)]	$ 1.05	$ 5,775,000
Proceeds to Milestone Pharmaceuticals Inc. (before expenses)	$ 13.95	$ 76,725,000

(1) We refer you to "Underwriting" beginning on page 154 for additional information regarding underwriter compensation.

Delivery of the shares is expected to be made on or about May 13, 2019. We have granted certain of the underwriters an option for a period of 30 days to purchase up to 825,000 additional common shares. If these underwriters exercise the option in full, the total underwriting discounts and commissions payable by us will be $6,641,250, and the total proceeds to us, before expenses, will be $88,233,750.

Joint Book-Running Managers

Jefferies **Cowen** **Piper Jaffray**

Lead Manager

Oppenheimer & Co.

The date of this prospectus is May 8, 2019

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Neither we nor the underwriters have done anything that would permit this offering or possession or distribution of this prospectus or any free writing prospectus we may provide to you in connection with this offering in any jurisdiction where action for that purpose is required, other than in the United States. You are required to inform yourselves about and to observe any restrictions relating to this offering and the distribution of this prospectus and any such free writing prospectus outside of the United States.

This prospectus contains references to United States dollars and Canadian dollars. All dollar amounts referenced, unless otherwise indicated, are expressed in United States dollars. References to "$" are to United States dollars and references to "C$" are to Canadian dollars.

PROSPECTUS SUMMARY

This summary highlights information contained elsewhere in this prospectus. This summary is not complete and does not contain all of the information you should consider in making your investment decision. Before investing in our common shares, you should carefully read this entire prospectus, especially the sections titled "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our consolidated financial statements and the related notes included elsewhere in this prospectus. Unless the context otherwise requires, the terms "Milestone," "Milestone Pharmaceuticals," "the company," "we," "us," "our" and similar references in this prospectus refer to Milestone Pharmaceuticals Inc. and its consolidated subsidiary.

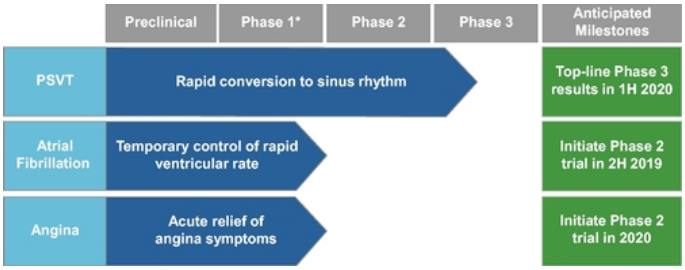
Overview

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. Investigators reported an 87% termination rate of PSVT within 15 minutes at the dose selected for Phase 3 versus a 35% termination rate for placebo. We are actively recruiting patients for a Phase 3 clinical trial of etripamil, which may serve as a single pivotal efficacy trial, and we expect top-line data in the first half of 2020. In addition to the efficacy trial, our Phase 3 clinical program for etripamil for PSVT includes two open-label safety studies, one of which we initiated in December 2018, and the other we expect to initiate in the second half of 2019. We are also planning to initiate a Phase 2 clinical trial in the second half of 2019 in atrial fibrillation, another rapid heart rate condition, and expect to subsequently initiate an additional Phase 2 clinical trial in angina to establish proof-of-concept for the broader use of etripamil in 2020.

Our Pipeline

The following table sets forth the status and initial focus of etripamil.



* We are relying on our Phase 1 clinical trial of etripamil to support further clinical development of etripamil in PSVT, atrial fibrillation and angina.

PSVT

PSVT is a serious and recurring disorder of the heart, which is caused by altered electrical conductivity, resulting in a rapid heart rate. PSVT originates in the heart's upper chambers, or atria, with abrupt onset and termination. There is an abnormal electrical pathway in patients with PSVT that allows the electrical signal to travel very rapidly in a circle, which sends impulses out to both the atria and the heart's lower chambers, or ventricles. The cycle continues repeatedly, resulting in the rapid heart rate, which often exceeds 200 beats per minute. Patients experiencing an episode of PSVT are usually highly symptomatic, with symptoms including palpitations, sweating, chest pressure or pain, shortness of breath, sudden onset of fatigue, lightheadedness or dizziness, fainting and anxiety.

Uncertainty of the timing and duration of episodes of PSVT can significantly impact patient quality of life. These episodes can be debilitating for patients who can be left unable to focus on family or work during an episode. The symptoms can mimic other conditions and are often mistaken for anxiety or panic attacks, especially in women, who represent approximately 60% of the PSVT patient population. Researchers have noted that up to 27% of PSVT patients stopped driving for fear of temporary loss of consciousness, fainting or passing out. Patients report that the duration of PSVT episodes varies widely from seconds to hours or more. Our market research indicates that in the year of diagnosis almost 40% of patients experience two or more episodes of PSVT per year that last more than 10 minutes each, and a similar percentage visit the emergency department at least once per year for treatment of their PSVT. We also estimate that 65% of PSVT patients have used chronic medications prophylactically to reduce episode frequency. Our market research also shows that after the first year of diagnosis the percentage of patients with PSVT episodes lasting longer than 10 minutes and the percentage visiting the emergency department for treatment decreases modestly to approximately one-third of those surveyed. Based upon our survey responses, we believe these decreases in both duration of episodes and emergency department visits are attributable to a combination of prophylactic medication use and proper implementation of vagal maneuvers. We estimate that PSVT patients experience a median of four to seven episodes of PSVT per year, approximately half suffer from other cardiovascular comorbidities, and approximately 60% are women. It is generally believed that patients are born with the anomaly that causes PSVT, and, following their first episode, will experience periodic and unpredictable episodes for the rest of their lives.

We believe that PSVT is a large and under-recognized market that we estimate affects approximately two million Americans, and results in over 600,000 healthcare claims in the United States per year, including emergency department visits, hospital admissions and ablations. Current treatment approaches for PSVT consume significant healthcare resources. An analysis of longitudinal Medicare and employer-based medical claims data from a recent peer-reviewed abstract that we sponsored has shown that mean annual costs per PSVT patient increase by more than $17,000 after diagnosis to approximately $30,000, with the largest increases coming from outpatient hospital and inpatient spending. In addition, this analysis concluded that rates of emergency department visits and hospitalizations were 1.8 and 3.0 times higher, respectively, following diagnosis. We believe that, if approved, etripamil could prevent many of these healthcare encounters, saving the patient time and inconvenience, and potentially providing a cost-effective solution for the healthcare system.

Limitations of Current PSVT Treatments

Currently available pharmacological therapy for the treatment of an acute episode of PSVT includes intravenous, or IV, administration of drugs in an acute care setting. The current standard of care for treatment of episodes of PSVT is adenosine, but prior to its approval in 1990, episodes of PSVT were treated with IV calcium channel blockers, such as verapamil or diltiazem. When given as a rapid IV bolus, adenosine blocks conduction over the atrio-ventricular, or AV, node, a piece of electrical tissue in the heart, thereby interrupting the arrhythmia and restoring the heart rate back to normal, also known as sinus rhythm. Adenosine temporarily stops the heart and patients have reported experiencing chest tightness, flushing and a sense of impending death. Physicians report that patients tell them that they feel like they are going to die. Adenosine is eliminated from the body in less than one minute, but cannot be self-administered as it requires IV access. IV calcium channel blockers also slow conduction over the AV node during the course of

several minutes. However, they are associated with the risk of excessive slowing of the heart rate and low blood pressure. In-hospital IV administrations are associated with higher health care costs, and are also unsettling and inconvenient for the patient.

In an attempt to prophylactically control the frequency and duration of future PSVT episodes, many patients will take chronic daily oral medications that modulate AV nodal conduction, such as beta blockers, calcium channel blockers or antiarrhythmic drugs. Despite chronic daily oral medication, breakthrough PSVT episodes that require visits to the emergency department may still occur, albeit at a reduced frequency. Chronic medication can lead to side effects such as sexual dysfunction or fatigue in the case of beta blockers and constipation in the case of verapamil. Some patients discontinue chronic oral medication due to intolerable side effects.

The only potentially curative treatment available at the present time for PSVT is ablation, an invasive procedure, which works by directly cauterizing the short circuit that is the cause of the abnormal rhythm. This is achieved via catheters that are run through the patient's groin vessels and into the heart and uses burning or freezing techniques to destroy the heart's abnormal electrical tissue. However, we estimate that less than 10% of patients with PSVT per year resort to this option.

Our Solution: Etripamil

We designed and are developing etripamil, a novel, potent, rapid-onset and short-acting calcium channel blocker, as a nasal spray to be administered by the patient to terminate episodes of transient cardiovascular conditions as they occur. Short pharmacological action is sufficient to resolve an episode of PSVT. Accordingly, long-lasting drugs that remain in the body at significant concentrations long after the episode is resolved subject patients to unnecessary risk, given the potential for prolonged adverse events. Currently, we are in Phase 3 clinical development for PSVT. We are also developing etripamil to provide rapid rate control and associated symptom relief for patients with acute episodes of atrial fibrillation and as an acute therapy for angina.

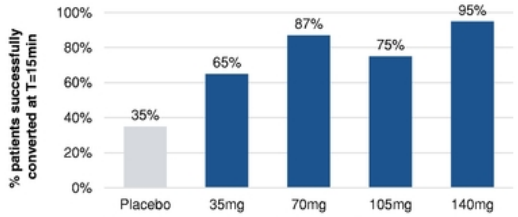
In our effort to develop potential therapies, we sought to create new chemical entities as analogs of known molecular classes with clinically-validated mechanisms of action. Our goal was to preserve the beneficial pharmacology of existing molecules while altering their pharmacokinetic profile with focused medicinal chemistry to produce drugs that are fast-acting and rapidly inactivated in the blood to minimize potential side effects. As a result, we created a series of novel non-dihydropyridine L-type calcium channel blockers with the desired properties. Etripamil resulted from this effort as a new chemical entity with a very short effective half-life of approximately 20 minutes in humans, compared with other calcium channel blockers, which have longer half-lives of several hours.

We believe that the following qualities of etripamil make it a better treatment for certain episodic cardiovascular conditions than current standards of care:

- *Short half-life:* As etripamil is a short-acting drug product, any adverse side effects that might occur should be short lived.
- *Fast onset:* Etripamil is designed to be rapidly absorbed into the bloodstream with a clinically meaningful concentration, allowing it to act quickly on the desired target (electrical conduction system or coronary blood vessels).
- *Convenient administration:* We developed etripamil as a convenient nasal spray that can be administered by patients to deliver a single dose of drug via a nasal spray device.

We completed a Phase 2 multi-center, randomized, double-blind, placebo-controlled clinical trial in the United States and Canada to evaluate the effects of four different doses of etripamil in 104 patients with PSVT. The primary objective of the trial was to demonstrate the superiority of at least one dose of etripamil over placebo in terminating PSVT. The secondary objectives included determining the Phase 3 dose of etripamil. The primary endpoint in this clinical trial was the conversion of PSVT to sinus rhythm within 15 minutes after administration of etripamil or placebo. As shown in the figure below, the percentage of patients in whom PSVT converted to sinus rhythm within 15 minutes of study drug administration was 65%

with 35 mg etripamil, 87% with 70 mg, 75% with 105 mg and 95% with 140 mg, compared with 35% in the placebo arm.



# patients converted at 15 min	7/20	13/20	20/23	15/20	20/21
p-value		0.1128	0.0006	0.0248	<.0001

Additional Pipeline Indications: Atrial Fibrillation and Angina

Atrial fibrillation is a common form of arrhythmia with an irregular and often rapid heart rate that can increase the risk of stroke, heart failure and other heart-related complications. There are currently two pharmacological approaches to managing atrial fibrillation: rate control to lower a rapid heart rate and rhythm control to restore and maintain the regular rhythm between heart beats. Oral rate control drugs do not provide immediate ventricular rate control due to the delayed 30 to 60 minute onset of action by the oral route. Breakthrough episodes of symptomatic atrial fibrillation often require urgent medical treatment with IV calcium channel blockers or beta blockers, usually in the emergency department to quickly reduce heart rate. We believe that etripamil can be used by patients to rapidly reduce their heart rate in the outpatient setting in combination with the oral rate or rhythm control strategy their physician has already prescribed.

Angina is a type of chest pain caused by an imbalance between the supply of oxygen to and the demand for oxygen by the heart. It may be due to a number of factors, but is primarily caused by either occlusion or spasm of the coronary arteries. Nitrates are prescribed to provide immediate relief of angina due to occlusion. Nitroglycerin is a common form of nitrate that is available primarily in sublingual formulations. In up to 20% of patients, nitroglycerin is not tolerated and additional patients do not respond to the treatment. It can also cause severe hypotension, circulatory collapse, and death if used together with phosphodiesterase type 5 inhibitor drugs that are prescribed for erectile dysfunction, such as Viagra, Cialis and Levitra. Calcium channel blockers are used to treat angina associated with coronary spasm, however, they do not provide immediate relief. We are not aware of any approved rapid-onset, short acting treatments for coronary spasm. We believe that etripamil can be used to rapidly reduce angina symptoms in the outpatient setting in patients with angina who cannot tolerate or do not respond to nitrates, and in patients experiencing coronary spasm.

Our Strategy

Our goal is to develop and commercialize etripamil for the treatment of PSVT and other cardiovascular indications, and to expand our pipeline to include additional clinical-stage compounds for other acute and/or episodic medical conditions. The key elements of our business strategy to achieve this goal include the following:

- ***Successfully complete development and obtain regulatory approval of etripamil for the treatment of PSVT.*** We are focused on efficiently developing and obtaining approval for etripamil to treat patients with PSVT. We are actively recruiting patients for a Phase 3 clinical trial of etripamil, which may serve as a single pivotal efficacy trial in the United States. We expect top-line data in the first half of 2020. We intend to first seek regulatory approval in the United States, followed by Europe and other major markets.

- ***Expand the scope of cardiovascular indications for etripamil beyond PSVT.*** We are exploring the use of etripamil for the treatment of patients with atrial fibrillation, another condition associated with a fast heart rate. We believe that etripamil could benefit patients with atrial fibrillation based on the approved use of IV calcium channel blockers in these indications. We are also exploring the use of etripamil for the treatment of angina, which is chest pain typically associated with an imbalance between the supply of oxygen to and the demand for oxygen by the heart. Calcium channel blockers have already been approved for chronic management of angina. We believe there is an opportunity to treat angina with etripamil. We plan to test etripamil in Phase 2 proof-of-concept clinical trials in patients with atrial fibrillation and angina.
- ***Maximize the value of our programs by maintaining flexibility to commercialize our product candidates independently or through collaborative partnerships.*** We currently have exclusive development and commercialization rights for etripamil for our initial indications of PSVT, atrial fibrillation and angina. We plan to establish commercialization and marketing capabilities using a direct sales force to commercialize etripamil in the United States. Outside of the United States, we are considering commercialization strategies that may include collaborations with other companies.
- ***Leverage our expertise and experience to expand our pipeline of product candidates.*** We seek to maximize our commercial opportunities by acquiring or in-licensing product candidates for indications with significant unmet need with a focus on clinically validated mechanisms that can yield novel treatments. We believe this approach may provide a more rapid path to regulatory approval, faster adoption by medical professionals, nearer-term commercial value and more immediate clinical benefit for patients with significant need. Our leadership team has extensive experience in developing and commercializing successful drugs. We intend to leverage the collective talent within our organization and our network to guide our development plans and pipeline expansion.

Intellectual Property

We developed etripamil as a new chemical entity. Our composition-of-matter claims for etripamil provide us an intellectual property position with patents issued in the United Stated through 2028, and with patent term extensions possible to 2031. In addition, we have corresponding issued patients in Europe and other major markets. We also have an issued U.S. patent that extends the exclusivity period for the commercial formulation of etripamil to 2036 and we have corresponding pending patent applications in Europe and other major markets.

Management

We are led by a team of executives who have extensive experience in successfully developing and commercializing therapies in cardiovascular and other indications at both major pharmaceutical and emerging life sciences companies. These therapies include Vytorin (ezetimibe and simvastatin), Ranexa (ranolazine), Effient (prasugrel), Northera (droxidopa), and Cologuard as well as several ACE Inhibitors, ARBs, and novel oral anticoagulants. We have raised approximately $139.2 million in gross proceeds from equity financings with a number of United States, Canadian and European healthcare specialist investment firms, including BDC Capital, Inc., Boxer Capital of Tavistock Group, Domain Associates, LLC, Fonds de solidarité FTQ, Forbion Capital Partners, iNovia Capital, Novo Holdings A/S, Pappas Ventures, RTW Investments, LP, Tekla Capital Management LLC, and Venrock Healthcare Capital Partners.

Risks Associated with Our Business

Our business is subject to a number of risks of which you should be aware before making a decision to invest in our common shares. These risks are more fully described in the section titled "Risk Factors," including the following:

- We have a limited operating history, have never generated any revenues from product sales and have incurred significant operating losses since inception.
- We anticipate that we will continue to incur substantial operating losses for the foreseeable future and may never achieve or maintain profitability.

- We will require additional capital to finance our operations, which may not be available on acceptable terms, if at all.
- Our future success is dependent on the successful clinical development, regulatory approval and commercialization of etripamil, which is currently our only product candidate and without which our ability to generate revenue will be adversely affected.
- 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.
- 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 trial for the treatment of PSVT.
- Etripamil is intended to be used with a nasal spray device, which may result in additional regulatory and supply risks.
- 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, or achieve market acceptance we may not be successful in commercializing etripamil or any future product candidates, if and when they are approved.
- 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, we may not be able to compete effectively in our markets.
- If we are a passive foreign investment company following this offering, there could be adverse U.S. federal income tax consequences to U.S. Holders.
- 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.

Our Corporate Information

We were incorporated under the laws of the province of Québec in 2003. Our principal executive offices are located at 1111 Dr. Frederik-Philips Blvd., Suite 420, Montréal, Québec, Canada H4M 2X6, and our telephone number is (514) 336-0444. In January 2017, we incorporated our wholly owned subsidiary, Milestone Pharmaceuticals USA, Inc., a Delaware corporation. Our corporate website address is www.milestonepharma.com. Information contained on, or accessible through, our website is not a part of this prospectus. We have included our website in this prospectus solely as an inactive textual reference.

Implications of Being an Emerging Growth Company

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act, or the JOBS Act, enacted in April 2012, and we may remain an emerging company for up to five years after the completion of this offering. For so long as we remain an emerging growth company, we are permitted and intend to rely on certain exemptions from various public company reporting requirements, including not being required to have our internal control over financial reporting audited by our independent registered public accounting firm pursuant to Section 404(b) of the Sarbanes-Oxley Act of 2002, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements, and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and any golden parachute payments not previously approved. In particular, in this prospectus, we have provided only two years of audited financial statements and have not included all of the executive compensation related information that would be required if we were not an emerging growth company. Accordingly, the information contained herein may be different than the information you receive from other public companies in which you hold shares.

In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This provision allows an emerging growth company to delay the adoption of some accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of delayed adoption of new or revised accounting standards, and therefore we will be subject to the same requirements to adopt new or revised accounting standards as other public companies that are not emerging growth companies.

THE OFFERING

Common shares to be offered	5,500,000 shares
Common shares to be outstanding after this offering	23,647,589 shares
Option to purchase additional common shares	825,000 shares
Use of proceeds	We estimate that the net proceeds from this offering will be approximately $74.0 million (or approximately $85.5 million if the underwriters exercise in full their option to purchase up to 825,000 additional common shares), after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. We currently intend to use the net proceeds from this offering, together with our existing cash, cash equivalents and short-term investments, as follows: § approximately $85.0 million for our Phase 3 clinical trials of etripamil in PSVT; § approximately $20.0 million for pre-commercialization activities; § approximately $6.0 million for our Phase 2 clinical trials of etripamil in atrial fibrillation and angina; and § the remainder to fund other research and development activities, working capital and other general corporate purposes. See "Use of Proceeds" for additional information.
Risk factors	You should read the section titled "Risk Factors" for a discussion of factors to consider carefully, together with all the other information included in this prospectus, before deciding to invest in our common shares.
Nasdaq Global Select Market symbol	"MIST"

The number of common shares to be outstanding after this offering is based on 18,147,589 common shares outstanding as of December 31, 2018, and excludes:

- 2,295,045 common shares issuable upon the exercise of 2,295,045 outstanding options as of December 31, 2018, at a weighted-average exercise price of $1.771 per share;
- 2,369,571 common shares reserved for future issuance under our 2019 Equity Incentive Plan, or the 2019 Plan, which became effective immediately prior to the execution of the underwriting agreement related to this offering, as well as any future increases in the number of common shares reserved for issuance under our 2019 Plan; and
- 278,764 common shares reserved for future issuance under our 2019 Employee Share Purchase Plan, or ESPP, which became effective immediately prior to the execution of the underwriting

agreement related to this offering, as well as any future increases in the number of common shares reserved for issuance under our ESPP.

Unless otherwise indicated, all information contained in this prospectus assumes or gives effect to:

- the filing and effectiveness of an amendment to our articles of incorporation upon the completion of this offering and the adoption of our amended and restated bylaws upon the completion of this offering;
- the automatic conversion of all outstanding preferred shares as of December 31, 2018 into an aggregate of 17,550,802 common shares immediately prior to the completion of this offering;
- a 1-for-5.3193 reverse split of our common shares and preferred shares effected on April 26, 2019;
- no exercise of the outstanding options described above; and
- no exercise by the underwriters of their option to purchase up to 825,000 additional common shares.

SUMMARY CONSOLIDATED FINANCIAL DATA

The following tables set forth our summary consolidated statements of operations data for the years ended December 31, 2017 and 2018, which has been derived from our audited consolidated financial statements appearing elsewhere in this prospectus. Our historical results are not necessarily indicative of the results to be expected in the future. You should read this consolidated summary financial data together with our consolidated financial statements and related notes to those statements, as well as the section titled "Management's Discussion and Analysis of Financial Condition and Results of Operations," which are included elsewhere in this prospectus.

(In thousands, except share and per share amounts)	YEAR ENDED DECEMBER 31, 2017	2018
Summary of Consolidated Operations Data:		
Operating expenses:		
Research and development, net of tax credits	$ 5,636	$ 16,849
General and administrative	1,502	3,052
Commercial	1,130	3,921
Total operating expenses	8,268	23,822
Loss from operations	(8,268)	(23,822)
Interest income, net of bank charges	186	711
Net loss and comprehensive loss before income taxes	(8,082)	(23,111)
Income tax expense	4	74
Net loss and comprehensive loss	$ (8,086)	$ (23,185)
Net loss per share:[1]		
Basic and diluted	$ (34.15)	$ (72.63)
Weighted average shares used in computing net loss per share:[1]		
Basic and diluted	236,750	319,202
Pro forma net loss per share:[1]		
Basic and diluted		$ (63.14)
Weighted average shares outstanding used in computing pro forma net loss per share:[1]		
Basic and diluted		367,287

(1) See Note 8 to our audited consolidated financial statements included elsewhere in this prospectus for an explanation of the calculations of our basic and diluted net loss per share and the weighted-average number of shares used in the computation of the per share amounts.

(In thousands)	AS OF DECEMBER 31, 2018 ACTUAL	PRO FORMA(1)	PRO FORMA AS ADJUSTED(2)
Consolidated Balance Sheet Data:			
Cash, cash equivalents and short-term investments	$ 85,976	$ 85,976	$ 159,986
Working capital	83,518	83,518	157,528
Total assets	88,081	88,081	162,091
Preferred shares	138,758	—	—
Accumulated deficit	(58,270)	(58,270)	(58,270)
Total shareholders' (deficit) equity	(55,210)	83,548	157,558

(1) The pro forma column reflects the conversion of all of the outstanding preferred shares into an aggregate of 17,550,802 common shares upon completion of this offering.

(2) The pro forma as adjusted column reflects the pro forma adjustments set forth above and: (i) the sale of 5,500,000 common shares in this offering at the initial public offering price of $15.00 per share, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us; and (ii) the filing and effectiveness of our amendment to our articles of incorporation.

RISK FACTORS

Investing in our common shares involves a high degree of risk. You should carefully consider the risks described below, as well as the other information in this prospectus, including our consolidated financial statements and the related notes and "Management's Discussion and Analysis of Financial Condition and Results of Operations," before deciding whether to invest in our common shares. The occurrence of any of the events or developments described below could harm our business, financial condition, results of operations and prospects. In such an event, the market price of our common shares could decline and you may lose all or part of your investment.

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. As of December 31, 2018, we had an accumulated deficit of $58.3 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 the net proceeds from this offering, together with our existing cash, cash equivalents and short-term investments, will be sufficient to fund our operations into the second 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, including purchasers of our common shares in this offering, 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 after this public offering, 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 approximately $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 abroad 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 abroad, 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, with a threshold p-value of $p<0.01$ as is the common standard when single efficacy trials are used to support an NDA submission. While we believe that this is sufficient to support our NDA submission based on our end-of-Phase 2 meeting with the FDA, the typical guidelines generally involve two efficacy trials with a threshold p-value of $p<0.05$. 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 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 will 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, and therefore, enrollment is still relatively limited at this stage. 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 will be completed when a total of 100 to 120 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. For example, in December 2016, the 21st Century Cures Act, or Cures Act, was signed into law. The Cures Act, among other things, is intended to modernize the regulation of drugs and to spur innovation, but its ultimate implementation is unclear. 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. For additional information on the healthcare laws and regulations that we may be subject to, see "Business — Government Regulation and Product Approval."

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. For additional information on the healthcare reform, see "Business — Government Regulation and Product Approval."

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 a CRO 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. To protect our proprietary positions, we file patent applications in the United States and abroad related to our product candidates that are important to our business. 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 issues. 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 preissuance submission of prior art to the U.S. Patent and Trademark Office, or USPTO, or become involved in opposition, derivation, reexamination, inter partes 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 and will continue to be able to do so after the closing of this offering. 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 December 31, 2018, we had 20 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 may be required to conduct clinical trial activities in Europe, which could 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 This Offering and Ownership of Our Common Shares

No public market for our common shares currently exists, and a public market may not develop or be liquid enough for you to sell your shares quickly or at market price.

Prior to this offering, there has not been a public market for our common shares. If an active trading market for our common shares does not develop following this offering, 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. The initial public offering price of our common shares will be determined by negotiations between us and representatives of the underwriters and may not be indicative of the market prices of our common shares that will prevail in the trading market.

The market price of our common shares may be volatile and fluctuate substantially, which could result in substantial losses for purchasers of our common shares in this offering.

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 initial public offering price. In addition to the factors discussed in this "Risk Factors" section and elsewhere in this prospectus, 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.

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 December 31, 2018, upon the completion of this offering, our executive officers, directors and shareholders who owned more than 5% of our outstanding common shares before this offering will, in the aggregate, beneficially own shares representing approximately 68% 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. We do not currently have, and may never obtain, research coverage by industry or financial analysts. Equity research analysts may elect not to provide research coverage of our common shares after the completion of this offering, and such lack of research coverage may adversely affect the market price of our common shares. In the event we do have equity research analyst coverage, we will 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.

If you purchase our common shares in this offering, you will suffer immediate dilution of your investment.

The initial public offering price of our common shares is substantially higher than the net tangible book value per common share. Therefore, if you purchase our common shares in this offering, you will pay a price per share that substantially exceeds our net tangible book value per share after this offering. Based on the initial public offering price of $15.00 per share, you will experience immediate dilution of $8.35 per share, representing the difference between our pro forma as adjusted net tangible book value per share after this offering and the initial public offering price per share. After this offering, we will also have outstanding options to purchase common shares with exercise prices lower than the initial public offering price. To the extent these outstanding options are exercised, there will be further dilution to investors in this offering. See the section titled "Dilution" for additional information.

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. Investors seeking cash dividends should not purchase our common shares in this offering.

We have broad discretion in the use of our cash, cash equivalents and short-term investments, including the net proceeds from this offering, and may use them ineffectively, 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, including the net proceeds from this offering, 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, including the net proceeds from this offering, in a manner that does not produce income or that loses value. See the section titled "Use of Proceeds" for additional information.

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. After this offering, we will have outstanding 23,647,589 common shares based on the number of shares outstanding as of December 31, 2018 assuming no exercise by the underwriters of their option to purchase additional common shares. This includes the shares that we are selling in this offering, 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 but will be able to be sold after the offering as described in the sections titled "Shares Eligible for Future Sale" and "Underwriting." Moreover, upon the completion of this offering, holders of an aggregate of approximately 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 described in the section titled "Underwriting."

If we are a passive foreign investment company following this offering, 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, including this 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. For further discussion of the PFIC rules and the adverse U.S. federal income tax consequences in the event we are classified as a PFIC, see the section titled "Material Income Tax Considerations — Material U.S. Federal Income Considerations for U.S. Holders" in this prospectus.

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 (as defined below under "Material Income Tax Considerations — Material U.S. Federal Income Tax Considerations for U.S. Holders") 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 Organisation 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:

- being permitted to provide only two years of audited financial statements, in addition to any required unaudited interim financial statements, with correspondingly reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure;
- 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 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. We may take advantage of some or all of these reporting exemptions until we are no longer an EGC. We will remain an EGC until the earlier of (i) five years following the completion of this offering, (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.

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 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 Québec, which in some cases have a different effect on shareholders than the corporate laws of Delaware.

We are governed by the Business Corporations Act (Québec), 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. Refer to the section titled "Material Differences between the Business Corporations Act (Québec) and the Delaware General in Corporation Law" for more information.

Our amended and restated bylaws to be in effect following completion of this offering 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 to be in effect following completion of this offering and certain Canadian legislation, together or separately, could discourage or delay certain change in control transactions or shareholder proposals.

Our amended and restated bylaws to be in effect following completion of this offering 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 Québec, 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.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

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

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

- the initiation, timing, progress and results of our current and future clinical trials of etripamil, including our Phase 3 clinical trials of etripamil for the treatment of 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;
- our expected use of proceeds from this offering;
- developments relating to our competitors and our industry; and
- the factors that may impact our financial results.

The foregoing list of risks is not exhaustive. Other sections of this prospectus may include additional factors that could harm our business and financial performance. Moreover, we operate in a very competitive and rapidly changing environment. New risk factors emerge from time to time, and it is not possible for our management to predict all risk factors nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in, or implied by, any forward-looking statements.

In light of the significant uncertainties in these forward-looking statements, you should not rely upon forward-looking statements as predictions of future events. Although we believe that we have a reasonable basis for each forward-looking statement contained in this prospectus, we cannot guarantee that the future results, levels of activity, performance or events and circumstances reflected in the forward-looking statements will be achieved or occur at all. You should refer to the section titled "Risk Factors" for a discussion of important factors that may cause our actual results to differ materially from those expressed or implied by our forward-looking statements. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. Except as required by law, we undertake no obligation to publicly update any forward-looking statements, whether as a result of new information, future events or otherwise. The Private Securities Litigation Reform Act of 1995 and Section 27A of the Securities Act of 1933, as amended, do not protect any forward-looking statements that we make in connection with this offering.

You should read this prospectus and the documents that we reference in this prospectus and have filed as exhibits to the registration statement, of which this prospectus is a part, completely and with the understanding that our actual future results may be materially different from what we expect. We qualify all of the forward-looking statements in this prospectus by these cautionary statements.

MARKET AND INDUSTRY DATA

Certain market and industry data included in this prospectus were obtained from independent third-party surveys, market research, publicly available information, reports of governmental agencies and industry publications and surveys as well as our own internal estimates and research, including both qualitative and quantitative market research in the United States and Europe with patients, healthcare providers, and payors, supplemented with analyses of longitudinal healthcare claims data in the United States between 2008 and 2016 for patients with claims for PSVT. All of the market and industry data used in this prospectus involve a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. Although we are responsible for all of the disclosure contained in this prospectus and we believe the information from the industry publications and other third-party sources included in this prospectus is reliable, such information is inherently imprecise. No independent sources have evaluated the reasonableness or accuracy of our internal estimates or research used in this prospectus. The industry in which we operate is subject to a high degree of uncertainty and risk due to a variety of factors, including those described in the section titled "Risk Factors." These and other factors could cause results to differ materially from those expressed in the estimates made by the independent parties and by us.

USE OF PROCEEDS

We estimate that the net proceeds to us from this offering will be approximately $74.0 million (or approximately $85.5 million if the underwriters exercise in full their option to purchase up to 825,000 additional common shares), based on the initial public offering price of $15.00 per share, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

The principal purposes of this offering are to increase our capitalization and financial flexibility, establish a public market for our common shares and to facilitate future access to the public equity markets by us, our employees and our shareholders, obtain additional capital to support our operations and increase our visibility in the marketplace.

As of December 31, 2018, we had cash, cash equivalents and short-term investments of $86.0 million. We currently intend to use the net proceeds from this offering, together with our existing cash, cash equivalents and short-term investments, as follows:

- approximately $85.0 million for our Phase 3 clinical trials of etripamil in PSVT;
- approximately $20.0 million for pre-commercialization activities;
- approximately $6.0 million for our Phase 2 clinical trials of etripamil in atrial fibrillation and angina; and
- the remainder to fund other research and development activities, working capital and other general corporate purposes.

We may also use a portion of the remaining net proceeds to in-license, acquire or invest in complementary businesses, technologies, products or assets. However, we have no current commitments or obligations to do so.

This expected use of the net proceeds from this offering represents our intentions based on our current plans and business conditions, which could change in the future as our plans and business conditions evolve. Further, due to the uncertainties inherent in the drug development process, it is difficult to estimate with certainty the exact amounts of the net proceeds from this offering that may be used for the above purposes.

Our management will have broad discretion over the use of the net proceeds from this offering, and our investors will be relying on the judgment of our management regarding the application of the net proceeds of this offering. The amounts and timing of our expenditures will depend upon numerous factors including the results of our research and development efforts, the timing and success of preclinical studies and any ongoing clinical trials or clinical trials we may commence in the future, the timing of regulatory submissions and the amount of cash obtained through current and any future collaborations.

While we anticipate that the amount of funds allocated for the Phase 3 clinical trials of PSVT will be sufficient to complete the Phase 3 clinical trials as currently planned, we expect that we will need to raise additional funds to complete the regulatory approval and commercialization of etripamil for PSVT. We also anticipate that the amount of funds allocated for the planned Phase 2 clinical trials of etripamil in atrial fibrillation and angina will be sufficient to complete such trials. However, we expect that we will need to raise additional capital to continue the clinical development, regulatory approval and commercialization of etripamil in these or any other indications, or to pursue the development and commercialization of any other product candidates. We expect to finance our cash needs through a combination of equity offerings, debt financings and potential collaborations, and license and development agreements. We have based these estimates on assumptions that may prove to be incorrect, and we could expend our available capital resources at a rate greater than we currently expect.

Pending the use of the net proceeds from this offering as described above, we intend to invest the net proceeds in a variety of capital preservation instruments, including short-term, interest-bearing obligations, investment-grade instruments, certificates of deposit or direct or guaranteed obligations of the U.S. and Canadian governments.

DIVIDEND POLICY

We have never declared or paid cash dividends on our share capital, and we do not currently intend to pay any cash dividends on our share capital in the foreseeable future. We currently intend to retain all available funds and any future earnings, if any, to fund the development and expansion of our business. Any future determination related to dividend policy will be made at the discretion of our board of directors, subject to applicable laws, and will depend upon, among other factors, our results of operations, financial condition, contractual restrictions and capital requirements. In addition, our ability to pay cash dividends on our share capital in the future may be limited by the terms of any future debt or preferred securities we issue or any credit facilities we enter into.

CAPITALIZATION

The following table sets forth our cash, cash equivalents and short-term investments, and our capitalization as of December 31, 2018 on:

- an actual basis;
- a pro forma basis, giving effect to the automatic conversion of all outstanding preferred shares into an aggregate of 17,550,802 common shares upon the completion of this offering; and
- a pro forma as adjusted basis, giving effect to the pro forma adjustments discussed above, and giving further effect to: (i) the sale of 5,500,000 common shares in this offering at the initial public offering price of $15.00 per share, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us; and (ii) the filing and effectiveness of our amendment to our articles of incorporation.

You should read this table together with the sections titled "Selected Consolidated Financial Data," "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our consolidated financial statements and the related notes included elsewhere in this prospectus.

	AS OF DECEMBER 31, 2018		
(In thousands, except share and per share amounts)	ACTUAL	PRO FORMA	PRO FORMA AS ADJUSTED
Cash, cash equivalents and short-term investments	$ 85,976	$ 85,976	$ 159,986
Preferred shares, no par value, unlimited shares authorized; 17,550,802 shares issued and outstanding, actual; unlimited shares authorized, no shares issued or outstanding, pro forma; no shares authorized, issued or outstanding, pro forma as adjusted	$ 138,758	$ —	$ —
Shareholders' (deficit) equity:			
Preferred shares, no par value, no shares authorized, issued and outstanding, actual and pro forma; unlimited shares authorized and no shares issued and outstanding, pro forma as adjusted	—	—	—
Common shares, no par value, unlimited shares authorized, 596,787 shares issued and outstanding, actual; unlimited shares authorized, 18,147,589 shares issued and outstanding, pro forma; unlimited authorized, 23,647,589 shares issued and outstanding, pro forma as adjusted	2,039	140,797	214,807
Additional paid-in capital	2,655	2,655	2,655
Accumulated other comprehensive loss			
Cumulative translation adjustment	(1,634)	(1,634)	(1,634)
Accumulated deficit	(58,270)	(58,270)	(58,270)
Total shareholders' (deficit) equity	(55,210)	83,548	157,558
Total capitalization	$ 83,548	$ 83,548	$ 157,558

The number of common shares outstanding after this offering is based on 18,147,589 common shares outstanding as of December 31, 2018, and excludes:

- 2,295,045 common shares issuable upon the exercise of 2,295,045 outstanding options as of December 31, 2018, at a weighted-average exercise price of $1.7713 per share;
- 2,369,571 common shares reserved for future issuance under our 2019 Plan, which became effective immediately prior to the execution of the underwriting agreement related to this offering, as well as any future increases in the number of common shares reserved for issuance under our 2019 Plan; and
- 278,764 common shares reserved for future issuance under our ESPP, which became effective immediately prior to the execution of the underwriting agreement related to this offering, as well as any future increases in the number of common shares reserved for issuance under our ESPP.

DILUTION

If you invest in our common shares in this offering, your ownership interest will be diluted to the extent of the difference between the initial public offering price per common share and the pro forma as adjusted net tangible book value per common share after this offering.

Our historical net tangible book deficit as of December 31, 2018 was $(55.4) million, or $(92.79) per common share. Our historical net tangible book deficit represents our total tangible assets (which excludes deferred offering costs) less total liabilities and preferred shares. Historical net tangible book deficit per share is our historical net tangible book deficit divided by the number of common shares outstanding as of December 31, 2018.

Our pro forma net tangible book value as of December 31, 2018 was $83.4 million, or $4.59 per common share, which gives effect to the automatic conversion of all outstanding preferred shares into an aggregate of 17,550,802 common shares immediately prior to the completion of this offering. Pro forma net tangible book value per share is our pro forma net tangible book value divided by the number of common shares deemed to be outstanding as of December 31, 2018.

After giving effect to the sale of 5,500,000 common shares in this offering at the initial public offering price of $15.00 per share, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us, our pro forma as adjusted net tangible book value as of December 31, 2018 would have been $157.4 million, or $6.65 per share. This represents an immediate increase in pro forma as adjusted net tangible book value of $2.06 per share to our existing shareholders and an immediate dilution of $8.35 per share to new investors participating in this offering.

The following table illustrates this dilution on a per share basis:

Initial public offering price per share		$ 15.00
Historical net tangible book deficit per share as of December 31, 2018	$ (92.79)	
Pro forma increase in net tangible book value per share as of December 31, 2018 attributable to pro forma transactions described above	97.38	
Pro forma net tangible book value per share as of December 31, 2018	4.59	
Increase in pro forma net tangible book value per share attributable to new investors participating in this offering	2.06	
Pro forma as adjusted net tangible book value per share after this offering		6.65
Dilution per share to new investors participating in this offering		$ 8.35

If the underwriters exercise in full their option to purchase up to 825,000 additional common shares, the pro forma as adjusted net tangible book value per share after giving effect to this offering would be $6.90 per share and dilution to new investors participating in this offering would be $8.10 per share.

The following table summarizes, on the pro forma as adjusted basis described above, the differences between the number of shares purchased from us on an as converted basis, the total consideration paid and the weighted average price per share paid by existing shareholders and by investors purchasing shares in

this offering at the initial public offering price of $15.00 per share, before deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us:

	SHARES PURCHASED		TOTAL CONSIDERATION		AVERAGE PRICE PER SHARE
	NUMBER	PERCENT	AMOUNT	PERCENT	
Existing shareholders	18,147,589	77%	$ 143,106,862	63%	$ 7.89
New investors	5,500,000	23%	82,500,000	37%	15.00
Total	23,647,589	100%	$ 218,106,862	100%	

If the underwriters exercise their option to purchase additional shares in full, our existing shareholders would own 74% and our new investors would own 26% of the total number of our common shares outstanding upon the completion of this offering.

The foregoing discussion and tables are based on 18,147,589 common shares outstanding as of December 31, 2018, which gives effect to the pro forma transactions described above and excludes:

- 2,295,045 common shares issuable upon the exercise of 2,295,045 outstanding options as of December 31, 2018, at a weighted-average exercise price of $1.7713 per share;
- 2,369,571 common shares reserved for future issuance under our 2019 Plan, which became effective immediately prior to the execution of the underwriting agreement related to this offering, as well as any future increases in the number of common shares reserved for issuance under our 2019 Plan; and
- 278,764 common shares reserved for future issuance under our ESPP, which became effective immediately prior to the execution of the underwriting agreement related to this offering, as well as any future increases in the number of common shares reserved for issuance under our ESPP.

To the extent that outstanding options are exercised, new options or other equity awards are issued under our equity incentive plans, or we issue additional shares in the future, there will be further dilution to investors purchasing shares in this offering. Assuming the exercise of all of our outstanding options as of December 31, 2018, the number of shares held by existing shareholders would increase to 79% of the total number of shares to be outstanding after this offering, and the number of shares held by investors participating in this offering would be reduced to 21% of the total number of shares to be outstanding after this offering. Additionally, the total consideration paid to us by existing shareholders would be 64% of the total consideration paid for our outstanding shares, and the total consideration paid to us by investors participating in this offering would be 36% of the total consideration paid for our outstanding shares. In addition, we may choose to raise additional capital because of market conditions or strategic considerations, even if we believe that we have sufficient funds for our current or future operating plans. If we raise additional capital through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our shareholders.

SELECTED CONSOLIDATED FINANCIAL DATA

You should read the following selected consolidated financial data together with the section titled "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our consolidated financial statements and the related notes included elsewhere in this prospectus. The selected consolidated financial data included in this section are not intended to replace the consolidated financial statements and are qualified in their entirety by the consolidated financial statements and the related notes included elsewhere in this prospectus.

The following tables set forth our selected consolidated statement of operations data for the years ended December 31, 2017 and 2018, and our selected consolidated balance sheet data as of December 31, 2017 and 2018, all of which has been derived from our audited consolidated financial statements appearing elsewhere in this prospectus. Our historical results are not necessarily indicative of the results that may be expected for any period in the future.

(In thousands, except share and per share amounts)	YEAR ENDED DECEMBER 31, 2017	2018
Summary of Consolidated Operations Data:		
Operating expenses:		
Research and development, net of tax credits	$ 5,636	$ 16,849
General and administrative	1,502	3,052
Commercial	1,130	3,921
Total operating expenses	8,268	23,822
Loss from operations	(8,268)	(23,822)
Interest income, net of bank charges	186	711
Net loss and comprehensive loss before income taxes	(8,082)	(23,111)
Income tax expense	4	74
Net loss and comprehensive loss	$ (8,086)	$ (23,185)
Net loss per share:[1]		
Basic and diluted	$ (34.15)	$ (72.63)
Weighted average shares used in computing net loss per share:[1]		
Basic and diluted	236,750	319,202
Pro forma net loss per share:[1]		
Basic and diluted		$ (63.14)
Weighted average shares outstanding used in computing pro forma net loss per share:[1]		
Basic and diluted		367,287

(1) See Note 8 to our audited consolidated financial statements included elsewhere in this prospectus for an explanation of the calculations of our basic and diluted net loss per share, and the weighted-average number of shares used in the computation of the per share amounts.

(In thousands)	AS OF DECEMBER 31, 2017	2018
Consolidated Balance Sheet Data:		
Cash, cash equivalents and short-term investments	$ 26,912	$ 85,976
Working capital	25,950	83,518
Total assets	27,590	88,081
Convertible preferred shares	59,104	138,758
Accumulated deficit	(35,085)	(58,270)
Total shareholders' deficit	(33,119)	(55,210)

MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

You should read the following discussion and analysis of our financial condition and results of operations together with "Selected Consolidated Financial Data" and our consolidated financial statements and related notes included elsewhere in this prospectus. This discussion contains forward-looking statements based upon current expectations that involve risks and uncertainties. Our actual results may differ materially from those anticipated in these forward-looking statements as a result of various factors, including those discussed in "Risk Factors" and in other parts of this 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. Investigators reported an 87% termination rate of induced PSVT within 15 minutes at the dose selected for Phase 3 versus a 35% termination rate for placebo. We are actively recruiting patients for our Phase 3 clinical trial of etripamil, which may serve as a single pivotal efficacy trial, and we expect top-line data in the first half of 2020. In addition to the efficacy trial, our Phase 3 clinical program for etripamil for PSVT includes two open-label safety studies, one of which we initiated in December 2018, and the other we expect to initiate in the second half of 2019. We are also planning to initiate a Phase 2 clinical trial in the second half of 2019 in atrial fibrillation, another rapid heart rate condition, and expect to subsequently initiate an additional Phase 2 clinical trial in angina to establish proof-of-concept for the broader use of etripamil in 2020.

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 and providing general and administrative support for these operations. 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 years ended December 31, 2018 and 2017, we recorded net losses of $23.2 million and $8.1 million, respectively. As of December 31, 2018, we had an accumulated deficit of $58.3 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, 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 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; and
- add operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts;

Furthermore, following the closing of this offering, we expect to incur additional costs associated with operating as a public company, including significant legal, accounting, investor relations and other expenses that we did not incur as a private company.

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 in preparation 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 research and development expenses. The following table shows our research and development expenses by type of activity for the years ended December 31, 2017 and 2018.

	Year Ended December 31,	
(in thousands)	2017	2018
Clinical and pre-clinical	$ 3,446	$ 12,546
Drug manufacturing and formulation	1,661	3,320
Regulatory and other costs	1,052	1,240
Less: investment tax credits	(523)	(257)
Total research and development expenses	$ 5,636	$ 16,849

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, rent 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.

Interest Income

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

Results of Operations

Comparison of the Years Ended December 31, 2017 and 2018

The following table summarizes our results of operations:

	Year ended December 31,			
(in thousands)	**2017**	**2018**	**$ Change**	**% Change**
Operating expenses				
Research and development, net of tax credits	5,636	16,849	11,213	199%
General and administrative	1,502	3,052	1,550	103%
Commercial	1,130	3,921	2,791	247%
Total operating expenses	8,268	23,822	15,554	188%
Loss from operations	(8,268)	(23,822)	(15,554)	188%
Interest income, net of bank charges	186	711	525	282%
Loss and comprehensive loss before income taxes	(8,082)	(23,111)	(15,029)	186%
Income tax expense	4	74	70	1,750%
Net loss and comprehensive loss	(8,086)	(23,185)	(15,099)	187%

Research and Development Expenses

Research and development expenses increased by $11.2 million, or 199%, for the year ended December 31, 2018 compared to the year ended December 31, 2017. Approximately $8.8 million of the

increase is related to the initiation of our Phase 3 pivotal efficacy trial of etripamil for the treatment of PSVT and increases in clinical management headcount and related costs during the year ended December 31, 2018. In addition, we increased our spending on formulation and manufacturing activities in the year ended December 31, 2018 by approximately $1.7 million reflecting the manufacture and packaging of additional clinical trial materials to support our Phase 3 program as well as activities undertaken in the year ended December 31, 2018 to qualify additional manufacturing vendors. We also recognized $0.3 million and $0.5 million of research and development investment tax credits provided by the federal and provincial governments of Canada and Québec in the years ended December 31, 2018 and 2017, respectively, which is recorded as a reduction in our research and development expenses.

General and Administrative Expenses

General and administrative expenses increased by $1.6 million, or 103% for the year ended December 31, 2018 compared to the year ended December 31, 2017. During 2018, we increased our administrative headcount and, as a result, the related personnel costs. In addition, we incurred increased spending for consulting fees, recruiting fees and professional fees, including legal and accounting services incurred to support this offering.

Commercial Expenses

Commercial expenses increased by $2.8 million, or 247%, for the year ended December 31, 2018 when compared to 2017, primarily to support increased commercial headcount and related costs, conduct additional commercial and market research, increase the scope of our patient advocacy activities and initiate a small medical affairs team focused on KOL engagement and disease awareness.

Interest Income, Net

Interest income, net of bank charges was $0.7 million and $0.2 million for the years ended December 31, 2018 and 2017, respectively, which increase in 2018 reflects increased earnings on cash, cash equivalents and short-term investments related to the proceeds from our October 2018 Series D preferred share financing.

Net Loss

For the foregoing reasons, we had net losses of $23.2 million and $8.1 million for the years ended December 31, 2018 and 2017, respectively.

Liquidity and Capital Resources

Sources of Liquidity

We have financed our operations primarily through sales of our convertible preferred shares to accredited investors generating net proceeds of approximately $138.8 million.

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 December 31, 2018, we had cash, cash equivalents and short-term investments of $86.0 million and an accumulated deficit of $58.3 million.

Based on our research and development plans, we expect that the net proceeds from this offering, together with our existing cash, cash equivalents and short-term investments, will be sufficient to fund our operations into the second 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 operating expenses, primarily research and development expenditures. We plan to increase our research and development expenses and 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:

	Year ended December 31,			
(in thousands)	2017	2018	$ Change	% Change
Net cash (used in) provided by:				
Operating activities	(8,052)	(21,046)	(12,994)	161%
Investing activities	(16,023)	15,998	32,021	(200)%
Financing activities	30,722	80,115	49,393	161%
Net increase in cash and cash equivalents during the year	6,647	75,067	68,420	

Operating Activities

In 2018, we used $21.0 million of cash in operating activities, which consisted of a net loss of $23.2 million offset by a net change of $1.5 million in our net operating assets and non-cash charges of $0.6 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 a net increase of $2.9 million for accounts payable and accrued liabilities offset by an increase of $1.3 million for prepaid expenses and a net increase of $0.1 million for research and development tax credits, interest and sales tax receivable.

In 2017, we used $8.1 million of cash in operating activities, which consisted of a net loss of $8.1 million and a net change of $0.2 million in our net operating assets, partially offset adjusted by non-cash charges of $0.2 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 a net decrease of $0.2 million for accounts payable and accrued liabilities, an increase of $0.1 million for prepaid expenses and a net decrease of $0.1 million for research and development tax credits, interest and sales tax receivable.

Investing Activities

In 2018, our investing activities provided $16.0 million of cash due to the redemption of approximately $16.0 million of short-term investments that we had acquired during the year ended December 31, 2017. In 2017, we used $16.0 million of cash in investing activities attributable to the acquisition of short-term investments that consisted of guaranteed investment certificates with maturities greater than 90 days and less than 12 months.

Financing Activities

In 2018, our financing activities provided $80.1 million of cash, primarily consisting of the proceeds from the issuance of Class D1 and Class D2 preferred shares in October 2018. During 2017, our financing activities provided $30.7 million of cash, primarily consisting of proceeds from the issuance of Class C preferred shares, and to a lesser extent, the issuance of Class B preferred shares.

Off-Balance Sheet Arrangements

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

Contractual Obligations

The following table summarizes our contractual obligations as of December 31, 2018:

	Payments due by period				
(in thousands)	**Total**	**Less Than 1 Year**	**1 to 3 Years**	**3 to 5 Years**	**More than 5 Years**
Operating lease commitments[(1)]	$ 380	$ 216	$ 164	$ —	$ —
Total	$ 380	$ 216	$ 164	$ —	$ —

(1) The operating lease consists primarily of costs related to the company's corporate headquarters location in Montréal, Québec, Canada.

We enter into contracts in the normal course of business with CROs, CMOs and other third parties for clinical trials, preclinical research studies and testing and manufacturing services. These contracts are generally cancelable at our option with various notice requirements as defined in the contract. Payments

due upon cancellation consist of payments for services provided or expenses incurred, including noncancelable obligations of our service providers, up to and through the date of cancellation. These payments are not included in the preceding table as the amount and timing of these payments are not known.

Critical Accounting Policies and Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with United States generally accepted accounting principles, or U.S. GAAP. The preparation of these 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. 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.

Research & Development Expenses — Accruals and Tax Credits

Research and development costs are charged against income in the period of expenditure. Our research and development costs consist primarily of salaries and fees paid to contract research organizations, CROs, and to contract manufacturing organizations, or CMOs.

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

Share-Based Compensation

We recognize compensation costs related to share options granted to employees and directors based on the estimated fair value of the awards on the date of grant. We estimate the grant date fair value, and the resulting share-based compensation expense, using the Black-Scholes option-pricing model. This Black-Scholes option pricing model uses various inputs to measure fair value, including estimated fair value of our underlying common shares at the grant date, expected term, estimated volatility, risk-free interest rate and expected dividend yields of our common shares. The grant date fair value of the share-based awards is recognized on a straight-line basis over the requisite service periods, which are generally the vesting period of the respective awards. Forfeitures are accounted for as they occur.

For share-based awards granted to consultants and non-employees, we recognize compensation costs over the period during which services are rendered by such consultants and non-employees until completed. At the end of each financial reporting period prior to completion of the service, the estimated fair value of these awards is re-measured using the then-current fair value of our ordinary shares and updated assumption inputs in the Black-Scholes option-pricing model.

As there has been no public market for our common shares to date, the estimated fair value of our common shares has been determined by our board of directors as of the date of each option grant, with input from management, considering third-party valuations of our common shares as well as our board of directors' assessment of additional objective and subjective factors that it believed were relevant and which may have changed from the date of the most recent third-party valuation through the date of the grant. These third-party valuations were performed in accordance with the guidance outlined in the American Institute of Certified Public Accountants' Accounting and Valuation Guide, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation*. The assumptions underlying these valuations represent management's best estimates, which involve inherent uncertainties and the application of management judgment. As a result, if factors or expected outcomes change and we use significantly different assumptions or estimates, our share-based compensation expense could be materially different. After the completion of this offering, we will determine the per share fair value of our common shares based on the closing price of our common shares as reported by The Nasdaq Stock Market on the date of grant.

The following table summarizes, by grant date, the number of underlying common shares and the associated per-share exercise price, which was the fair value per share as determined by our board of directors on the applicable grant date, for share options granted during the years ended December 31, 2017 and 2018:

	Number of Common Shares Subject to Options Granted	Exercise Price Per Common Share	Estimated Fair Value per Common Share at Grant Date	Estimated Per-Share Fair Value of Options
January 3, 2017	18,382	$ 1.117	$ 1.117	$ 0.766
December 12, 2017	260,372	$ 1.543	$ 1.543	$ 1.064
February 21, 2018	820,450	$ 1.543	$ 1.543	$ 1.112
May 31, 2018	67,001	$ 1.543	$ 1.543	$ 1.112
August 15, 2018	82,774	$ 1.915	$ 1.915	$ 1.378
October 26, 2018	212,747	$ 2.660	$ 2.660	$ 1.904
November 21, 2018	493,485	$ 2.660	$ 2.660	$ 1.904
November 27, 2018	18,799	$ 2.660	$ 2.660	$ 1.904

The intrinsic value of all outstanding options as of December 31, 2018 was $31.4 million, based on the estimated fair value of our common shares of $15.00 per share, of which approximately $8.1 million related to vested options and approximately $23.3 million related to unvested options.

Quantitative and Qualitative Disclosures about Market 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 and cash equivalents and short-term investments of $86.0 million and $26.9 million as of December 31, 2018 and 2017, respectively, which consist primarily of bank deposits and guaranteed investment certificates. The primary objective of our investment activities is to preserve principal and liquidity while maximizing income without significantly increasing risk. 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 December 31, 2018 and 2017, our net monetary assets denominated in Canadian dollars was $0.8 million and $0.6 million, respectively.

Our operating results and financial position are reported in U.S. dollars in our 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.

Recent Accounting Pronouncements

Refer to Note 2, "Summary of Significant Accounting Policies," in the accompanying notes to our consolidated financial statements appearing elsewhere in this prospectus for a discussion of recent accounting pronouncements.

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 will comply with new or revised accounting standards when they are required to be adopted by public companies that are not emerging growth companies.

BUSINESS

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 or 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. Investigators reported an 87% termination rate of PSVT within 15 minutes at the dose selected for Phase 3 versus a 35% termination rate for placebo. We are actively recruiting patients for a Phase 3 clinical trial of etripamil, which may serve as a single pivotal efficacy trial, and we expect top-line data in the first half of 2020. In addition to the efficacy trial, our Phase 3 clinical program for etripamil for PSVT includes two open-label safety studies, one of which we initiated in December 2018, and the other we expect to initiate in the second half of 2019. We are also planning to initiate a Phase 2 clinical trial in the second half of 2019 in atrial fibrillation, another rapid heart rate condition, and expect to subsequently initiate an additional Phase 2 clinical trial in angina to establish proof-of-concept for the broader use of etripamil in 2020.

We believe that PSVT is a large and under-recognized market that we estimate affects approximately two million Americans, and results in over 600,000 healthcare claims in the United States per year, including emergency department visits, hospital admissions and ablations. We believe that, if approved, etripamil could prevent many of these healthcare encounters, saving the patient time and inconvenience, and potentially providing a cost-effective solution for the healthcare system. It is generally believed that patients are born with the anomaly that causes PSVT, and will have life-long episodes periodically and unpredictably. Patients experiencing an episode of PSVT are usually highly symptomatic, with a rapid heart rate, often over 200 beats per minute, causing palpitations, sweating, chest pressure or pain, shortness of breath, sudden onset of fatigue, lightheadedness or dizziness, fainting and anxiety.

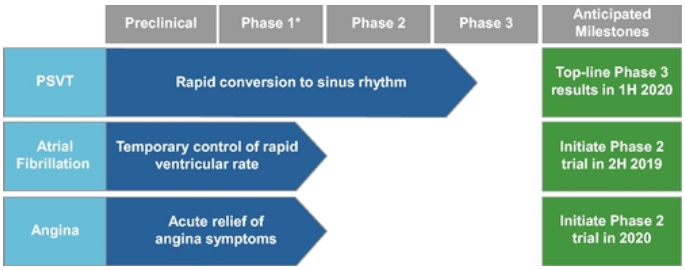
We currently have exclusive development and commercialization rights for etripamil for all indications that we may pursue. The composition-of-matter claims for etripamil as a new chemical entity give us a strong intellectual property position with patents issued in the United Stated through 2028, and with patent term extensions possible to 2031. In addition, we have an issued U.S. patent that extends the exclusivity period for the commercial formulation of etripamil to 2036.

We are led by a team of executives with extensive experience in successfully developing and commercializing therapies in cardiovascular and other indications at both major pharmaceutical and emerging life sciences companies. These therapies include Vytorin (ezetimibe & simvastatin), Ranexa (ranolazine), Effient (prasugrel), Northera (droxidopa), and Cologuard as well as several cardiac drugs in the classes of angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, and novel oral anticoagulants. We have raised approximately $139.2 million in gross proceeds from equity financings with a number of United States, Canadian and European healthcare specialist investment firms, including BDC Capital, Inc., Boxer Capital of Tavistock Group, Domain Associates, LLC, Fonds de solidarité FTQ, Forbion

Capital Partners, iNovia Capital, Novo Holdings A/S, Pappas Ventures, RTW Investments, LP, Tekla Capital Management LLC and Venrock Healthcare Capital Partners.

Our Pipeline

The following table sets forth the status and initial focus of etripamil.



* We are relying on our Phase 1 clinical trial of etripamil to support further clinical development of etripamil in PSVT, atrial fibrillation and angina.

Our Strategy

Our goal is to develop and commercialize etripamil for the treatment of PSVT and other cardiovascular indications, and to expand our pipeline to include additional clinical-stage compounds for other acute and/or episodic medical conditions. The key elements of our business strategy to achieve this goal include the following:

- ***Successfully complete development and obtain regulatory approval of etripamil for the treatment of PSVT.*** We are focused on efficiently developing and obtaining approval for etripamil to treat patients with PSVT. We are actively recruiting patients for a Phase 3 clinical trial of etripamil, which may serve as a single pivotal efficacy trial in the United States. We expect top-line data in the first half of 2020. We intend to first seek regulatory approval in the United States, followed by Europe and other major markets.

- ***Expand the scope of cardiovascular indications for etripamil beyond PSVT.*** We are exploring the use of etripamil for the treatment of patients with atrial fibrillation, another condition associated with a fast heart rate. We believe that etripamil could benefit patients with atrial fibrillation based on the approved use of intravenous, or IV, calcium channel blockers in these indications. We are also exploring the use of etripamil for the treatment of angina, which is chest pain typically associated with an imbalance between the supply of oxygen to and the demand for oxygen by the heart. Calcium channel blockers have already been approved for chronic management of angina. We believe there is an opportunity to treat angina with etripamil. We plan to test etripamil in Phase 2 proof-of-concept clinical trials with patients with atrial fibrillation and angina.

- ***Maximize the value of our programs by maintaining flexibility to commercialize our product candidates independently or through collaborative partnerships.*** We currently have exclusive development and commercialization rights for etripamil for our initial indications of PSVT, atrial fibrillation and angina. We plan to establish commercialization and marketing capabilities using a direct sales force to commercialize etripamil in the United States. Outside of the United States, we are considering commercialization strategies that may include collaborations with other companies.

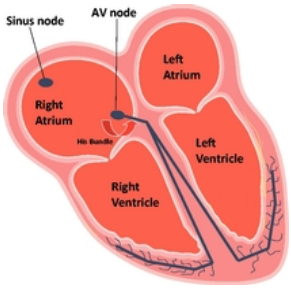
- ***Leverage our expertise and experience to expand our pipeline of product candidates.*** We seek to maximize our commercial opportunities by acquiring or in-licensing product candidates for indications with significant unmet need with a focus on clinically validated mechanisms that can yield novel treatments. We believe this approach may provide a more rapid path to regulatory

approval, faster adoption by medical professionals, nearer-term commercial value and more immediate clinical benefit for patients with significant need. Our leadership team has extensive experience in developing and commercializing successful drugs. We intend to leverage the collective talent within our organization and our network to guide our development plans and pipeline expansion.

Cardiac Conduction

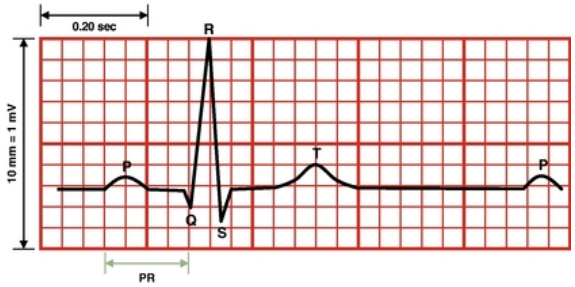
Normal Conduction

Within the right atrium, one of the heart's upper chambers, sits a specialized structure called the sinus node. The sinus node generates its own electrical signal, which spreads throughout both atria and is transmitted down to the lower chambers, the ventricles, and over another piece of electrical tissue called the atrio-ventricular, or AV, node, which is shown in the figure below. Once the signal reaches the ventricles, it causes them to contract, pumping blood out to the body. Another heart beat does not occur until a new signal is generated from the sinus node and the cycle repeats. Under normal conditions, passage from the sinus node over the AV node is the only way for the electrical impulse to travel from the atria down to the ventricles.



The electrical signal of each heart beat can be detected by placing sensors known as electrodes over the skin, and recorded over time in a tracing known as an electrocardiogram, or ECG. The ECG measures signal voltage and duration. To the trained interpreter, an ECG conveys a large amount of information about the structure and function of the heart, including among other things, heart rate and rhythm. Under normal physiologic conditions, an ECG has a characteristic pattern of waves corresponding to the electrical activity, contraction and relaxation of each heart chamber. This normal functioning is referred to as sinus rhythm and occurs at a heart rate of between 60 and 100 beats per minute at regular intervals.

As seen in the figure below, the various waves of an ECG tracing corresponding to the events of a single heart beat are named with the letters P, Q, R, S and T. The interval between the P wave and the R wave, known as the PR interval, is a measure of conduction over the AV node. A normal PR interval is 0.12-0.20 seconds in duration.



Arrhythmias

A disruption in the heart's normal rate or rhythm is called an arrhythmia. With an arrhythmia, the heart can beat too quickly, too slowly or with an irregular pattern. A faster than normal heat rate is called tachycardia; a slower than normal heart rate is called bradycardia. Symptoms of an arrhythmia can include palpitations, lightheadedness or dizziness, chest pain, shortness of breath or sweating. PSVT and atrial fibrillation are two of the most commonly occurring arrhythmias. While PSVT is characterized by a faster than normal heart rate where the heart beats at regular intervals, with atrial fibrillation the heart often beats faster than normal and always with a random, irregular rhythm. Pharmacologic treatment of PSVT focuses on terminating the arrhythmia using an agent to slow conduction over the AV node. With atrial fibrillation, there are two approaches to treatment: rate control to reduce the heart rate and rhythm control to restore sinus rhythm and prevent AF recurrences.

Etripamil

We designed and are developing etripamil, a novel, potent, rapid-onset and short-acting calcium channel blocker, as a nasal spray to be administered by the patient to terminate episodes of transient cardiovascular conditions as they occur. Short pharmacological action is sufficient to resolve an episode of PSVT. Accordingly, long-lasting drugs that remain in the body at significant concentrations long after the episode is resolved subject patients to unnecessary risk, given the potential for prolonged adverse events. Currently, we are in Phase 3 development for PSVT. We are also developing etripamil to provide rapid rate control and associated symptom relief for patients with acute episodes of atrial fibrillation and as an acute therapy for angina.

In our effort to develop potential therapies, we sought to create new chemical entities as analogs of known molecular classes with clinically-validated mechanisms of action. Our goal was to preserve the beneficial pharmacology of existing molecules while altering their pharmacokinetic profile with focused medicinal chemistry to produce drugs that are fast-acting and rapidly inactivated. As a result, we created a series of novel non-dihydropyridine L-type calcium channel blockers containing chemical ester moieties that preserved the desired pharmacology on the heart but that could be rapidly metabolized and inactivated in the blood by serum esterases. Etripamil resulted from this effort as a new chemical entity with a very short effective half-life of approximately 20 minutes in humans, compared with other calcium channel blockers that have half-lives of several hours.

We believe that the following qualities of etripamil make it a better treatment for certain episodic cardiovascular conditions than current standards of care:

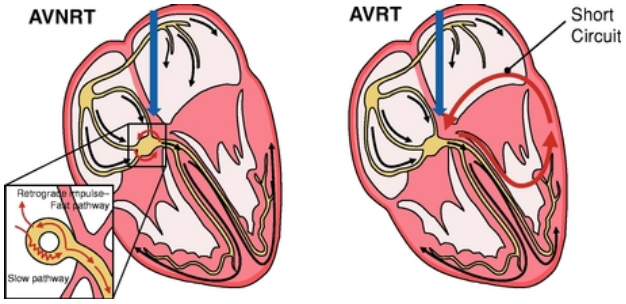
- *Short half-life*: Etripamil is a short-acting drug, and any adverse side effects that might occur should be short lived.
- *Fast onset*: Etripamil is designed to be rapidly absorbed into the bloodstream with a clinically meaningful concentration, allowing it to act quickly on the desired target (electrical conduction system or coronary blood vessels).
- *Convenient administration*: We developed etripamil so that it can be conveniently self-administered by patients via a nasal spray device.

To better understand the opportunity for etripamil in the United States and Europe, we have commissioned multiple market research studies. In 2017, we commissioned a study that involved qualitative in-depth interviews with 121 cardiologists, electrophysiologists, emergency medicine physicians, primary care physicians, PSVT patients and private and public payors in the United States, Germany, France, United Kingdom, Italy and Spain. In this research, physicians in these countries were exposed to a target product profile of etripamil based on our Phase 2 trial results and reported that they would use etripamil in 3.5 times as many PSVT patients as those receiving a catheter ablation, which they report as 10% of their PSVT patients. From the same research, PSVT patients in the United States reported going to the emergency department for approximately 10% of their PSVT episodes and anticipated being able to avoid 50% to 75%

of these emergency department visits per year by using etripamil. PSVT patients in this market research also reported a desire to use etripamil three to five times per year.

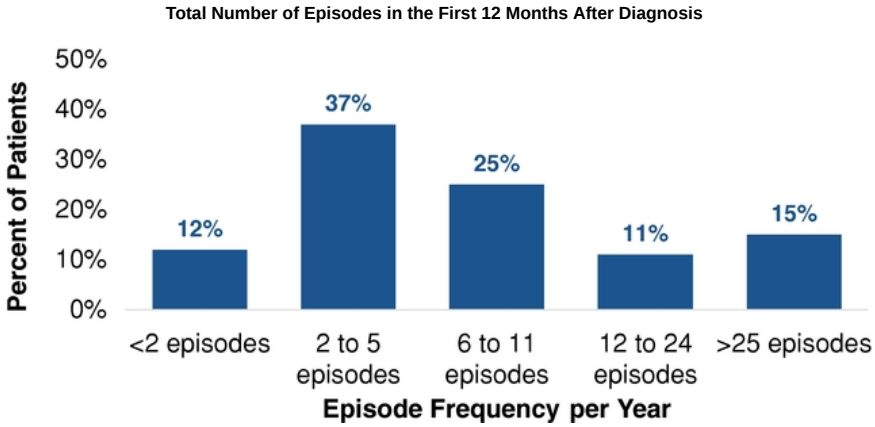
PSVT

PSVT is a serious and recurring electrical disorder of the heart, which is caused by altered electrical conductivity over the AV node. PSVT refers to a rapid heart rate condition of the heart's upper chambers (atria) of abrupt onset and termination. In the most common form of PSVT called AV nodal reentrant tachycardia, or AVNRT, there is an extra piece of electrical tissue that allows the electrical signal to travel very rapidly in a circle. As shown in the figure below, when that extra tissue forms within or near the AV node, the signal can now travel down one part of the AV node and up the other in a small circle, sending impulses out to both the atria and ventricles along the way. The cycle continues over and over, resulting in a rapid heart rate.



In the next most common form of PSVT, called atrio-ventricular reciprocating tachycardia, or AVRT, there is an extra piece of electrical tissue that directly connects the atria and the ventricles. In AVRT, the electrical signal begins like it would in a normal heart beat by traveling from the atria to the ventricles over the AV node. However, as shown in the figure above, in AVRT, the extra piece of electrical tissue allows the signal to travel back up to the atria, creating a "short circuit." Once the signal gets back to the atria, it goes back down the AV node and the cycle continues over and over, resulting in a rapid heart rate.

Uncertainty of the timing and duration of episodes of PSVT can significantly impact patient quality of life. In 2018, we conducted a quantitative internet survey involving 256 patients with PSVT. The survey was designed to assess the impact of PSVT on patients prior to and after their diagnosis and explored the key patient drivers of disease burden, including episode frequency, duration, perceived severity of symptoms and emergency department visits. The survey included both newly-diagnosed PSVT patients and patients who had been diagnosed with PSVT for some time. The previously diagnosed patients had an average time since diagnosis of seven years. We estimate that, overall, 60% of PSVT patients are women and approximately half suffer from cardiovascular comorbidities. The figure below shows the surveyed patients' total number of PSVT episodes in the first 12 months after diagnosis.



Patients reported episode frequencies that vary from less than one per year to greater than 25 per year. Based on this market research, we estimate that patients with PSVT experience a median of four to seven episodes of PSVT per year. These episodes can be debilitating for patients, who can be left unable to focus on family or work during an episode. While experiencing an episode of PSVT, patients may experience symptoms including palpitations, sweating, chest pressure or pain, shortness of breath, sudden onset of fatigue, fainting and anxiety. Symptoms commonly reported by patients with PSVT mimic other conditions and are often mistaken for anxiety or panic attacks, especially in women. Researchers have noted that up to 27% of PSVT patients stopped driving for fear of temporary loss of consciousness, fainting or passing out. Patients have reported that the duration of PSVT episodes varies widely from minutes to hours, or more. Our market research indicates that in the year of diagnosis almost 40% of patients experience two or more episodes of PSVT per year that last more than 10 minutes each, and a similar percentage visit the emergency department for treatment of their PSVT at least once per year. We also estimate that 65% of PSVT patients have used chronic medications prophylactically to reduce episode frequency. Our market research also shows that after the first year of diagnosis the percentage of patients with PSVT episodes lasting longer than 10 minutes and the percentage visiting the emergency department for treatment decreases modestly to approximately one-third of those surveyed. Based upon our survey responses, we believe these decreases in both duration of episodes and emergency department visits are attributable to a combination of prophylactic medication use and proper implementation of vagal maneuvers.

Current Treatment Options for PSVT

Treatment for PSVT depends on the frequency, duration, and severity of the episodes as well as patient preference. Current options for PSVT patients to terminate an episode include vagal maneuvers, IV medication or external shock delivered in the emergency department. Additionally, some practitioners prescribe oral medications, such as calcium channel blockers, beta blockers and anti-arryhthmic drugs to be taken at the onset of an episode. However, these interventions are generally not acutely effective. Long-term strategies include chronic drug therapy to reduce the frequency of episodes and cardiac ablation to potentially cure the disease. Patients may also elect to not treat their symptoms and simply endure episodes when they occur.

Vagal maneuvers can be attempted to terminate an episode, with low to modest success rates. These are physiological maneuvers that stimulate the vagus nerve, which can terminate a PSVT episode. These include gagging, massaging the carotid artery, holding one's breath and bearing down (Valsalva maneuver), immersing one's face in ice-cold water, or coughing.

Currently approved acute pharmacological therapy for the treatment of an acute episode of PSVT includes IV administration of approved AV nodal-blocking agents in an acute care setting. The current standard of care for treatment of episodes of PSVT is adenosine, but prior to its approval in 1990, episodes of PSVT were treated with IV calcium channel blockers, such as verapamil or diltiazem. When given as a rapid IV bolus, adenosine blocks conduction over the AV node, thereby interrupting the arrhythmia circuit and restoring the heart back to sinus rhythm. Adenosine temporarily stops the heart and patients have reported experiencing chest tightness, flushing and a sense of impending death. Physicians report that patients tell them that they feel like they are going to die. Adenosine is eliminated from the body in less than one minute, but cannot be self-administered as it requires IV access. In-hospital IV administrations are associated with higher healthcare costs, and are also unsettling and inconvenient for the patient. IV calcium channel blockers also slow conduction over the AV node during the course of several minutes. However, they are associated with the risk of excessive slowing of the heart rate and low blood pressure. According to treatment guidelines, patients in the acute care setting who fail pharmacologic treatment for PSVT could then receive direct current cardioversion, where an electric shock is applied to the heart to return it to sinus rhythm.

In an attempt to prophylactically control the frequency and duration of future PSVT episodes, many patients will take chronic daily oral medications that modulate AV nodal conduction, such as beta blockers, L-type non-dihydropyridine calcium channel blockers, or anti-arrhythmic drugs. Despite chronic daily oral medication, breakthrough PSVT episodes that require visits to the emergency department may still occur, albeit at a reduced frequency. Chronic medication can lead to side effects such as sexual dysfunction or fatigue in the case of beta blockers and constipation in the case of verapamil. Some patients discontinue chronic oral medication due to intolerable side effects. Based on our market research, we estimate that approximately two-thirds of PSVT patients have been prescribed chronic medications such as beta blockers or calcium channel blockers to prevent PSVT episodes.

The only potentially curative treatment available at the present time for PSVT is ablation, an invasive procedure, which works by directly cauterizing or freezing the short circuit that is the cause of the abnormal rhythm. This is achieved in an electrophysiology lab via catheters that are run through the patient's groin vessels and into the heart and uses burning or freezing techniques to destroy the heart's abnormal electrical tissue. Ablation single-procedure success rates for PSVT are reported to be 91% to 96%. However, we estimate that less than 10% of patients with PSVT per year choose this option, which we believe is due primarily to anxiety related to the procedure. Although ablations are generally considered to be safe by the treating community, as with any invasive procedure there are potential complications, which include bleeding, blood clots, pericardial tamponade, and transient or permanent heart block, with the latter requiring permanent pacemaker implantation.

Market Opportunity

We believe that PSVT is a large and under-recognized market that we estimate affects approximately two million Americans and results in over 600,000 healthcare claims in the United States alone per year, including more than 150,000 emergency department visits and hospital admissions and up to 80,000 ablations. Published sources documenting the epidemiology of PSVT rely on a single medical encounter that is confirmed by an ECG to estimate incidence and prevalence, which we believe significantly underestimates the prevalence due to the episodic nature of the disease as well as the variability in the duration of the episodes. Our use of longitudinal claims data has identified a larger prevalence of PSVT in the United States. Based on an analysis of longitudinal Medicare claims data for patients age 65 and older and employer-based medical claims data for patients under age 65 between 2012 and 2016, we project prevalence for all ages to be approximately two million, with approximately 300,000 new PSVT patients being diagnosed each year in the United States. The prevalence analyses were recently published and presented at the 2018 International Academy of Cardiology's Scientific Sessions. From market research conducted in 2017 and 2018, we estimate a target addressable market of approximately 40-65% of the prevalent population that we estimate has a higher burden of PSVT as measured by episode duration, emergency department visits and prophylactic use of chronic medications to reduce episode frequency.

Current treatment approaches for PSVT consume significant healthcare resources. Our longitudinal analysis has shown that mean annual costs per PSVT patient increase by more than $17,000 after diagnosis to approximately $30,000, with the largest increases coming from outpatient hospital and inpatient spending. In addition, this analysis concluded that rates of emergency department visits and hospitalizations were 1.8 and 3.0 times higher, respectively, following diagnosis. In total, we estimate from these claims data that approximately $3 billion is spent each year in the United States on treatments for PSVT.

Our Clinical Development Program for the Treatment of PSVT

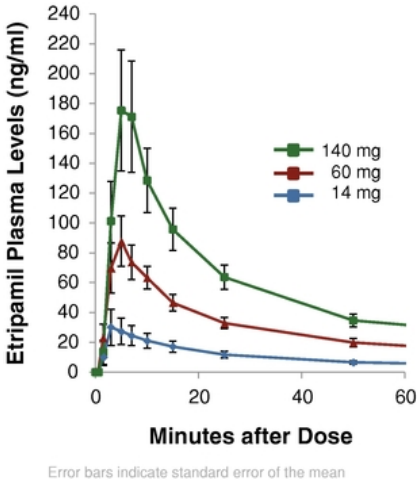
Current treatments do not address the unmet medical need for a rapidly-acting, effective, and safe patient-administered treatment that can be taken outside of a hospital or acute care setting at the onset of a PSVT episode to restore the heart back to sinus rhythm. We believe that etripamil fills this need. We completed a Phase 1 clinical trial, which supported the selection of four doses of etripamil for Phase 2 development, followed by a Phase 2 clinical trial in adult patients to evaluate the effects of those four doses in patients with PSVT. Both trials were conducted to assess nasally-administered etripamil compared to placebo. Based on discussions with the FDA, we initiated a single pivotal Phase 3 clinical trial in July 2018 to assess the efficacy and safety of etripamil in the outpatient setting, and expect top-line data in the first half of 2020. We also intend to conduct two open label safety trials. The FDA agreed that our Phase 3 clinical trial and these safety trials could support an NDA filing in the United States.

Phase 1 Clinical Data

We completed a Phase 1 clinical trial in healthy volunteers, which was designed to assess the safety, pharmacokinetic, or PK, profile, and cardiac pharmacology of intra-nasally administered etripamil in a randomized, double-blind, placebo-controlled, single ascending dose trial. The primary objective of this trial was to determine the maximum tolerated dose or maximum feasible dose of two different etripamil formulations administered via the nasal route in healthy, adult male subjects. All etripamil doses were generally well tolerated, and there was no difference in the safety profile and PK between the two etripamil formulations, referred to as MSP-2017A and MSP-2017B. The study of MSP-2017A was stopped at 60 mg and MSP-2017B was further studied at higher doses (105 mg and 140 mg). The Phase 1 results supported the selection of four doses of etripamil for Phase 2 development. We are using this Phase 1 data to support further clinical development of etripamil in three indications: PSVT, atrial fibrillation and angina.

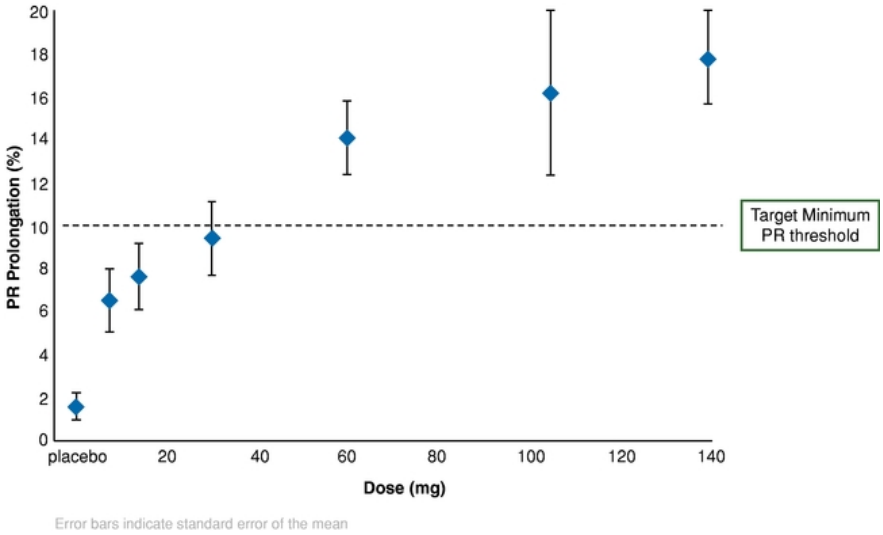
Following nasal administration of etripamil, PK analyses demonstrated rapid absorption and elimination, a dose-proportional systemic exposure, or area under the curve, and maximum plasma concentration for etripamil and its primary inactive metabolite. These findings were consistent across a range of six doses tested up to 140 mg, i.e., two sprays of 100 µL of solution of 35 mg of etripamil in each nostril. The 140 mg dose was the maximal feasible dose because neither the concentration (350 mg/mL) nor the volume (200 µL) of solution administered in each nostril could be increased. Due to these characteristics of formulation and delivery, a maximum tolerated dose of etripamil was not established. The figure below shows the rapid absorption via the nasal route and the rapid decrease in plasma concentration of etripamil.

Pharmacokinetic Profile of Etripamil Plasma Concentrations in Phase 1



Prolongation of the PR interval as measured by ECGs was taken as the pharmacodynamic measure. A linear relationship was observed between the etripamil dose and prolongation of the PR interval. The 60 mg, 105 mg, and 140 mg doses demonstrated a 10% or greater PR prolongation, which is shown in the figure below. This correlates with the reported slowing of conduction over the AV node that is necessary to convert a PSVT episode to sinus rhythm. Such slowing of conduction has already been observed clinically with IV AV nodal agents such as adenosine, verapamil and tecadenoson.

Phase 1 Pharmacology

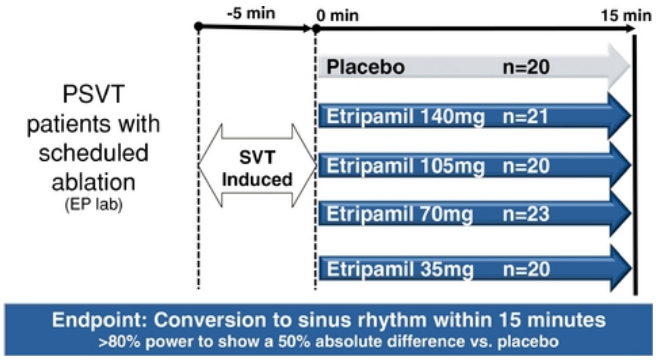


Phase 2 Clinical Data

We completed a Phase 2 multi-center, randomized, double-blind, placebo-controlled clinical trial in the United States and Canada to evaluate the effects of four different doses of etripamil in patients with PSVT. In order to demonstrate the ability of etripamil to terminate PSVT in a controlled setting, we conducted the study in the electrophysiology, or EP, laboratory setting, where the PSVT episode could be induced in patients scheduled to undergo an EP study and ablation. The primary objective of this trial was to demonstrate the superiority of at least one dose of etripamil over placebo in terminating PSVT. The secondary objectives were to determine the minimally effective dose of etripamil, to establish a dose-related efficacy trend for etripamil, and to evaluate the safety of etripamil in a clinical setting. The trial was statistically powered at more than 80% to show a 50% absolute difference of etripamil versus placebo.

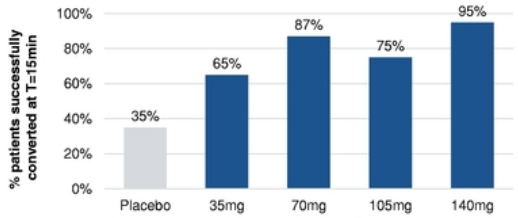
The trial enrolled 199 patients, of which 95 withdrew prior to dosing: 70 due to inability to induce (n=42) or sustain (n=28) PSVT, 5 based on physician discretion, 1 lost to follow up, 1 due to withdrawal of consent, and 18 for other reasons. The mean age of patients was 52.2 years, with the study enrolling patients as young as 19 and as old as 85. As shown in the figure below, PSVT was induced and sustained for ³5 minutes in 104 patients, who were then randomized into one of five dosing cohorts. Four cohorts received active doses of etripamil (35 mg, 70 mg, 105 mg or 140 mg) and one cohort received placebo. All doses of the study drug were delivered in a blind randomized fashion in which healthcare providers administered four 100 µL sprays from four different single-spray devices. There were no imbalances in baseline characteristics across the five treatment groups. The mean heart rate in PSVT at time 0 was 177 bpm in the placebo group and 168 bpm, 173 bpm, 180 bpm and 155 bpm in the etripamil 35 mg, 70 mg, 105 mg and 140 mg groups, respectively.

Phase 2 Clinical Trial Design



The primary endpoint in this clinical trial was the conversion of PSVT to sinus rhythm within 15 minutes after administration of etripamil or placebo. As shown in the figure below, the percentage of patients in whom PSVT converted to sinus rhythm within 15 minutes of study drug administration was 65% with 35 mg etripamil, 87% with 70 mg, 75% with 105 mg and 95% with 140 mg, compared with 35% in the placebo arm. The three highest doses of etripamil showed statistically significant conversion rates compared with placebo. Statistical significance expresses the probability that the results of a particular study could have occurred purely by chance. Statistical significance is assessed by the FDA and other health regulatory agencies in evaluating marketing approval applications. FDA and other regulatory agencies review the strength of the statistical evidence and whether it supports the claims of the applicant. The primary endpoint, statistical methods for the trial and a p-value boundary for achieving statistical significance for a clinical trial are typically defined before the trial begins. If the probability of observing the calculated statistic is smaller than the p-value boundary, the primary endpoint is considered statistically significant. P-value is a conventional statistical method for measuring the statistical significance of clinical results. A p-value of 0.05 or less represents statistical significance, meaning there is a less than 1-in-20 likelihood that the observed results occurred by chance. The FDA utilizes statistical significance, as measured by p-value, as an evidentiary standard of efficacy and typically requires a p-value of 0.05 or less to demonstrate statistical significance.

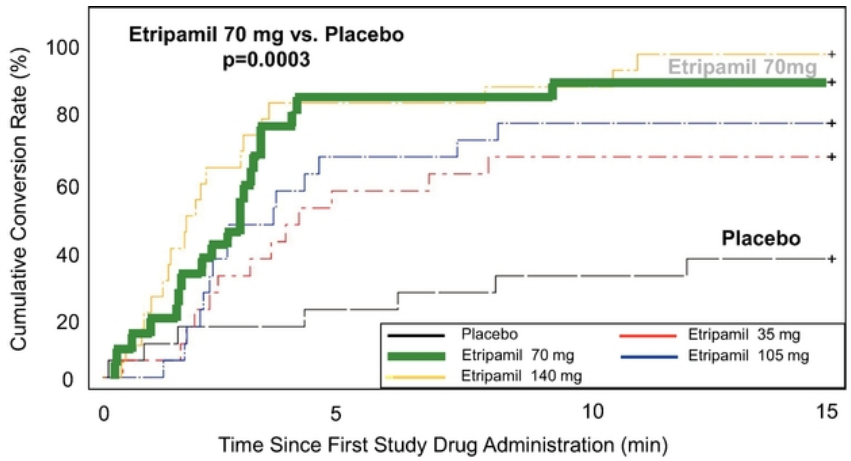
Etripamil Conversion Rates from PSVT to Sinus Rhythm in Phase 2



# patients converted at 15 min	7/20	13/20	20/23	15/20	20/21
p-value		0.1128	0.0006	0.0248	<.0001

In a post-hoc analysis conducted to help inform our Phase 3 trial design, the patients' time to conversion to sinus rhythm was examined. As shown in the following Kaplan-Meier plot of patients successfully converting to sinus rhythm during the 15 minute study window, the three highest etripamil doses of 140 mg, 105 mg and 70 mg showed statistically significant shorter time to conversion compared with placebo. The 70 mg dose showed a rapid onset of action with a median time to conversion of less than three minutes after nasal administration of etripamil.

Etripamil Time to Conversion from PSVT to Sinus Rhythm in Phase 2



		Patients Converting at Each Time Interval			
		0 min	5 min	10 min	15 min
Placebo		20	4	6	7
Etripamil	35 mg	20	11	13	14
Etripamil	70 mg	23	19	20	21
Etripamil	105 mg	20	13	15	16
Etripamil	140 mg	21	17	18	20

Overall, etripamil was well tolerated, and the most common adverse events were related to the nasal route of administration, e.g., nasal irritation or nasal congestion, reported by up to 60% and 45% of patients, respectively, after etripamil versus none after placebo administration. The 70 mg dose was reported to have 48% nasal irritation and 26% nasal congestion. However, these were transient. Most adverse events were mild (44.2%) or moderate (24.0%) across all treatment groups. At least one adverse event considered related to the study drug, according to the investigator assessment, was reported in 17 (85.0%) patients in the etripamil 35 mg group, 18 (78.3%) in the 70 mg group, 15 (75.0%) in the 105 mg group, 20 (95.2%) in the 140 mg group and 4 (20.0%) in the placebo group. The incidence of adverse events was not dose dependent. Hypotension, or low blood pressure, was reported as an adverse event in two patients, one in the etripamil 105 mg dose group and one in the 140 mg group.

A total of three patients experienced severe adverse events that were considered possibly related to etripamil. One patient who received an etripamil dose of 35 mg experienced facial flushing, shortness of breath, and chest discomfort. One patient who received an etripamil dose of 105 mg had nausea and

vomiting, as well as a severe and serious cough. One patient who received an etripamil dose of 140 mg experienced a severe adverse event of second degree AV block with hypotension beginning five minutes after conversion to sinus rhythm. The AV block resolved after 43 minutes and ablation was subsequently performed. There were no adverse events that led to study discontinuation or death.

Calcium channel blockers have the potential to cause hypotension as a side effect. In our Phase 2 clinical trial, we recorded vital signs, including heart rate and blood pressure, before induction of PSVT and every two minutes for 30 minutes after study drug was given. We observed no meaningful reduction in mean blood pressure in the 35 mg or 70 mg etripamil cohorts, but observed a transient decrease in the mean blood pressure in the two highest cohorts, 105 mg and 140 mg. Due to the induction of PSVT, the mean systolic blood pressure decreased at time 0 compared to the average at 20 and 10 minutes before PSVT induction. Compared to baseline and time 0, systolic blood pressure measurements recorded from 2 minutes to 16 minutes post study drug administration showed no decrease in mean systolic blood pressure in the placebo or 35 mg groups, and maximum mean decreases of 2 mmHg four minutes post-dose in the 70 mg group, 17 mmHg six minutes post-dose in the 105 mg group, and 20 mmHg six minutes and eight minutes post-dose in the 140 mg group.

Based on the combination of efficacy and safety data from our Phase 2 trial, we selected the 70 mg dose for our subsequent clinical trials. There was no decrease in mean systolic blood pressure compared to baseline from 16 to 30 minutes post-study drug administration.

Ongoing and Planned Clinical Development of PSVT

We had an end-of-Phase 2 meeting with the FDA in September 2017 to review our Phase 2 clinical trial results and to discuss our proposed Phase 3 clinical program. The FDA agreed with our proposal to assess the efficacy of etripamil in PSVT patients in the outpatient setting and suggested that we consider conducting a single pivotal trial to assess the efficacy of etripamil, followed by two open label safety trials. The FDA further confirmed that a large outcome trial would not be required for etripamil and that the total NDA safety database could consist of up to 1,500 patients. Finally, the FDA agreed that our upcoming Phase 3 program, if successful, could support efficacy claims in an NDA filing in the United States. We also had a meeting to obtain Scientific Advice from the European Medicines Agency, or EMA, in April 2018. The EMA agreed that our planned Phase 3 program could support a registration in the European Union but recommended additional safety data in non-induced episodes of PSVT.

Based on our interactions with the regulatory agencies, our planned Phase 3 clinical program includes:

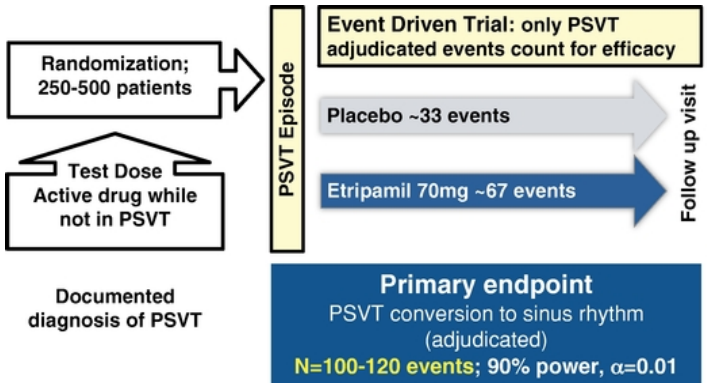
- NODE-301, a pivotal efficacy trial to assess the time to conversion of etripamil compared to placebo in outpatients;
- NODE-302, an open-label extension of NODE-301 to enroll patients who have completed NODE-301 in order to collect safety data on subsequent episodes; and
- NODE-303, an open-label global safety trial to complete the safety assessment of etripamil in outpatients to support an NDA.

Phase 3 Clinical Trials

NODE-301. NODE-301 is our ongoing placebo-controlled Phase 3 clinical trial being conducted in the United States and Canada to evaluate etripamil 70 mg versus placebo in terminating a PSVT episode in the outpatient setting. As shown in the figure below, the primary endpoint is the time to conversion over a five-hour monitoring period following the start of the episode. Prior to randomization, eligible patients are administered a test dose of 70 mg etripamil in the investigators' office while in sinus rhythm in order to ensure tolerability. Patients successfully completing the test dose are randomly assigned to the etripamil or placebo cohorts (2:1 randomization) and sent home with the study drug and a small portable cardiac monitor that can be used during the patient's subsequent PSVT episode. Upon experiencing their next PSVT episode, patients are instructed to first apply the cardiac monitoring device to record ECG data, then attempt a vagal maneuver, and if that is not successful in terminating the episode, to then dose the drug. The ECG data will be reviewed by an adjudication committee to determine the type of arrhythmia during the

episode and the time to conversion to sinus rhythm. NODE-301 will enroll up to 500 diagnosed PSVT patients meeting inclusion and exclusion criteria and will be completed when a total of 100 to 120 adjudicated PSVT events are treated.

Phase 3 Clinical Trial Design



In moving from the monitored setting of our Phase 2 trial to the outpatient setting of NODE-301, we conducted several human factor studies to optimize the operational parameters, such as use of the cardiac monitoring device, how to conduct vagal maneuvers and how to correctly use the nasal spray device. We plan to conduct additional human factor studies to evaluate the final commercial instructions for use for etripamil. The results of these studies will be submitted with the NDA for etripamil.

Each patient will stay in the NODE-301 trial until one episode of PSVT is treated with etripamil or placebo. All the patients completing a study closure visit for the NODE-301 trial will have the opportunity to continue in the open-label NODE-302 clinical trial and self-manage subsequent episodes of PSVT with etripamil. Topline results from NODE-301 are expected in the first half of 2020.

NODE-302. NODE-302 is the open-label extension trial of NODE-301. We designed NODE-302 to evaluate the safety of etripamil when self-administered without medical supervision and to monitor the safety and efficacy of etripamil for the treatment of multiple episodes of PSVT.

Patients who have successfully dosed with the study drug in NODE-301 and completed a study closure visit will be eligible to enroll in NODE-302 to manage any subsequent episodes of PSVT. Patients who were randomized in NODE-301, but did not experience any PSVT episode, or had not used the study drug at the time of the NODE-301 trial completion, will also be eligible for NODE-302. Eligibility will also be contingent on satisfying all inclusion and exclusion criteria, including not experiencing a serious adverse event related to the study drug or the study procedure that precludes the self-administration of etripamil.

We initiated NODE-302 in December 2018, the trial is ongoing and enrollment is still relatively limited at this stage. Trial safety results will contribute to the etripamil safety database.

NODE-303. NODE-303 will be an open-label global safety trial consisting of up to 1,500 patients who did not participate in NODE-301 or NODE-302. We designed NODE-303 to evaluate the safety of etripamil when self-administered without medical supervision, and to evaluate the safety and efficacy of etripamil on multiple PSVT episodes. The patients have the opportunity to manage several episodes of PSVT in NODE-303.

We expect to initiate NODE-303 in the second half of 2019.

Etripamil in Other Indications

Our goal in expanding our pipeline is to apply the same treatment paradigm-changing aspiration that we have for PSVT to other cardiac conditions where we believe that a rapid-onset, short-acting calcium channel blocker could potentially deliver significant clinical and quality of life benefits for patients. We believe that the same insights that led to the development of etripamil for the treatment of PSVT are relevant in other indications in which AV-nodal blocking agents and vasodilators have demonstrated clinical utility. Both calcium channel blockers and beta blockers are indicated to manage not only PSVT, but also to provide temporary control of rapid ventricular rate in atrial fibrillation and acute relief of angina symptoms.

Atrial Fibrillation

Overview

Atrial fibrillation is a common form of arrhythmia with an irregular and often rapid heart rate that can increase the risk of stroke, heart failure and other heart-related complications. During atrial fibrillation, the heart's two upper chambers, the atria, beat chaotically and irregularly — out of coordination with the two lower chambers, the ventricles, of the heart. Atrial fibrillation symptoms often include heart palpitations, shortness of breath and weakness. Episodes of atrial fibrillation can come and go, or patients may have atrial fibrillation that does not go away and may require treatment. Although the heart arrhythmia in atrial fibrillation itself usually is not life-threatening, it is a serious medical condition that sometimes requires emergency treatment. Prevalence estimates range from four to six million patients suffering from atrial fibrillation in the United States. Approximately 25% of these patients have paroxysmal atrial fibrillation, another 25% have persistent atrial fibrillation, while 50% have permanent atrial fibrillation.

Acute episodes of symptomatic atrial fibrillation are often treated with IV calcium channel blockers and beta blockers under medical supervision, usually in the emergency department to quickly reduce heart rate before transitioning a patient back to oral therapy.

Our Solution

There are currently two pharmacological approaches to managing atrial fibrillation: rate control to lower a rapid heart rate and rhythm control to restore and maintain a regular rhythm. For rate control, the rapid heart rate of atrial fibrillation is often treated with calcium channel blockers or beta blockers to control symptoms and improve cardiac function. Oral rate control drugs do not provide immediate ventricular rate control due to the delayed 30 to 60 minute onset of action by the oral route. Breakthrough episodes of symptomatic atrial fibrillation often require urgent medical treatment with IV calcium channel blockers and beta blockers under medical supervision, usually in the emergency department to quickly reduce heart rate before transitioning a patient back to oral therapy. We believe that etripamil can be used by patients to rapidly reduce their heart rate in the outpatient setting on top of the oral rate or rhythm control strategy their physician has already prescribed. We believe that the combination of convenient delivery, potency, rapid-onset, and short duration of action of etripamil has the potential to move the current treatment setting for some acute symptomatic episodes of atrial fibrillation out of the burdensome and costly emergency department.

Clinical Development Plan for Atrial Fibrillation

We are using the Phase 1 clinical trial data regarding the safety, PK profile and cardiac pharmacology of etripamil (see "—PSVT—Our Clinical Development Program of the Treatment of PSVT—Phase 1 Clinical Data"), to pursue clinical development of etripamil in atrial fibrillation. We believe this Phase 1 clinical trial data is sufficient to support Phase 2 development of etripamil for this additional indication. We are planning a small Phase 2 trial in patients with atrial fibrillation as a proof-of-concept to test the efficacy of one or two doses of etripamil against placebo in reducing heart rate and to test the onset and duration of effect. We expect to initiate this trial in the second half of 2019 after submission of the appropriate regulatory filing (IND or equivalent) in the country where the trial is planned to be conducted.

Angina

Overview

Angina is chest pain caused by an imbalance between the supply of oxygen to and the demand for oxygen by the heart. It can feel like pain, pressure or squeezing in the chest, but the discomfort also can occur in the shoulders, arms, neck, jaw, or back. Angina may be due to a number of factors, but is primarily caused by either occlusion or spasm of the coronary arteries. The coronary arteries sit on the surface of the heart muscle and supply it with oxygen and nutrients with each heart beat. Coronary occlusion is most often caused by the deposition of fatty plaques that narrow the arteries and reduce blood flow, a condition known as coronary artery disease, or CAD, which can lead to a heart attack. Coronary spasm is the sudden and involuntary tightening of the muscles within the coronary arteries, which narrows them and reduces blood flow to the heart. It may be due to high blood pressure, high cholesterol, or certain drugs. The coronary spasm form of angina, also known as variant or Prinzmetal's angina, represents two out of every hundred cases of angina. Angina from CAD is characterized as one of two forms: stable or unstable. Stable angina is the most common form, affecting approximately 3% of the adult population, or almost approximately nine million patients in the United States. It manifests when the heart works harder than usual to pump blood through narrowed coronary arteries and can be triggered by physical exertion or other factors such as emotional stress. Episodes are typically short-lasting, five minutes or less, and disappear soon after exercise is terminated or after using angina medication. Symptoms resolve with rest. Unstable angina is new onset chest pain or angina that gets worse or becomes more frequent, and can be a sign of an impending heart attack.

Our Solution

There are several medical treatments available to treat stable angina caused by CAD, including nitrates, beta blockers and calcium channel blockers. Only nitrates provide immediate relief, but all three classes of drug are indicated for prophylactic use. Nitrates work by dilating or widening coronary blood vessels, allowing more blood to flow to the heart muscle. Short-acting nitrates are used acutely to relieve angina-related chest discomfort, or prophylactically before doing something that normally triggers angina, such as physical exertion. Nitroglycerin is a common form of nitrate that is available primarily in sublingual formulations for rapid symptom relief. It is also available as a cream or patch that can be applied to the skin. In up to 20% of patients, nitroglycerin is not tolerated and additional patients do not respond to the treatment. For example, nitroglycerin can cause severe headaches that necessitate analgesic intervention for pain relief, the painful nature of which can have a marked negative effect on patient compliance. Nitroglycerin also can cause severe hypotension, circulatory collapse, and death if used together with phosphodiesterase type 5 inhibitor drugs that are used for the treatment of erectile dysfunction, such as Viagra (sildenafil), Adcirca and Cialis (tadalafil), and Levitra and Staxyn (vardenafil). In addition to their use in CAD, calcium channel blockers are also prescribed for coronary spasm, however, they do not provide immediate relief. We are not aware of any approved rapid-onset, short acting treatments for coronary spasm.

We believe that etripamil can be used to rapidly reduce or relieve angina symptoms in the outpatient setting in both patients with stable angina who cannot tolerate or do not respond to nitrates, and in patients experiencing coronary spasm.

Clinical Development Plan for Angina

We are using the Phase 1 clinical trial data regarding the safety, PK profile and cardiac pharmacology of etripamil (see "—PSVT—Our Clinical Development Program of the Treatment of PSVT—Phase 1 Clinical Data"), to pursue clinical development of etripamil in angina. We believe this Phase 1 clinical trial data is sufficient to support Phase 2 development of etripamil for this additional indication. We are in the early stages of planning small Phase 2 clinical trials as proof-of-concepts to test the efficacy and safety of etripamil in various forms of angina. We expect to initiate a Phase 2 clinical trial in angina in 2020 after submission of the appropriate regulatory filing (IND or equivalent) in the country where the trial is planned to be conducted.

Sales and Marketing

Given our stage of development, we have not yet established a commercial sales and marketing organization or distribution capabilities. We currently have exclusive global development and commercialization rights for etripamil for all indications that we may pursue and believe that we can maximize the value of etripamil by retaining commercialization rights in the United States and entering into collaboration agreements for certain territories outside the United States. Our current strategy is to market etripamil in the United States for the treatment of PSVT using a targeted direct sales force focused on clinical cardiologists, electrophysiologists, and high-volume primary care physicians who have a history of prescribing anti-arrhythmic therapies. We believe that a majority of PSVT patients are managed by these cardiovascular specialists and that a targeted sales force will be able to reach a substantial portion of the market for etripamil.

Manufacturing

We currently rely on third-party contract manufacturing organizations, or CMOs, for all of our required raw materials, nasal spray device, API and finished product for our clinical trials and for our preclinical research. We require all of our CMOs to conduct manufacturing activities in compliance with current good manufacturing practice, or cGMP, requirements. We have assembled a team of experienced employees and consultants to provide the necessary technical, quality and regulatory oversight over our CMOs and have implemented a comprehensive plan for audits of our CMOs. Currently, we have development contracts and quality agreements with our CMOs for the manufacturing of etripamil drug substance and drug product. We currently have enough manufactured supply of etripamil to complete our ongoing NODE-301 and NODE-302 trials. We also may elect to pursue additional CMOs for manufacturing supplies of regulatory starting materials in the future and for the filling of the nasal spray device, labeling, packaging, storage and distribution of investigational drug products. We plan to continue to rely on third-party manufacturers for any future trials and commercialization of etripamil, if approved. We anticipate that these CMOs will have capacity to support commercial scale production, but we do not have any formal agreements at this time with these CMOs to cover commercial production. We believe we can identify and establish additional CMOs to provide API and finished drug product without significant disruption to our business or clinical development timelines. If etripamil is approved by any regulatory agency, we intend to enter into agreements with a third-party contract manufacturer and one or more backup manufacturers for the commercial production of etripamil.

Competition

Drug development is highly competitive and subject to rapid and significant technological advancements. Our ability to compete will significantly depend upon our ability to complete necessary clinical trials and regulatory approval processes, and effectively market any drug that we may successfully develop. Our current and potential future competitors include pharmaceutical and biotechnology companies, academic institutions and government agencies. The primary competitive factors that will affect the commercial success of etripamil or any other product candidate for which we may receive marketing approval include efficacy, safety, tolerability, dosing convenience, price, coverage and reimbursement. Many of our existing or potential competitors have substantially greater financial, technical and human resources than we do and significantly greater experience in the discovery and development of product candidates, as well as in obtaining regulatory approvals of those product candidates in the United States and in foreign countries.

Our current and potential future competitors may also have significantly more experience commercializing drugs that have been approved for marketing. Mergers and acquisitions in the pharmaceutical and biotechnology industries could result in even more resources being concentrated among a small number of our competitors.

Accordingly, our competitors may be more successful than us in obtaining regulatory approval for therapies and in achieving widespread market acceptance of their drugs. It is also possible that a competitor may

develop a cure or more effective treatment method for the diseases we are targeting, which could render our current or future product candidates non-competitive or obsolete, or reduce the demand for our product candidates before we can recover our development and commercialization expenses.

We are not aware of any approved drug or drug in clinical development for a patient self-administered treatment to terminate PSVT episodes. InCarda Therapeutics, Inc., or InCarda, is developing InRhythm, an inhaled version of flecainide, in preclinical development. To our knowledge, there are no other treatments in development for acute episodic treatment of PSVT. In the acute setting, IV treatments of generic drugs such as adenosine, verapamil and diltiazem, are routinely given. Additionally, some practitioners prescribe oral medications, such as calcium channel blockers, beta blockers and anti-arrhythmics to be taken at the onset of an episode. However, these interventions are not acutely effective.

For atrial fibrillation, there are a number of marketed generic anti-arrhythmic drugs that are used for chronic and/or acute rate control, such as metoprolol, propranolol, esmolol, pindolol, atenolol, nadolol, verapamil and diltiazem. There are also several drugs under development for atrial fibrillation, including: Ranexa (ranolazine), a sodium channel blocker in Phase 2 (ex-U.S.) from Gilead Sciences, Inc., or Gilead; Gencaro (bucindolol hydrochloride), a beta blocker in Phase 2 from ARCA biopharma, Inc..

For acute relief of angina symptoms, approved drugs include short-acting nitrates such as nitroglycerin, isosorbide dinitrate, and pentaerythritol. We are not aware of any approved drug or drug in clinical development for rapid-onset, short-acting treatment for coronary spasm.

Intellectual Property

We have filed numerous patent applications pertaining to etripamil and possible future product candidates, formulations containing etripamil, methods of making such formulations and clinical use. We strive to protect and enhance the proprietary technology, invention and improvements that are commercially important to the development of our business by seeking, maintaining, and defending our intellectual property. We also rely on know-how, continuing technological innovation and potential in-licensing opportunities to develop, strengthen and maintain our position in the field of cardiac arrhythmias, such as PSVT, and immediate rate control in atrial fibrillation, as well as other medical conditions affecting the cardiovascular system. Additionally, we intend to rely on regulatory protection afforded through data exclusivity and market exclusivity, as well as patent term extensions, where available.

As of March 31, 2019, our patent portfolio as it pertains to etripamil included:

- a patent family containing six U.S. patents, projected to expire in 2028, a pending U.S. patent application, which, if granted, is projected to expire in 2028, as well as corresponding patents in Australia, Brazil, Canada, China, Europe, Hong Kong, India, Japan, Mexico, New Zealand and South Korea, directed to etripamil, pharmaceutical compositions including etripamil, and uses of etripamil such as to treat angina or cardiac arrhythmias, including PSVT and atrial fibrillation; and

- a patent family containing one U.S. patent, projected to expire in 2036, a pending U.S. patent application, which, if granted, is projected to expire in 2036, as well as corresponding patent applications in Australia, Brazil, Canada, China, Europe, Hong Kong, India, Israel, Japan, Mexico, New Zealand, Russia, South Africa, South Korea and Ukraine, directed to formulations including etripamil, methods of making such formulations, and uses of such formulations to treat angina or cardiac arrhythmias, such as PSVT and atrial fibrillation.

The terms of individual patents may vary based on the countries in which they are obtained. Generally, patents issued for applications filed in the United States are effective for 20 years from the earliest effective non-provisional filing date in the absence, for example, of a terminal disclaimer shortening the term of the patent or patent term adjustment increasing the term of the patent. In addition, in certain instances, a patent term can be extended to recapture a portion of the term effectively lost as a results of FDA regulatory review periods. The restoration period cannot be longer than five years and the total term,

including the restoration period, must not exceed 14 years following FDA approval. The duration of patents outside the United States varies in accordance with provisions of applicable local law, but typically is also 20 years from the earliest non-provisional filing date.

In addition to patents and patent applications that we own, we rely on know-how to develop and maintain our competitive position. We seek to protect our proprietary technology and processes, and obtain and maintain ownership of certain technologies, in part, through confidentiality agreements and invention assignment agreements with our employees, consultants, scientific advisors, contractors and commercial partners.

Our future commercial success depends, in part, on our ability to obtain and maintain patent and other proprietary protection for commercially important technology, inventions and know-how related to our business; defend and enforce our patents; and operate without infringing valid enforceable patents and proprietary rights of third parties. Our ability to stop third parties from making, using, selling, offering to sell or importing our products may depend on the extent to which we have rights under valid and enforceable patents that cover these activities. With respect to our owned intellectual property, we cannot be sure that patents will issue from any of the pending patent applications to which we own or from any patent applications that we may file in the future, nor can we be sure that any patents that may be issued in the future to us will be commercially useful in protecting etripamil or any future product candidates and methods of using or manufacturing the same. Moreover, we may be unable to obtain patent protection for certain aspects of etripamil or future product candidates generally, as well as with respect to certain indications. See the section entitled "Risk Factors — Risks Related to Our Intellectual Property" for a more comprehensive description of risks related to our intellectual property.

Government Regulation and Product Approval

Government authorities in the United States, at the federal, state and local levels, and in other countries, extensively regulate, among other things, the research, development, testing, manufacture, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, import and export of pharmaceutical products, such as those we are developing. The processes for obtaining regulatory approvals in the United States and in foreign countries, along with subsequent compliance with applicable statutes and regulations, require the expenditure of substantial time and financial resources.

United States Government Regulation

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and its implementing regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable United States requirements at any time during the drug development process, approval process or after approval, may subject an applicant to a variety of administrative or judicial sanctions, such as the FDA's refusal to approve a pending New Drug Application, or NDA, withdrawal of an approval, imposition of a clinical hold, issuance of warning or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement or civil or criminal penalties.

The process required by the FDA before a drug may be marketed in the United States generally involves:

- § completion of preclinical laboratory tests, animal studies and formulation studies in compliance with the FDA's good laboratory practice, or GLP, regulations;
- § submission to the FDA of an IND, which must become effective before human clinical trials may begin;
- § approval by an independent institutional review board, or IRB, at each clinical site before each trial may be initiated;

- performance of adequate and well-controlled clinical trials, in accordance with good clinical practice, or GCP, requirements to establish the safety and efficacy of the proposed drug for each indication;
- submission to the FDA of an NDA;
- satisfactory completion of an FDA advisory committee review, if applicable;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with cGMP requirements, and to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity;
- satisfactory completion of an FDA inspection of selected clinical sites to assure compliance with GCPs and the integrity of the clinical data;
- payment of user fees; and
- FDA review and approval of the NDA.

Preclinical Studies

Preclinical studies include laboratory evaluation of product chemistry, toxicity and formulation, as well as animal studies to assess potential safety and efficacy. An IND sponsor must submit the results of the nonclinical tests, together with manufacturing information, analytical data and any available clinical data or literature, among other things, to the FDA as part of an IND. Some nonclinical testing may continue even after the IND is submitted. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to one or more proposed clinical trials and places the clinical trial on a clinical hold.

In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. As a result, submission of an IND may not result in the FDA allowing clinical trials to commence.

Clinical Trials

Clinical trials involve the administration of the investigational new drug to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include the requirement that all research subjects provide their informed consent in writing for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the trial, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. In addition, an IRB at each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must continue to oversee the clinical trial while it is being conducted. Information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health, or NIH, for public dissemination on their ClinicalTrials.gov website.

Human clinical trials are typically conducted in three sequential phases, which may overlap or be combined. In Phase 1, the drug is initially introduced into healthy human subjects or patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an initial indication of its effectiveness. In Phase 2, the drug typically is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage. In Phase 3, the drug is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to statistically evaluate the safety and efficacy of the product for approval, to establish the overall risk-benefit profile of the product and to provide adequate information for the labeling of the product.

Progress reports detailing the results of the clinical trials must be submitted, at least annually, to the FDA, and more frequently if serious adverse events occur. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, or at all. Furthermore, the FDA or the sponsor may

suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements, or if the drug has been associated with unexpected serious harm to patients.

Marketing Approval

Assuming successful completion of the required clinical testing, the results of the preclinical and clinical studies, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA requesting approval to market the product for one or more indications. In most cases, the submission of an NDA is subject to a substantial application user fee. Under the Prescription Drug User Fee Act, or PDUFA, guidelines that are currently in effect, the FDA has a goal of ten months from the date of "filing" of a standard NDA for a new molecular entity to review and act on the submission. This review typically takes twelve months from the date the NDA is submitted to the FDA because the FDA has approximately two months to make a "filing" decision.

In addition, under the Pediatric Research Equity Act, certain NDAs or supplements to an NDA must contain data that are adequate to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. Unless otherwise required by regulation, the pediatric data requirements do not apply to products with orphan designation.

The FDA also may require submission of a risk evaluation and mitigation strategy, or REMS, plan to ensure that the benefits of the drug outweigh its risks. The REMS plan could include medication guides, physician communication plans, assessment plans, and/or elements to assure safe use, such as restricted distribution methods, patient registries or other risk minimization tools.

The FDA conducts a preliminary review of all NDAs within the first 60 days after submission, before accepting them for filing, to determine whether they are sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA reviews an NDA to determine, among other things, whether the drug is safe and effective and whether the facility in which it is manufactured, processed, packaged or held meets standards designed to assure the product's continued safety, quality and purity.

The FDA may refer an application for a novel drug to an advisory committee. An advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA will typically inspect one or more clinical trial sites to assure compliance with GCP requirements.

The testing and approval process for an NDA requires substantial time, effort and financial resources, and takes several years to complete. Data obtained from preclinical and clinical testing are not always

conclusive and may be susceptible to varying interpretations, which could delay, limit or prevent regulatory approval. The FDA may not grant approval of an NDA on a timely basis, or at all.

After evaluating the NDA and all related information, including the advisory committee recommendation, if any, and inspection reports regarding the manufacturing facilities and clinical trial sites, the FDA may issue an approval letter, or, in some cases, a complete response letter. A complete response letter generally contains a statement of specific conditions that must be met in order to secure final approval of the NDA and may require additional clinical or preclinical testing in order for FDA to reconsider the application. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. If and when those conditions have been met to the FDA's satisfaction, the FDA will typically issue an approval letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications.

Even if the FDA approves a product, it may limit the approved indications for use of the product, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies, including Phase 4 clinical trials, be conducted to further assess a drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution and use restrictions or other risk management mechanisms under a REMS, which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-marketing studies or surveillance programs. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes, and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Special FDA Expedited Review and Approval Programs

The FDA has various programs, including fast track designation, accelerated approval, priority review, and breakthrough therapy designation, which are intended to expedite or simplify the process for the development and FDA review of drugs that are intended for the treatment of serious or life threatening diseases or conditions and demonstrate the potential to address unmet medical needs. The purpose of these programs is to provide important new drugs to patients earlier than under standard FDA review procedures.

To be eligible for a fast track designation, the FDA must determine, based on the request of a sponsor, that a product is intended to treat a serious or life-threatening disease or condition and demonstrates the potential to address an unmet medical need. The FDA will determine that a product will fill an unmet medical need if it will provide a therapy where none exists or provide a therapy that may be potentially superior to existing therapy based on efficacy or safety factors. The FDA may review sections of the NDA for a fast track product on a rolling basis before the complete application is submitted. If the sponsor provides a schedule for the submission of the sections of the NDA, the FDA agrees to accept sections of the NDA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the NDA.

The FDA may give a priority review designation to drugs that are designed to treat serious conditions, and if approved, would provide a significant improvement in treatment, or provide a treatment where no adequate therapy exists. A priority review means that the goal for the FDA to review an application is six months, rather than the standard review of ten months under current PDUFA guidelines. Under the current PDUFA agreement, these six and ten month review periods are measured from the "filing" date rather than the receipt date for NDAs for new molecular entities, which typically adds approximately two months to the timeline for review and decision from the date of submission. Most products that are eligible for fast track designation are also likely to be considered appropriate to receive a priority review.

In addition, products studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may be eligible for accelerated approval and may be approved on the basis of adequate and well-controlled clinical trials

establishing that the drug product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA may require a sponsor of a drug receiving accelerated approval to perform post-marketing studies to verify and describe the predicted effect on irreversible morbidity or mortality or other clinical endpoint, and the drug may be subject to accelerated withdrawal procedures.

Breakthrough therapy designation is for a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The FDA must take certain actions, such as holding timely meetings and providing advice, intended to expedite the development and review of an application for approval of a breakthrough therapy.

Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened. We may explore some of these opportunities for our product candidates as appropriate.

Rare pediatric disease designation by the FDA enables priority review voucher, or PRV, eligibility upon U.S. market approval of a designated drug for rare pediatric diseases. The RPD-PRV program is intended to encourage development of therapies to prevent and treat rare pediatric diseases. The voucher, which is awarded upon NDA or BLA approval to the sponsor of a designated RPD can be sold or transferred to another entity and used by the holder to receive priority review for a future NDA or BLA submission, which reduces the FDA review time of such future submission from ten to six months.

Post-Approval Requirements

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications, manufacturing changes or other labeling claims, are subject to further testing requirements and prior FDA review and approval. There also are continuing annual user fee requirements for any marketed products and the establishments at which such products are manufactured, as well as application fees for supplemental applications with clinical data.

Even if the FDA approves a product, it may limit the approved indications for use of the product, require that contraindications, warnings or precautions be included in the product labeling, including a boxed warning, require that post-approval studies, including Phase 4 clinical trials, be conducted to further assess a drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution restrictions or other risk management mechanisms under a REMS, which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-marketing studies or surveillance programs.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state agencies, and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon the sponsor and any

third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain cGMP compliance.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market.

Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in mandatory revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- § restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- § fines, warning letters or holds on post-approval clinical trials;
- § refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product approvals;
- § product seizure or detention, or refusal to permit the import or export of products; or
- § injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label, although physicians, in the practice of medicine, may prescribe approved drugs for unapproved indications. 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 their 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 liability.

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act, or PDMA, which regulates the distribution of drugs and drug samples at the federal level, and sets minimum standards for the registration and regulation of drug distributors by the states. Both the PDMA and state laws limit the distribution of prescription pharmaceutical product samples and impose requirements to ensure accountability in distribution.

Federal and State Fraud and Abuse, Data Privacy and Security, and Transparency Laws and Regulations

In addition to FDA restrictions on marketing of pharmaceutical products, federal and state healthcare laws and regulations restrict business practices in the biopharmaceutical industry. These laws may impact, among other things, our current and future business operations, including our clinical research activities, and proposed sales, marketing and education programs and constrain the business or financial arrangements and relationships with healthcare providers and other parties through which we market, sell and distribute our products for which we obtain marketing approval. These laws include anti-kickback and false claims laws and regulations, data privacy and security, and transparency laws and regulations, including, without limitation, those laws described below.

The federal Anti-Kickback Statute prohibits any person or entity from, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration to induce or in return for purchasing, leasing, ordering or arranging for or recommending the purchase, lease or order of any item or service reimbursable under Medicare, Medicaid or other federal healthcare programs. The term "remuneration" has been broadly interpreted to include anything of value. The federal Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers and formulary managers on the other. Although there are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution, the exceptions and safe harbors are drawn narrowly. Practices that involve remuneration that may be alleged to be intended to induce prescribing,

purchases or recommendations may be subject to scrutiny if they do not qualify for an exception or safe harbor. Several courts have interpreted the statute's intent requirement to mean that if any one purpose of an arrangement involving remuneration is to induce referrals of federal healthcare covered business, the statute has been violated.

A person or entity does not need to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act or the civil monetary penalties laws.

Federal civil and criminal false claims laws and civil monetary penalties laws, including the federal civil False Claims Act, which can be enforced by individuals through civil whistleblower and qui tam actions, prohibits any person or entity from, among other things, knowingly presenting, or causing to be presented, a false claim for payment to the federal government or knowingly making, using or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government. A claim includes "any request or demand" for money or property presented to the U.S. government. Several pharmaceutical and other healthcare companies have been prosecuted under these laws for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. Other companies have been prosecuted for causing false claims to be submitted because of the companies' marketing of products for unapproved, and thus non-reimbursable, uses.

The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, created additional federal criminal statutes that prohibit, among other things, knowingly and willfully executing a scheme to defraud any healthcare benefit program, including private third-party payors and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. Also, many states have similar fraud and abuse statutes or regulations that apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor.

In addition, we may be subject to data privacy and security regulation by both the federal government and the states in which we conduct our business. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and their respective implementing regulations, impose specified requirements on certain types of individuals and entities relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH makes HIPAA's security standards directly applicable to "business associates," defined as independent contractors or agents of covered entities, which include certain healthcare providers, healthcare clearinghouse and health plans, that create, receive, maintain or transmit individually identifiable health information in connection with providing a service for or on behalf of a covered entity. HITECH also increased the civil and criminal penalties that may be imposed against covered entities, business associates and possibly other persons, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce HIPAA and seek attorney's fees and costs associated with pursuing federal civil actions. In addition, state laws govern the privacy and security of health information in certain circumstances, many of which are not pre-empted by HIPAA, differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

The federal Physician Payments Sunshine Act requires certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program, with specific exceptions, to report annually to the Centers for Medicare & Medicaid Services, or CMS, information related to payments or other transfers of value made to physicians and teaching hospitals, and applicable manufacturers and applicable group purchasing organizations to report annually to CMS ownership and investment interests held by physicians and their immediate family members.

We may also be subject to state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures, state laws that require drug manufacturers to report information on the pricing of certain drugs, and state and local laws that require the registration of pharmaceutical sales representatives.

Because of the breadth of these laws and the narrowness of available statutory exceptions and regulatory safe harbors, it is possible that some of our business activities could be subject to challenge under one or more of such laws. If our operations are found to be in violation of any of the federal and state laws described above or any other governmental regulations that apply to us, we may be subject to significant criminal, civil and administrative penalties including damages, fines, imprisonment, 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, diminished profits and future earnings, disgorgement, exclusion from participation in government healthcare programs and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations. To the extent that any of our products are sold in a foreign country, we may be subject to similar foreign laws and regulations, which may include, for instance, applicable post-marketing requirements, including safety surveillance, anti-fraud and abuse laws, implementation of corporate compliance programs, reporting of payments or transfers of value to healthcare professionals, and additional data privacy and security requirements.

Coverage and Reimbursement

The future commercial success of our, or any of our collaborators', product candidates, if approved, will depend in part on the extent to which third-party payors, such as governmental payor programs at the federal and state levels, including Medicare and Medicaid, private health insurers and other third-party payors, provide coverage of and establish adequate reimbursement levels for our product candidates. Third-party payors generally decide which products they will pay for and establish reimbursement levels for those products. In particular, in the United States, no uniform policy for coverage and reimbursement exists. Private health insurers and other third-party payors often provide coverage and reimbursement for products based on the level at which the government, through the Medicare program, provides coverage and reimbursement for such products, but also have their own methods and approval process apart from Medicare determinations. Therefore, coverage and reimbursement can differ significantly from payor to payor.

In the United States, the European Union, or EU, and other potentially significant markets for our product candidates, government authorities and third-party payors are increasingly attempting to limit or regulate the price of products, particularly for new and innovative products, which often has resulted in average selling prices lower than they would otherwise be. Further, the increased emphasis on managed healthcare in the United States and on country and regional pricing and reimbursement controls in the EU will put additional pressure on product pricing, reimbursement and usage. These pressures can arise from rules and practices of managed care groups, judicial decisions and laws and regulations related to Medicare, Medicaid and healthcare reform, pharmaceutical coverage and reimbursement policies and pricing in general.

Third-party payors are increasingly imposing additional requirements and restrictions on coverage and limiting reimbursement levels for products. For example, federal and state governments reimburse products at varying rates generally below average wholesale price. These restrictions and limitations influence the purchase of products. Third-party payors may limit coverage to specific products on an approved list, or formulary, which might not include all of the FDA-approved products for a particular indication. Third-party payors are increasingly challenging the price and examining the medical necessity and cost-effectiveness of products , in addition to their safety and efficacy. We may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of our product candidates, in addition to the costs required to obtain the FDA approvals. Our product candidates may not be considered

medically necessary or cost-effective. A payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Adequate third-party payor reimbursement may not be available to enable us to realize an appropriate return on our investment in product development. Legislative proposals to reform healthcare or reduce costs under government insurance programs may result in lower reimbursement for our product candidates, if approved, or exclusion of our product candidates from coverage and reimbursement. The cost containment measures that third-party payors and providers are instituting and any healthcare reform could significantly reduce our revenues from the sale of any approved product candidates.

Healthcare Reform

The United States and some foreign jurisdictions are considering enacting or have enacted a number of additional legislative and regulatory proposals to change the healthcare system in ways that could affect our ability to sell our product candidates profitably, if approved. Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts, which include major legislative initiatives to reduce the cost of care through changes in the healthcare system, including limits on the pricing, coverage, and reimbursement of pharmaceutical and biopharmaceutical products, especially under government-funded health care programs, and increased governmental control of drug pricing.

There have been several U.S. government initiatives over the past few years to fund and incentivize certain comparative effectiveness research, including creation of the Patient-Centered Outcomes Research Institute under 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. It is also possible that comparative effectiveness research demonstrating benefits in a competitor's product could adversely affect the sales of our product candidates

The PPACA became law in March 2010 and substantially changed the way healthcare is financed by both third-party payors. Among other measures that may have an impact on our business, the PPACA establishes an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents; a new Medicare Part D coverage gap discount program; and a new formula that increases the rebates a manufacturer must pay under the Medicaid Drug Rebate Program. Additionally, the PPACA extends manufacturers' Medicaid rebate liability, expands eligibility criteria for Medicaid programs, and expands entities eligible for discounts under the Public Health Service Act. At this time, we are unsure of the full impact that the PPACA will have on our business.

Since its enactment, there have been judicial and Congressional challenges to certain aspects of the PPACA, as well as recent efforts by the Trump administration to repeal or replace certain aspects of the PPACA, and we expect such challenges and amendments to continue. Since January 2017, President Trump has signed two Executive Orders and other directives designed to delay the implementation of certain provisions of the PPACA or otherwise circumvent some of the requirements for health insurance mandated by the PPACA. Concurrently, Congress has considered legislation that would repeal or repeal and replace all or part of the PPACA. While Congress has not passed comprehensive repeal legislation, two bills affecting the implementation of certain taxes under the PPACA have been signed into law. The Tax Cuts and Jobs Act of 2017, or Tax Act, 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." On January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain PPACA-mandated fees, including the so-called "Cadillac" tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the medical device excise tax on non-exempt medical devices. The Bipartisan Budget Act of 2018, or the BBA, among other things, amended the PPACA, effective January 1, 2019, to increase from 50% to 70% the point-of-sale discount that is owed by pharmaceutical manufacturers who

participate in Medicare Part D and to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole." In July 2018, CMS published a final rule permitting further collections and payments to and from certain PPACA qualified health plans and health insurance issuers under the PPACA adjustment program in response to the outcome of federal district court litigation regarding the method CMS uses to determine this risk adjustment. On December 14, 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.

In addition, other legislative changes have been proposed and adopted since the PPACA was enacted. In August 2011, the President signed into law the Budget Control Act of 2011, as amended, which, among other things, included aggregate reductions to Medicare payments to providers of 2% per fiscal year, which began in 2013 and, following passage of subsequent legislation, including the BBA, will continue through 2027 unless additional Congressional action is taken. In January 2013, the American Taxpayer Relief Act of 2012 was enacted and, among other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Further, there has been increasing legislative and enforcement interest in the United States with respect to drug pricing practices. Specifically, there have been several recent U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. At the federal level, the Trump administration's budget proposal for fiscal year 2019 contains further drug price control measures that could be enacted during the 2019 budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. Additionally, the Trump administration released a "Blueprint" to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products and reduce the out of pocket costs of drug products paid by consumers. The U.S. Department of Health and Human Services, or HHS, has already started the process of soliciting feedback on some of these measures and, at the same, is immediately implementing others under its existing authority. For example, in September 2018, CMS announced that it will allow Medicare Advantage plans the option to use step therapy for Part B drugs beginning January 1, 2019, and in October 2018, CMS proposed a new rule that would require direct-to-consumer television advertisements of prescription drugs and biological products, for which payment is available through or under Medicare or Medicaid, to include in the advertisement the Wholesale Acquisition Cost, or list price, of that drug or biological product. On January 31, 2019, the HHS Office of Inspector General proposed modifications to federal Anti-Kickback Statute safe harbors that among other things, may affect rebates paid by manufacturers to Medicare Part D plans, the purpose of which is to further reduce the cost of drug products to consumers. Although a number of these, and other proposed measures will require additional authorization to become effective, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

Additionally, on May 30, 2018, the Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017, or the Right to Try Act, was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a Phase I clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a drug manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act.

Foreign Regulation

In order to market any product outside of the United States, we would need to comply with numerous and varying regulatory requirements of other countries regarding safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of our product candidates. For example, in the EU, we must obtain authorization of a clinical trial application, or CTA, in each member state in which we intend to conduct a clinical trial. Whether or not we obtain FDA approval for a drug, we would need to obtain the necessary approvals by the comparable regulatory authorities of foreign countries before we can commence clinical trials or marketing of the drug in those countries. The approval process varies from country to country and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country may negatively impact the regulatory process in others.

Employees

As of March 31, 2019, we had 23 full-time employees, 15 of whom were primarily engaged in research and development activities and 8 of whom had an M.D. or Ph.D. degree. None of our employees is represented by a labor union and we consider our employee relations to be good.

Facilities

Our headquarters is currently located in Montréal (Québec), Canada and consists of 7,700 square feet of leased office space under a lease that expires in November 2020. We also have a U.S. subsidiary in Charlotte, North Carolina. We believe that our facilities are adequate to meet our current needs.

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.

MANAGEMENT

The following table sets forth information regarding our executive officers and directors, including their ages as of March 31, 2019:

NAME	AGE	POSITION(S)
Executive Officers		
Joseph Oliveto	51	President, Chief Executive Officer and Director
Lorenz Muller	55	Chief Commercial Officer
Francis Plat, M.D.	61	Chief Medical Officer
Philippe Douville, Ph.D.	57	Founder and Chief Scientific Officer
Timothy L. Maness	58	Vice President, Finance
Non-Employee Directors		
Paul Edick[2][3]	63	Director and Chairperson of the Board
Marco Boorsma[1][3]	44	Director
Nilesh Kumar, Ph.D.[2]	43	Director
Debra K. Liebert[2]	62	Director
Michael Tomsicek[1]	53	Director
Paul Truex[1][3]	50	Director

(1) Member of our audit committee.

(2) Member of our compensation committee.

(3) Member of our nominating and corporate governance committee.

Executive Officers

Joseph Oliveto has served as our President and Chief Executive Officer since March 2017 and as a member of our board of directors since July 2017. Prior to becoming our President and Chief Executive Officer, Mr. Oliveto served as a consultant to the company from September 2016 to March 2017. Mr. Oliveto served as Chief Executive Officer at Galleon Pharmaceuticals, Inc. from July 2015 to June 2016. From June 2008 to June 2014, Mr. Oliveto was at Chelsea Therapeutics International, Ltd., where he held various roles, including serving as President and Chief Executive Officer and a member of the board of directors from January 2014 to June 2014, overseeing the company's sale to Lundbeck, Inc., following which he served as an Executive Advisor from July 2014 to July 2015. Mr. Oliveto received his B.A. degree in Chemistry and his M.B.A. degree from Rutgers University. We believe that Mr. Oliveto's significant experience in the areas of drug development, commercialization and manufacturing as well as business development, qualifies him to serve on our board of directors.

Philippe Douville, Ph.D., is our founder and has served as our Chief Scientific Officer since March 2017. Dr. Douville was a member of our board of directors from our inception in 2005 to 2017, including serving as Chairman from 2011 to 2012, and as our President and Chief Executive Officer from 2005 to March 2017. Prior to founding our company, Dr. Douville was the co-founder, Chief Executive Officer and Chief Business Officer of Galileo Genomics (later Genizon Biosciences), a population genomics company. Dr. Douville received his Ph.D. degree in Neuroscience from McGill University, Canada, and later pursued several years of post-doctoral research activities at the University of Zurich, Switzerland. He later received his M.B.A degree from the HEC at the University of Montréal, Canada.

Timothy L. Maness has served as our Vice President, Finance, since February 2018. Mr. Maness provided consulting services to several publicly-held life sciences companies with development and/or commercial activities. Prior to that, Mr. Maness served as the Chief Financial Officer of Ballantyne Therapeutics, Inc. a pharmaceutical company, from May 2015 to April 2016. From 2006 to 2014, Mr. Maness served as the Senior Director of Finance and Corporate Controller at Chelsea Therapeutics International Inc. until the sale of the company to Lundbeck, Inc. Prior to Chelsea Therapeutics, Mr. Maness provided consulting services and held a variety of senior financial management roles, primarily in software and technology services. Mr. Maness received a B.S. in Accounting from the University of North Carolina at Charlotte and is licensed as a Certified Public Accountant and as a Chartered Global Management Accountant.

Lorenz Muller has served as our Chief Commercial Officer since October 2017. Prior to joining our company, Mr. Muller served as the Vice President of Marketing at Exact Sciences Corporation, a molecular diagnostics company, from June 2016 through July 2017. Prior to that, Mr. Muller served as the Executive Director, Thrombosis at Daiichi Sankyo, Inc. from July 2008 through December 2015. Mr. Muller received his B.S. degrees in Chemical Engineering and Life Sciences and his M.S. degree in Chemical Engineering from the Massachusetts Institute of Technology. He received his M.B.A degree from the Harvard Graduate School of Business Administration.

Francis Plat, M.D., has served as our Chief Medical Officer since June 2015. Prior to joining our company, Dr. Plat was a clinical consultant from August 2013 to May 2015. From August 2009 to July 2013, Dr. Plat served as the Vice President and Therapeutic Area Head, Atherosclerosis and Cardiovascular, at Merck Research Laboratories. Prior to that, Dr. Plat was the Vice President of Cardiovascular Clinical Development at Daiichi Sankyo, Inc., a global pharmaceutical company. Dr. Plat received his M.D. from the University of Paris and is a board-certified cardiologist in France, where he spent 10 years practicing medicine, including post-cardiovascular surgery at the intensive care unit in the Hopital Marie Lannelongue and in cardiac rehabilitation at Broussais Hospital.

Non-Employee Directors

Marco Boorsma, Ph.D., has served as a member of our board of directors since July 2017. Dr. Boorsma served as a Partner of Forbion Capital Partners from October 2014 through April 2017, and has served as its General Partner since April 2017. Dr. Boorsma has served on the board of directors of various privately held life sciences and pharmaceutical companies. Dr. Boorsma received his Master's degree in molecular biology from the University of Groningen in Netherlands. He received his Ph.D. degree in biotechnology from the ETH Institute for Technology in Zürich, Switzerland, and completed part of his research at the Laboratory of Molecular Biology of the Medical Research Council in Cambridge, United Kingdom. We believe that Dr. Boorsma's extensive experience in life science investments and serving on the boards of directors of a number of life sciences and pharmaceutical companies qualifies him to serve on our board of directors.

Paul R. Edick has served as a member and Chairperson of our board of directors since April 2019. Since January 2017, Mr. Edick has served as President, Chief Executive Officer and as a member of the board of directors of Xeris Pharmaceuticals, Inc., a Nasdaq-listed biopharmaceutical company, and as its Chairman since June 2018. Previously, Mr. Edick served as founding partner of 3G Advisors, LLC, a consultancy to the pharmaceutical, healthcare and healthcare investor communities from November 2014 to January 2017. From July 2010 to November 2014, Mr. Edick served as Chief Executive Officer and as a member of the board of directors of Durata Therapeutics, Inc., a Nasdaq-listed pharmaceutical company, prior to its acquisition in November 2014. From 2008 to 2010, Mr. Edick served as Chief Executive Officer of GANIC Pharmaceuticals, Inc., a Warburg Pincus investment search vehicle. From 2002 to 2008, Mr. Edick served in a variety of roles at MedPointe, including as its president of pharmaceutical operations from 2006 to 2008. Mr Edick currently serves on the board of directors for Iterum Therapeutics Limited, a Nasdaq-listed pharmaceutical company. In addition, Mr. Edick has previously served as a member of the board of directors of Newlink Genetics Corporation, Sucampo Pharmaceuticals, Inc., Neos Therapeutics, Inc., PDL BioPharma, Inc., and Circassia Pharmaceuticals plc. Mr. Edick holds a B.A. in psychology from Hamilton

College in Clinton, New York. We believe Mr. Edick's management and industry experience, including his experience serving on public company boards of directors, qualifies him to serve on our board of directors.

Nilesh Kumar, Ph.D., has served as a member of our board of directors since July 2017. Dr. Kumar has been employed as a Partner at Novo Ventures (US), Inc. since January 2017. Prior to that, Dr. Kumar was Senior Investment Director at Merck Serono Ventures from June 2009 through March 2015. Dr. Kumar has served on the board of directors of various privately held life sciences and pharmaceutical companies. Dr. Kumar received his B.A. degree in Natural Sciences from the University of Cambridge, United Kingdom, and his Ph.D. and M.B.A degrees from Harvard University. We believe that Dr. Kumar's financial expertise and experience as both an investor in and member of the board of directors at numerous life sciences companies qualifies him to serve on our board of directors.

Debra K. Liebert has served as a member of our board of directors since June 2015. Ms. Liebert served as a Principal of Domain Associates, LLC, a healthcare venture capital firm with an exclusive focus on life sciences, since 2007, and has served as a Managing Director since January 2014. Ms. Liebert previously served in various positions at CancerVax Corporation, Atairgin Technologies and Trega Biosciences. Ms. Liebert received her B.S. degree in chemistry from Clarion University, her M.S. degree in pharmacology/toxicology from Duquesne University, and her M.B.A degree from University of California, Los Angeles. We believe that Ms. Liebert's over 35 years of scientific, strategic and management experience in the healthcare industry qualifies her to serve on our board of directors.

Michael Tomsicek has served as a member of our board of directors since April 2019. Mr. Tomsicek has served as the Chief Financial Officer of CRISPR Therapeutics AG, a Nasdaq-listed gene editing company, since November 2017. Prior to that, Mr. Tomsicek served as Chief Financial Officer of Abiomed, a Nasdaq-listed medical device company, from July 2015 to August 2017. Before that, he was Chief Financial Officer at Cubist Pharmaceuticals, Inc., a Nasdaq-listed biopharmaceutical company. He was at Cubist from August 2010 to January 2015, through the company's sale to Merck, and held a series of roles of increasing responsibility leading finance, investor relations and strategic sourcing. Prior to Cubist, Mike spent nearly eight years at General Electric Healthcare, ultimately as Chief Financial Officer of the global ultrasound business. Mike holds an M.B.A. and a B.S. in Engineering, both from the University of Wisconsin. We believe Mr. Tomsicek's management and industry experience, including his public company management experience, qualifies him to serve on our board of directors.

Paul Truex has served as a member of our board of directors since February 2012. From June 2012 to October 2018, Mr. Truex was the Chairman of our board of directors. Mr. Truex founded Anthera Pharmaceuticals, Inc., a currently publicly traded biopharmaceutical company, in September 2004 and has served as the Executive Chairman of the board of directors of Anthera since December 2016. He previously served as the President of Anthera from its inception in September 2004 until January 2016 and as its Chief Executive Officer from September 2004 to December 2016. Prior to founding Anthera, Mr. Truex served as a founder, director, President and Chief Executive Officer of Peninsula Pharmaceuticals, Inc. from the commencement of its operations in October 2001 until December 2005 after which Peninsula was acquired in a series of transactions by Johnson and Johnson and Forest Laboratories. Mr. Truex is currently a director at CymaBay Therapeutics Inc., a Nasdaq-listed company, where he has served since April 2016. From May 2012 to September 2013, he served on the board of directors of Trius Therapeutics Inc. (acquired by Cubist Pharmaceuticals, Inc. in July 2013). Mr. Truex obtained his M.B.A. in marketing and finance from Indiana University and his B.A. in economics from the University of Waterloo. We believe that Mr. Truex's extensive experience at both public and private pharmaceutical companies qualify him to serve on our board of directors.

Family Relationships and Other Arrangements

There are no family relationships among our directors and executive officers. Marco Boorsma, Nilesh Kumar and Debra K. Liebert were each designated as a director to our board of directors by Forbion Capital

Fund III Cooperatief U.A., Novo Holdings A/S and Domain Partners VIII, L.P., respectively, in connection with a shareholders agreement, which will terminate upon the closing of this offering.

Board Composition

Our board of directors currently consists of seven members. Our amended articles of incorporation and amended and restated by-laws provide that the number of directors shall be a minimum of three and a maximum of 15 members and will be fixed from time to time by resolution of the board of directors. Our board of directors are elected at each annual meeting of our shareholders and serve until their successors are elected or appointed, unless their office is vacated earlier. The term of office for each of the directors will expire at the time of our next annual shareholder's meeting.

Director Independence

Under The Nasdaq Stock Market LLC, or Nasdaq, Marketplace Rules, or the Nasdaq Listing Rules, independent directors must comprise a majority of our board of directors as a public company within one year of listing.

Our board of directors has undertaken a review of its composition, the composition of its committees and the independence of each director. Based upon information requested from and provided by each director concerning his or her background, employment and affiliations, including family relationships, our board of directors has determined that all of our directors except Joseph Oliveto do not have any relationships that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director and that each of these directors is "independent" as that term is defined under the applicable rules and regulations of the SEC and the listing requirements of the Nasdaq Listing Rules. Our board of directors has determined that Joseph Oliveto, by virtue of his employment with us, is not independent under applicable rules and regulations of the SEC and the Nasdaq Listing Rules. In making this determination, our board of directors considered the current and prior relationships that each non-employee director has with our company and all other facts and circumstances our board of directors deemed relevant in determining their independence, including the beneficial ownership of our share capital by each non-employee director.

Board Committees

Our board of directors has established an audit committee, a compensation committee and a nominating and corporate governance committee. Our board of directors may establish other committees to facilitate the management of our business. The composition and functions of each committee are described below. Members serve on these committees until their resignation or until otherwise determined by our board of directors. Each committee has adopted a written charter that satisfies the applicable rules and regulations of the SEC and Nasdaq Listing Rules, which we will post on our website at www.milestonepharmaceuticals.com upon completion of this offering.

Audit Committee

The audit committee is responsible for assisting our board of directors in its oversight of the integrity of our consolidated financial statements, the qualifications and independence of our independent auditors and our internal financial and accounting controls. The audit committee has direct responsibility for the appointment, compensation, retention (including termination) and oversight of our independent registered public accounting firm, and our independent auditors report directly to the audit committee. The audit committee also prepares the audit committee report that the SEC requires to be included in our annual proxy statement.

Our audit committee consists of Marco Boorsma, Paul Truex and Michael Tomsicek. Our board of directors has determined that all members are independent under the Nasdaq Listing Rules and Rule 10A-3(b)(1) of the Securities Exchange Act of 1934, as amended, or the Exchange Act. The chair of our audit committee is Michael Tomsicek. Our board of directors has determined that Mr. Tomsicek is an "audit committee financial expert" as such term is currently defined in Item 407(d)(5) of Regulations S-K. Our board of

directors has also determined that each member of our audit committee can read and understand fundamental financial statements, in accordance with applicable requirements. In arriving at these determinations, the board of directors has examined each audit committee member's scope of experience and the nature of their employment in the corporate finance sector.

Compensation Committee

The compensation committee approves the compensation objectives for the company, the compensation of the chief executive officer and approves, or recommends to our board of directors for approval, the compensation for other executives. The compensation committee reviews all compensation components, including base salary, bonus, benefits and other perquisites.

Our compensation committee consists of Nilesh Kumar, Paul Edick and Debra Liebert. Our board of directors has determined that all members are independent under the Nasdaq Listing Rules and are "non-employee directors" as defined in Rule 16b-3 promulgated under the Exchange Act. The chair of our compensation committee is Debra Liebert.

Nominating and Corporate Governance Committee

The nominating and corporate governance committee makes recommendations regarding corporate governance, the composition of our board of directors, identification, evaluation and nomination of director candidates and the structure and composition of committees of our board of directors. In addition, the nominating and corporate governance committee is responsible for developing and recommending corporate governance guidelines to our board of directors, as applicable to the company.

Our nominating and corporate governance committee consists of Marco Boorsma, Paul Truex and Paul Edick. The chair of our nominating and corporate governance committee is Paul Edick. Each member of the nominating and corporate governance committee is a non-employee director within the meaning of Rule 16b-3 of the rules promulgated under the Exchange Act, an independent director as defined by the Nasdaq Listing Rules and is free from any relationship that would interfere with the exercise of his or her independent judgment, as determined by the board of directors in accordance with the applicable Nasdaq Listing Rules.

Compensation Committee Interlocks and Insider Participation

None of the members of the compensation committee is currently, or has been at any time, one of our executive officers or employees. None of our executive officers currently serves, or has served during the last year, as a member of the board of directors or compensation committee of any entity that has one or more executive officers serving as a member of our board of directors or on our compensation committee.

Code of Business Conduct and Ethics

Effective upon completion of this offering, we will adopt a written code of business conduct and ethics that applies to all of our directors, officers and employees, including our principal executive officer, principal financial officer and principal accounting officer or controller, or persons performing similar functions, and agents and representatives. The full text of our code of business conduct and ethics will be posted on our website at www.milestonepharmaceuticals.com upon completion of this offering. The nominating and corporate governance committee of our board of directors will be responsible for overseeing our code of business conduct and ethics and any waivers applicable to any director, executive officer or employee. We intend to disclose future amendments to certain provisions of our code of business conduct and ethics, or waivers of such provisions applicable to our directors, officers and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions, and agents and representatives, on our website identified above.

In addition, under the *Civil Code of Québec,* to which we are subject as a legal person incorporated under the *Business Corporations Act* (Québec) (L.R.Q., c. S-31), or the BCA, and under the BCA, a director must

immediately disclose to the board any situation that may place him or her in a conflict of interest. Any such declaration of interest is recorded in the minutes of proceeding of the board of directors. The director abstains, except if required, from the discussion and voting on the question. In addition, it is our policy that an interested director recuse himself or herself from the decision-making process pertaining to a contract or transaction in which he or she has an interest.

Limitation on Liability and Indemnification Matters

Under the BCA and our amended and restated bylaws, we must indemnify our current or former directors and officers, agents or any other individuals who act or has acted at our request as a director or officer of a related entity, against all costs, charges and expenses reasonably incurred by such individual in connection with any civil, criminal, administrative, investigative or other proceeding in which such individual is involved because of his or her association with us or a related entity. The BCA also provides that we may, with the approval of the court, also make an advance payment to such individual for costs, charges and expenses reasonably incurred in connection with such a proceeding, provided, however, that such individual shall repay such payment if he or she does not fulfill the conditions described below.

Indemnification is prohibited under the BCA unless the individual:

- acted with honestly and loyalty in our interests, or in the interests of the other entity for which the individual acted as director or officer or in a similar capacity at our request;
- in the case of a proceeding that is enforced by a monetary penalty, the individual had reasonable grounds for believing that his or her conduct was lawful; and
- was not judged by the court to have committed an intentional or gross fault.

In addition, we have entered, and intend to continue to enter, into separate indemnity agreements with each of our directors and officers. These indemnity agreements, among other things, require us to indemnify our directors and officers for certain expenses, including attorneys' fees, judgments, fines and settlement amounts incurred by a director or officer in any action or proceeding arising out of their services as a director or officer, or any other company or enterprise to which the person provides services at our request.

We maintain a directors' and officers' insurance policy pursuant to which our directors and officers are insured against liability for actions taken in their capacities as directors and officers. We believe that these provisions in our amended articles of incorporation and amended and restated bylaws and these indemnity agreements are necessary to attract and retain qualified persons as directors and officers.

Insofar as indemnification for liabilities arising under the Securities Act of 1933, as amended, or the Securities Act, may be permitted to directors, officers or control persons, in the opinion of the SEC, such indemnification is against public policy, as expressed in the Securities Act and is therefore unenforceable.

EXECUTIVE AND DIRECTOR COMPENSATION

Our named executive officers for the year ended December 31, 2018, which consist of our principal executive officer and our next two most highly compensated executive officers, are:

- Joseph Oliveto;
- Francis Plat; and
- Lorenz Muller.

Summary Compensation Table

The following table provides information regarding the compensation provided to our named executive officers for the years ended December 31, 2018 and 2017.

NAME AND PRINCIPAL POSITION	YEAR	SALARY ($)[1][2]	NON-EQUITY INCENTIVE PLAN COMPENSATION ($)[2][3]	OPTION AWARDS ($)[4]	ALL OTHER COMPENSATION ($)[5]	TOTAL ($)
Joseph Oliveto	2018	360,000	190,000	866,653	20,184	1,436,837
Chief Executive Officer	2017	364,166[6]	180,000	283,597	23,175	850,938
Francis Plat	2018	330,000	83,000	223,609	—	636,609
Chief Medical Officer	2017	296,933[7]	66,000	—	—	362,933
Lorenz Muller	2018	300,000	87,000	248,183	10,534	645,717
Chief Commercial Officer						

(1) Salary amounts represent actual amounts paid during 2018 and 2017. See "—Narrative to the Summary Compensation Table—Annual Base Salary" below.

(2) Cash compensation amounts paid to Dr. Plat were paid in Canadian dollars through April 20, 2017 and have been converted to U.S. dollars for the purposes of the table. The U.S. dollar per Canadian dollar exchange rate used for such conversion was the average exchange rate in effect over the course of each payment period.

(3) Reflects performance-based cash bonuses awarded to our named executive officers. See "—Non Equity Incentive Plan Compensation" below for a description of the material terms pursuant to which this compensation was awarded.

(4) In accordance with SEC rules, this column reflects the aggregate grant date fair value of the option awards granted during fiscal years 2018 and 2017 computed in accordance with ASC 718 for share-based compensation transactions. Assumptions used in the calculation of these amounts are included in Note 7 to our audited consolidated financial statements included elsewhere in this prospectus. These amounts do not reflect the actual economic value that will be realized by the named executive officer upon the vesting of the share options, the exercise of the share options, or the sale of the common shares underlying such share options.

(5) Reflects reimbursements paid with respect to medical, dental, life and disability insurance policies obtained by Mr. Oliveto and Mr. Muller in 2017 and 2018, including (i) for Mr. Oliveto in 2017, medical ($17,800); dental ($1,661); life ($2,063) and disability ($1,651); (ii) for Mr. Oliveto in 2018, medical ($18,676); dental ($1,355); and life ($153); and for Mr. Muller in 2018, medical ($10,534).

(6) Reflects $300,000 in base salary and $64,166 in consulting fees paid prior to Mr. Oliveto's appointment as our Chief Executive Officer.

(7) In May 2017, our board of directors approved an increase in Dr. Plat's salary from C$300,000 to $330,000.

Narrative to the Summary Compensation Table

Our board of directors reviews compensation annually for all employees, including our named executive officers. In setting executive base salaries and bonuses and granting equity incentive awards, we consider compensation for comparable positions in the market, the historical compensation levels of our executives, individual performance as compared to our expectations and objectives, our desire to motivate our

employees to achieve short- and long-term results that are in the best interests of our shareholders and a long-term commitment to our company.

Either our board of directors or the compensation committee has historically determined our executive officers' compensation and has typically reviewed and discussed management's proposed compensation with our chief executive officer for all executives other than our chief executive officer. Based on those discussions and its discretion, the compensation committee and our full board of directors then approved the compensation of each executive officer. Upon the completion of this offering, the compensation committee will determine our executive officers' compensation and follow this process, but the compensation committee itself, rather than our board of directors, will approve the compensation of each executive officer.

Annual Base Salary

Base salaries for our executive officers are initially established through arm's-length negotiations at the time of the executive officer's hiring, taking into account such executive officer's qualifications, experience, the scope of his or her responsibilities and competitive market compensation paid by other companies for similar positions within the industry and geography. Base salaries are reviewed annually, typically in connection with our annual performance review process, and adjusted from time to time to realign salaries with market levels after taking into account individual responsibilities, performance and experience. For each of 2017 and 2018, the base salaries of Mr. Oliveto and Dr. Plat were $360,000 and $330,000, respectively. Mr. Muller's base salary for 2018 was $300,000. In making decisions regarding salary increases, we may also draw upon the experience of members of our board of directors with executives at other companies.

Non-Equity Incentive Plan Compensation

In accordance with the terms of their employment agreements, our named executive officers are eligible to receive discretionary annual bonuses of up to a percentage of each executive's gross base salary based on individual performance, company performance or as otherwise determined appropriate, as determined by our board of directors. The target bonus percentage for each of Mr. Oliveto and Dr. Plat in 2018 and 2017 were: Mr. Oliveto, 50% (2017 and 2018); and Dr. Plat, 20% (2017) and 25% (2018). Mr. Muller's target bonus percentage for 2018 was 25%.

Equity-Based Incentive Awards

Our equity-based incentive awards are designed to align our interests and those of our shareholders with those of our employees and consultants, including our executive officers. The board of directors is responsible for approving equity grants. As of the date of this prospectus, share option awards were the only form of equity awards we have granted to any of our executive officers.

We have historically used share options as an incentive for long-term compensation to our executive officers because the share options allow our executive officers to profit from this form of equity compensation only if our share price increases relative to the share option's exercise price, which exercise price is set at the fair market value of our common shares on the date of grant. We may grant equity awards at such times as our board of directors determines appropriate. Our executives generally are awarded an initial grant in the form of a share option in connection with their commencement of employment with us. Additional grants may occur periodically in order to specifically incentivize executives with respect to achieving certain corporate goals or to reward executives for exceptional performance.

Prior to this offering, we have granted all share options pursuant to our Stock Option Plan, or the 2011 Plan. Following this offering, we will grant equity incentive awards under the terms of the 2019 Equity Incentive Plan, or the 2019 Plan. The terms of our equity plans are described below under "— Equity Incentive Plans."

All options are granted with an exercise price per share that is no less than the fair market value of our common shares on the date of grant of such award. Our share option awards generally vest over a four-year period and may be subject to acceleration of vesting and exercisability under certain termination and change in control events. See "— Outstanding Equity Awards at Fiscal Year-End."

Outstanding Equity Awards at Fiscal Year-End

The following table provides information regarding the outstanding equity awards held by our named executive officers as of December 31, 2018. All awards were granted pursuant to the Stock Option Plan. See "— Equity Incentive Plans — 2011 Plan" below for additional information.

			OPTION AWARDS			
NAME AND PRINCIPAL POSITION	GRANT DATE	VESTING COMMENCEMENT DATE	NUMBER OF SECURITIES UNDERLYING UNEXERCISED OPTIONS (#) (EXERCISABLE)	NUMBER OF SECURITIES UNDERLYING UNEXERCISED OPTIONS (#) (UNEXERCISABLE)[1]	OPTION EXERCISE PRICE ($)	OPTION EXPIRATION DATE
Joseph Oliveto	10/27/2016	9/19/2016	10,569	111,004	1.12	09/19/2026
Chief Executive Officer	1/3/2017	9/19/2016	921	8,039	1.12	1/3/2027
	12/12/2017	9/19/2016	10,631	110,625	1.54	12/12/2027
	10/26/2018	9/19/2016	107,705	83,773	2.66	10/25/2028
	11/21/2018	11/21/2018	—	263,192	2.66	11/20/2028
Francis Plat	2/28/2014	12/18/2013	26,076	—	0.96 CA	12/18/2024
Chief Medical Officer	11/11/2014	7/25/2014	5,040	—	0.96 CA	7/25/2024
	08/26/2015	8/26/2015	16,441	3,288	1.12	8/26/2025
	2/21/2018	10/15/2018	—	53,202	1.54	10/15/2028
	2/21/2018	7/21/2017	29,572	53,928	1.54	7/21/2027
	11/21/2018	11/21/2018	—	37,598	2.66	11/20/2028
Lorenz Muller	2/21/2018	10/11/2017	—	99,238	1.54	10/11/2027
Chief Commercial Officer	2/21/2018	10/15/2018	—	50,946	1.54	10/15/2028
	11/21/2018	11/21/2018	—	18,799	2.66	11/20/2028

(1) The common shares underlying the options vest as to 25% on the first anniversary of the vesting commencement date, and the remaining shares vest in 36 equal monthly installments thereafter, subject to the officer's continued service through each vesting date.

(2) 79,016 of the common shares underlying the option vested on December 12, 2017, and the remaining shares vest in 33 equal monthly installments thereafter, subject to the officer's continued service through each vesting date.

Employment Arrangements

We have entered into employment agreements with each of our named executive officers. The agreements set forth the named executive officer's initial base salary, bonus potential, eligibility for employee benefits and severance benefits upon a qualifying termination of employment, subject to certain non-solicitation and non-competition provisions. Any potential payments and benefits due upon a qualifying termination of employment or a change in control are further described below under "— Potential Payments and Benefits upon Termination or Change in Control."

Agreement with Joseph Oliveto

We entered into an employment agreement with Mr. Oliveto, our President and Chief Executive Officer, in March 2017 that governed the terms of his employment with us prior to April 2019. Pursuant to his prior agreement, Mr. Oliveto was entitled to an annual base salary of $360,000, was eligible to receive an annual target performance bonus of up to 50% of his gross base salary, and was granted options to purchase an aggregate of 252,853 common shares.

In April 2019 in connection with this offering, we entered into an amended and restated employment agreement with Mr. Oliveto that governs the current terms of his employment with us. Pursuant to his amended and restated agreement, Mr. Oliveto is entitled to an annual base salary of $500,000 and is eligible to receive an annual target performance bonus of up to 50% of his gross base salary.

Agreement with Francis Plat

We entered into an employment agreement with Dr. Plat, our Chief Medical Officer, in April 2014 that governed the terms of his employment with us prior to April 2019. Pursuant to his prior agreement, Dr. Plat was entitled to an annual base salary C$300,000, was eligible to receive an annual target performance bonus of up to, as a percentage of his gross base salary, 20% for 2017 and 25% for 2018, and was granted an option to purchase 34,769 common shares. In May 2017, our board of directors approved an increase to Dr. Plat's annual base salary to $330,000.

In April 2019 in connection with this offering, we entered into an amended and restated employment agreement with Dr. Plat that governs the current terms of his employment with us. Pursuant to his amended and restated agreement, Dr. Plat is entitled to an annual base salary of $400,000 and is eligible to receive an annual target performance bonus of up to 35% of his gross base salary.

Agreement with Lorenz Muller

We entered into an employment agreement with Mr. Muller, our Chief Commercial Officer, in October 2017 that governed the terms of his employment with us prior to April 2019. Pursuant to his prior agreement, Mr. Muller was entitled to an annual base salary of $300,000, was eligible to receive an annual target performance bonus of up to 25% of his gross base salary, and was granted an option to purchase 190,310 common shares.

In April 2019 in connection with this offering, we entered into an amended and restated employment agreement with Mr. Muller that governs the current terms of his employment with us. Pursuant to his amended and restated agreement, Mr. Muller is entitled to an annual base salary of $350,000 and is eligible to receive an annual target performance bonus of up to 35% of his gross base salary.

Potential Payments and Benefits upon Termination or Change in Control

Regardless of the manner in which a named executive officer's employment with us terminates, the named executive officer is entitled to receive amounts earned during his term of service, including salary and accrued unused vacation pay. In addition, each of our named executive officers is eligible to receive certain benefits pursuant to his employment agreement with us as follows:

Joseph Oliveto

Under his amended and restated employment agreement, if Mr. Oliveto is terminated by us without cause or if Mr. Oliveto resigns for good reason, he is entitled to salary continuation and reimbursement of premiums to continue health care benefits for a period of 12 months, subject to his execution of a general release in favor of our company. If Mr. Oliveto is terminated without cause or resigns for good reason within 30 days prior to, or 12 months following, a change in control, he is entitled to receive (i) salary continuation and reimbursement of premiums to continue health care benefits for a period of 18 months, (ii) a one-time bonus equal to one and a half times his target bonus for the year in which he is terminated and (iii) accelerated vesting of any outstanding and unvested share options, subject in the case of the foregoing clauses (i) and (ii), to his execution of a general release in favor of our company.

Francis Plat

Under his amended and restated employment agreement, if Dr. Plat is terminated by us without cause or if Dr. Plat resigns for good reason, he is entitled to salary continuation for a period of nine months, as well as benefits coverage for a period of nine months or until Dr. Plat begins alternate employment, whichever occurs first, subject in each case to his release of claims in favor of our company. If Dr. Plat is terminated without cause or resigns for good reason within 30 days prior to, or 12 months following, a change in

control, he is entitled to receive (i) salary continuation for a period of 12 months, (ii) benefits coverage for a period of 12 months or until Dr. Plat begins alternate employment, whichever occurs first, (iii) a one-time bonus equal to his target bonus for the year in which he is terminated, and (iv) accelerated vesting of any outstanding and unvested share options, subject to his release of claims in favor of our company.

Lorenz Muller

Under his amended and restated employment agreement, if Mr. Muller is terminated by us without cause or if Mr. Muller resigns for good reason, he is entitled to salary continuation and reimbursement of premiums to continue health care benefits for a period of nine months, subject to his execution of a general release in favor of our company. If Mr. Muller is terminated without cause or resigns for good reason within 30 days prior to, or 12 months following, a change in control, he is entitled to receive (i) salary continuation and reimbursement of premiums to continue health care benefits for a period of 12 months, (ii) a one-time bonus equal to his target bonus for the year in which he is terminated and (iii) accelerated vesting of any outstanding and unvested share options, subject in the case of the foregoing clauses (i) and (ii), to his execution of a general release in favor of our company.

Health and Welfare and Retirement Benefits; Perquisites

Prior to 2018, we did not provide any health or welfare benefits to our U.S. employees. We did provide reimbursements or extra salary payments for employees, including Mr. Oliveto and Mr. Muller, to purchase personal health and welfare insurance. In 2018, our chief executive officer received medical, dental, vision, life and accidental death and dismemberment insurance generally made available to all of our U.S. employees. Our Chief Commercial Officer was provided reimbursement of personal health and welfare insurance through December 31, 2018. Beginning January 1, 2019, all employees either receive insurance coverage made available to the U.S. employees or group benefits insurance coverage made available to the Canadian employees. We do not provide a 401(k) plan or any other retirement plan to our employees in the United States or Canada. We generally do not provide perquisites or personal benefits to our named executive officers, except in limited circumstances. Our board of directors may elect to adopt qualified or nonqualified benefit plans in the future, if it determines that doing so is in our best interests.

Equity Incentive Plans

2019 Plan

Our board of directors adopted and our shareholders approved the 2019 Plan in April 2019. Our 2019 Plan is a successor to and continuation of our 2011 Plan. The 2019 Plan became effective upon, and no share awards were granted under the 2019 Plan until, the date of the underwriting agreement related to this offering. No further grants will be made under the 2011 Plan.

Awards. Our 2019 Plan provides for the grant of incentive stock options, or ISOs, within the meaning of Section 422 of the Code, to employees, including employees of any parent or subsidiary, and for the grant of nonstatutory stock options, or NSOs, share appreciation rights, restricted share awards, restricted share unit awards, performance share awards, performance cash awards and other forms of share awards to employees, directors and consultants, including employees and consultants of our affiliates.

Authorized Shares. Initially, the maximum number of our common shares that may be issued under our 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 our 2011 Plan at the time our 2019 Plan became effective, and (ii) any shares subject to outstanding options or other share awards that were granted under our 2011 Plan that terminate or expire prior to exercise or settlement; are forfeited because of the failure to vest; or are reacquired or withheld (or not issued) to satisfy a tax withholding obligation or the purchase or exercise price. In addition, the number of our common shares reserved for issuance under our 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 our 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 our board of directors. The maximum number of our common shares that may be issued on the exercise of ISOs under our 2019 Plan is 14,131,692 shares.

Shares subject to share awards granted under our 2019 Plan that expire or terminate without being exercised in full or that are paid out in cash rather than in shares do not reduce the number of shares available for issuance under our 2019 Plan. If any common shares issued pursuant to a share award are forfeited back to or repurchased by us because of the failure to meet a contingency or condition required to vest, the shares that are forfeited or repurchased will revert to and again become available for issuance under the 2019 Plan. Any shares subject to an award that are surrendered in satisfaction of tax withholding obligations or as consideration for the exercise or purchase price of a share award will again become available for issuance under the 2019 Plan.

The maximum number of common shares subject to share awards granted under the 2019 Plan or otherwise during any one calendar year to any non-employee director, taken together with any cash fees paid by us to such non-employee director during such calendar year for service on the board of directors, will not exceed $750,000 in total value (calculating the value of any such share awards based on the grant date fair value of such share awards for financial reporting purposes), or, with respect to the calendar year in which a non-employee director is first appointed or elected to our board of directors, $1,100,000.

Plan Administration. Our board of directors, or a duly authorized committee of our board of directors, will administer our 2019 Plan and is referred to as the "plan administrator" herein. Our board of directors may also delegate to one or more of our officers the authority to (1) designate employees (other than officers) to receive specified share awards and (2) determine the number of shares subject to such share awards. Under our 2019 Plan, our board of directors has the authority to determine award recipients, grant dates, the numbers and types of share awards to be granted, the applicable fair market value, and the provisions of each share award, including the period of exercisability and the vesting schedule applicable to a share award.

Under the 2019 Plan, the board of directors also generally has the authority to effect, with the consent of any adversely affected participant, (A) the reduction of the exercise, purchase, or strike price of any outstanding award; (B) the cancellation of any outstanding award and the grant in substitution therefore of other awards, cash, or other consideration; or (C) any other action that is treated as a repricing under generally accepted accounting principles.

Options. ISOs and NSOs are granted under option agreements adopted by the plan administrator. The plan administrator determines the exercise price for options, within the terms and conditions of the 2019 Plan, provided that the exercise price of a option generally cannot be less than 100% of the fair market value of our common shares on the date of grant. Options granted under the 2019 Plan vest at the rate specified in the option agreement as determined by the plan administrator.

The plan administrator determines the term of options granted under the 2019 Plan, up to a maximum of 10 years. Unless the terms of an optionholder's option agreement provide otherwise, if an optionholder's service relationship with us or any of our affiliates ceases for any reason other than disability, death, or cause, the optionholder may generally exercise any vested options for a period of three months following the cessation of service. This period may be extended in the event that exercise of the option is prohibited by applicable securities laws or our insider trading policy. If an optionholder's service relationship with us or any of our affiliates ceases due to death, or an optionholder dies within a certain period following cessation of service, the optionholder or a beneficiary may generally exercise any vested options for a period of 18 months following the date of death. If an optionholder's service relationship with us or any of our affiliates ceases due to disability, the optionholder may generally exercise any vested options for a period of 12 months following the cessation of service. In the event of a termination for cause, options generally

terminate upon the termination date. In no event may an option be exercised beyond the expiration of its term.

Acceptable consideration for the purchase of common shares issued upon the exercise of an option will be determined by the plan administrator and may include (1) cash, check, bank draft or money order, (2) a broker-assisted cashless exercise, (3) a net exercise of the option if it is an NSO, or (4) other legal consideration approved by the plan administrator.

Unless the plan administrator provides otherwise, options generally are not transferable except by will or the laws of descent and distribution. Subject to approval of the plan administrator or a duly authorized officer in each case, (i) an option may be transferred pursuant to a domestic relations order, official marital settlement agreement, or other divorce or separation instrument and (ii) an optionholder may designate a beneficiary who may exercise the option following the optionholder's death.

Tax Limitations on ISOs. The aggregate fair market value, determined at the time of grant, of our common shares with respect to ISOs that are exercisable for the first time by an award holder during any calendar year under all of our equity benefit plans may not exceed $100,000. Options or portions thereof that exceed such limit will generally be treated as NSOs. No ISO may be granted to any person who, at the time of the grant, owns or is deemed to own shares possessing more than 10% of our total combined voting power or that of any of our affiliates unless (1) the option exercise price is at least 110% of the fair market value of the shares subject to the option on the date of grant, and (2) the term of the ISO does not exceed five years from the date of grant.

Restricted Share Unit Awards. Restricted share unit awards are granted under restricted share unit award agreements adopted by the plan administrator. Restricted share unit awards may be granted in consideration for any form of legal consideration that may be acceptable to our board of directors and permissible under applicable law. A restricted share unit award may be settled by cash, delivery of shares, a combination of cash and shares as deemed appropriate by the plan administrator, or in any other form of consideration set forth in the restricted share unit award agreement. Additionally, dividend equivalents may be credited in respect of shares covered by a restricted share unit award. Except as otherwise provided in the applicable award agreement, restricted share unit awards that have not vested will be forfeited once the participant's continuous service ends for any reason.

Restricted Share Awards. Restricted share awards are granted under restricted share award agreements adopted by the plan administrator. A restricted share award may be awarded in consideration for cash, check, bank draft or money order, past or future services to us, or any other form of legal consideration that may be acceptable to our board of directors and permissible under applicable law. The plan administrator determines the terms and conditions of restricted share awards, including vesting and forfeiture terms. If a participant's service relationship with us ends for any reason, we may receive any or all of the common shares held by the participant that have not vested as of the date the participant terminates service with us through a forfeiture condition or a repurchase right.

Share Appreciation Rights. Share appreciation rights are granted under share appreciation right agreements adopted by the plan administrator. The plan administrator determines the purchase price or strike price for a share appreciation right, which generally cannot be less than 100% of the fair market value of our common shares on the date of grant. A share appreciation right granted under the 2019 Plan vests at the rate specified in the share appreciation right agreement as determined by the plan administrator.

The plan administrator determines the term of share appreciation rights granted under the 2019 Plan, up to a maximum of 10 years. If a participant's service relationship with us or any of our affiliates ceases for any reason other than cause, disability, or death, the participant may generally exercise any vested share appreciation right for a period of three months following the cessation of service. This period may be further

extended in the event that exercise of the share appreciation right following such a termination of service is prohibited by applicable securities laws or our insider trading policy. If a participant's service relationship with us, or any of our affiliates, ceases due to disability or death, or a participant dies within a certain period following cessation of service, the participant or a beneficiary may generally exercise any vested share appreciation right for a period of 12 months in the event of disability and 18 months in the event of death. In the event of a termination for cause, share appreciation rights generally terminate immediately upon the occurrence of the event giving rise to the termination of the individual for cause. In no event may a share appreciation right be exercised beyond the expiration of its term.

Performance Awards. The 2019 Plan permits the grant of performance-based share and cash awards. Our compensation committee may structure awards so that the share or cash will be issued or paid only following the achievement of certain pre-established performance goals during a designated performance period.

The performance goals that may be selected include one or more of the following: (i) sales; (ii) revenues; (iii) assets; (iv) expenses; (v) market penetration or expansion; (vi) earnings from operations; (vii) earnings before or after deduction for all or any portion of interest, taxes, depreciation, amortization, incentives, service fees or extraordinary or special items, whether or not on a continuing operations or an aggregate or per share basis; (viii) net income or net income per common share (basic or diluted); (ix) return on equity, investment, capital or assets; (x) one or more operating ratios; (xi) borrowing levels, leverage ratios or credit rating; (xii) market share; (xiii) capital expenditures; (xiv) cash flow, free cash flow, cash flow return on investment, or net cash provided by operations; (xv) share price, dividends or total shareholder return; (xvi) development of new technologies or products; (xvii) sales of particular products or services; (xviii) economic value created or added; (xix) operating margin or profit margin; (xx) customer acquisition or retention; (xxi) raising or refinancing of capital; (xxii) successful hiring of key individuals; (xxiii) resolution of significant litigation; (xxiv) acquisitions and divestitures (in whole or in part); (xxv) joint ventures and strategic alliances; (xxvi) spin-offs, split-ups and the like; (xxvii) reorganizations; (xxviii) recapitalizations, restructurings, financings (issuance of debt or equity) or refinancings; (xxix) or strategic business criteria, consisting of one or more objectives based on the following goals: achievement of timely development, design management or enrollment, meeting specified market penetration or value added, payor acceptance, patient adherence, peer reviewed publications, issuance of new patents, establishment of or securing of licenses to intellectual property, product development or introduction (including, without limitation, any clinical trial accomplishments, regulatory or other filings, approvals or milestones, discovery of novel products, maintenance of multiple products in pipeline, product launch or other product development milestones), geographic business expansion, cost targets, cost reductions or savings, customer satisfaction, operating efficiency, acquisition or retention, employee satisfaction, information technology, corporate development (including, without limitation, licenses, innovation, research or establishment of third-party collaborations), manufacturing or process development, legal compliance or risk reduction, patent application or issuance goals, or goals relating to acquisitions, divestitures or other business combinations (in whole or in part), joint ventures or strategic alliances; and (xxx) other measures of performance selected by the board of directors.

The performance goals may be based on company-wide performance or performance of one or more business units, divisions, affiliates, or business segments, and may be either absolute or relative to the performance of one or more comparable companies or the performance of one or more relevant indices. Our board of directors is authorized at any time in its sole discretion, to adjust or modify the calculation of a performance goal for such performance period in order to prevent the dilution or enlargement of the rights of participants, (a) in the event of, or in anticipation of, any unusual or extraordinary corporate item, transaction, event or development; (b) in recognition of, or in anticipation of, any other unusual or nonrecurring events affecting us, or our financial statements in response to, or in anticipation of, changes in applicable laws, regulations, accounting principles, or business conditions; or (c) in view of the board of director's assessment of our business strategy, performance of comparable organizations, economic and

business conditions, and any other circumstances deemed relevant. Specifically, the board of directors is authorized to make adjustment in the method of calculating attainment of performance goals and objectives for a performance period as follows: (i) to exclude the dilutive effects of acquisitions or joint ventures; (ii) to assume that any business divested by us achieved performance objectives at targeted levels during the balance of a performance period following such divestiture; and (iii) to exclude the effect of any change in our outstanding common share by reason of any share dividend or split, share repurchase, reorganization, recapitalization, merger, consolidation, spin-off, combination or exchange of shares or other similar corporate change, or any distributions to common shareholders other than regular cash dividends. In addition, the board of directors is authorized to make adjustment in the method of calculating attainment of performance goals and objectives for a performance period as follows: (i) to exclude restructuring and/or other nonrecurring charges; (ii) to exclude exchange rate effects, as applicable, for non-U.S. dollar denominated net sales and operating earnings; to exclude the effects of changes to generally accepted accounting standards required by the Financial Accounting Standards Board; (iv) to exclude the effects of any items that are "unusual" in nature or occur "infrequently" as determined under generally accepted accounting principles; (v) to exclude the effects to any statutory adjustments to corporate tax rates; and (vi) to make other appropriate adjustments selected by the board of directors.

Other Share Awards. The plan administrator may grant other awards based in whole or in part by reference to our common shares. The plan administrator will set the number of shares under the share award and all other terms and conditions of such awards.

Changes to Capital Structure. In the event there is a specified type of change in our capital structure, such as a share split, reverse share split, or recapitalization, appropriate adjustments will be made to (1) the class and maximum number of shares reserved for issuance under the 2019 Plan, (2) the class and maximum number of shares by which the share reserve may increase automatically each year, (3) the class and maximum number of shares that may be issued on the exercise of ISOs, (4) the class and maximum number of shares that may be awarded to any non-employee director and (5) the class and number of shares and exercise price, strike price, or purchase price, if applicable, of all outstanding share awards.

Corporate Transactions. Our 2019 Plan provides that in the event of certain specified significant corporate transactions (or a change in control, as defined below), unless otherwise provided in an award agreement or other written agreement between us and the award holder, the plan administrator may take one or more of the following actions with respect to such share awards:

- arrange for the assumption, continuation, or substitution of a share award by a successor corporation;
- arrange for the assignment of any reacquisition or repurchase rights held by us to a successor corporation;
- accelerate the vesting, in whole or in part, of the share award and provide for its termination if not exercised (if applicable) at or before the effective time of the transaction;
- arrange for the lapse, in whole or in part, of any reacquisition or repurchase rights held by us;
- cancel or arrange for the cancellation of the share award, to the extent not vested or not exercised before the effective time of the transaction, in exchange for a cash payment, if any; or
- make a payment equal to the excess, if any, of (A) the value of the property the participant would have received on exercise of the award immediately before the effective time of the transaction, over (B) any exercise price payable by the participant in connection with the exercise.

The plan administrator is not obligated to treat all share awards or portions of share awards in the same manner and is not obligated to take the same actions with respect to all participants.

Under the 2019 Plan, a corporate transaction is generally the consummation of: (1) a sale of all or substantially all of our assets, (2) the sale or disposition of more than 50% of our outstanding securities, (3) a merger, amalgamation, arrangement or consolidation where we do not survive the transaction, or (4) a merger or consolidation where we do survive the transaction but our common shares outstanding

immediately before such transaction are converted or exchanged into other property by virtue of the transaction.

Change in Control. In the event of a change in control, the plan administrator may take any of the above-mentioned actions. Awards granted under the 2019 Plan may be subject to additional acceleration of vesting and exercisability upon or after a change in control as may be provided in the applicable share award agreement or in any other written agreement between us or any affiliate and the participant, but in the absence of such provision, no such acceleration will automatically occur. Under the 2019 Plan, a change in control is generally (1) the acquisition by any person or company of more than 50% of the combined voting power of our then outstanding shares, (2) a merger, amalgamation, arrangement, consolidation or similar transaction in which our shareholders immediately before the transaction do not own, directly or indirectly, more than 50% of the combined voting power of the surviving entity (or the parent of the surviving entity) in substantially the same proportions as their ownership immediately prior to such transaction, (3) a sale, lease, exclusive license or other disposition of all or substantially all of our assets other than to an entity more than 50% of the combined voting power of which is owned by our shareholders in substantially the same proportions as their ownership of our outstanding voting securities immediately prior to such transaction, (4) a complete dissolution or liquidation of the company or (5) when a majority of our board of directors becomes comprised of individuals who were not serving on our board of directors on the date of the underwriting agreement related to this offering, or the incumbent board, or whose nomination, appointment, or election was not approved by a majority of the incumbent board still in office.

Plan Amendment or Termination. Our board of directors has the authority to amend, suspend, or terminate our 2019 Plan, provided that such action does not materially impair the existing rights of any participant without such participant's written consent. Certain material amendments also require the approval of our shareholders. No ISOs may be granted after the tenth anniversary of the date our board of directors adopts our 2019 Plan. No share awards may be granted under our 2019 Plan while it is suspended or after it is terminated.

2011 Plan

General. Our board of directors originally adopted and our shareholders initially approved our 2011 Plan in August 2011. We have subsequently amended and restated our 2011 Plan, most recently in October 2018, the purpose of which was to increase the number of shares available for issuance under our 2011 Plan. Our shareholders approved this recent amendment and restatement in October 2018. Our 2011 Plan was terminated upon the adoption of our 2019 Plan; however, awards outstanding under our 2011 Plan will continue in full effect in accordance with their existing terms.

Share Reserve. The aggregate number of common shares reserved for issuance under our 2011 Plan is 3,238,943. As of December 31, 2018, options to purchase 2,295,045 common shares, at exercise prices ranging from $0.7021 to $2.6597 per share, or a weighted-average exercise price of $1.7713 per share, were outstanding under our 2011 Plan.

Administration. The compensation committee of our board of directors administers our 2011 Plan. Our board of directors has full authority and discretion to take any actions it deems necessary or advisable for the administration of our 2011 Plan. Our board of directors may cancel, amend, adjust or otherwise change any outstanding options under such circumstances as it may consider appropriate in accordance with the provisions of the 2011 Plan.

Types of Awards. Our 2011 Plan provides for the grant of incentive share options and nonstatutory share options to purchase common shares of our share capital to employees, members of our board of directors and consultants. Incentive share options may be granted only to employees.

Options. The exercise price of options granted under our 2011 Plan will be equal to or exceed the fair market value of a common share of our share capital on the grant date. Options expire at the time

determined by the administrator, but in no event more than ten years after they are granted, and generally expire earlier if the optionholder's service terminates.

Capital Reorganization. If we effect a subdivision, consolidation, or similar reorganization, or any other change in capitalization that, in the option of the administrator, warrants the replacement or amendment of any existing options, the administrator may adjust: (i) the number of common shares that may be acquired on the exercise of any options; and/or (ii) the exercise price of any outstanding options, as necessary.

Other Events Affecting the Corporation. In the event of an amalgamation, combination, merger or other reorganization involving the exchange of our common shares, by sale or lease of assets or otherwise, that, in the opinion of the administrator, in its discretion, warrants the replacement or amendment of any existing options in order to adjust: (a) the number of common shares that may be acquired on the exercise of any outstanding options; and/or (b) the exercise price of any outstanding options in order to preserve proportionately the rights and obligations of the optionees, the administrator will authorize such steps to be taken as may be equitable and appropriate to that end.

Liquidity Event. Notwithstanding anything else provided in the 2011 Plan or any option agreement, upon a liquidity event, our board of directors (or a committee thereof) may:

- cause the conversion or exchange of any outstanding options into or for options, rights or other securities of substantially equivalent value (or greater value), in any entity participating in or resulting from such liquidity event; and/or
- accelerate the vesting of any or all outstanding options to provide that such outstanding options will be fully vested and exercisable contemporaneously with the completion of the transaction resulting in the liquidity event.

In general, a "liquidity event" means the acquisition of the company by another entity by means of any transaction or series of related transactions, which results in one person, together with any related entities of such person, acquiring beneficial ownership, or exercising direction or control, over more than 50% of the combined voting power attached to all of our outstanding securities; a sale, lease, transfer, exclusive license or disposition of all or substantially all of our assets; our adoption of a plan of liquidation providing for the distribution of all or substantially all of our assets; or any other event so specified by our board of directors, subject to certain exceptions.

Transferability. A participant may not transfer options under our 2011 Plan other than by will, the laws of descent and distribution, or as otherwise provided under our 2011 Plan.

Plan Amendment or Termination. Subject to any shareholders agreement, our board of directors may terminate the 2011 Plan at any time without shareholder approval. Our board of directors has the authority to amend our 2011 Plan, provided that such action is approved by our shareholders to the extent shareholder approval is necessary. As described above, our 2011 Plan was terminated upon the effective date of our 2019 Plan.

2019 Employee Share Purchase Plan

Our board of directors adopted and our shareholders approved the 2019 Employee Share Purchase Plan, or the ESPP, in April 2019. The ESPP became effective immediately prior to and contingent upon the date of the underwriting agreement related to this offering. The purpose of the ESPP is to secure the services of new employees, to retain the services of existing employees, and to provide incentives for such individuals to exert maximum efforts toward our success and that of our affiliates. The ESPP is intended to qualify as an "employee stock purchase plan" within the meaning of Section 423 of the Code for U.S. employees. In addition, the ESPP authorizes grants of purchase rights that do not comply with Section 423 of the Code under a separate non-423 component. In particular, where such purchase rights are granted to employees who are employed or located outside the United States, our board of directors may adopt rules that are beyond the scope of Section 423 of the Code.

Share Reserve. Following this offering, the ESPP authorizes the issuance of 278,764 common shares of our share capital under purchase rights granted to our employees or to employees of any of our designated affiliates. The number of shares of our share capital 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 our 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, our board of directors may determine that such increase will be less than the amount set forth in clauses (1) and (2). As of the date hereof, no shares of our share capital have been purchased under the ESPP.

Administration. Our board of directors administers the ESPP and may delegate its authority to administer the ESPP to our compensation committee. The ESPP is implemented through a series of offerings under which eligible employees are granted purchase rights to purchase shares of our share capital on specified dates during such offerings. Under the ESPP, we may specify offerings with durations of not more than 27 months, and may specify shorter purchase periods within each offering. Each offering will have one or more purchase dates on which shares of our share capital will be purchased for employees participating in the offering. An offering under the ESPP may be terminated under certain circumstances.

Payroll Deductions. Generally, all regular employees, including executive officers, employed by us or by any of our designated affiliates, may participate in the ESPP and may contribute, normally through payroll deductions, up to 15% of their earnings (as defined in the ESPP) for the purchase of our share capital under the ESPP. Unless otherwise determined by our board of directors, common shares will be purchased for the accounts of employees participating in the ESPP at a price per share that is at least the lesser of (1) 85% of the fair market value of a share of our share capital on the first date of an offering or (2) 85% of the fair market value of a share of our share capital on the date of purchase.

Limitations. Employees may have to satisfy one or more of the following service requirements before participating in the ESPP, as determined by our board of directors, including: (1) being customarily employed for more than 20 hours per week, (2) being customarily employed for more than five months per calendar year or (3) continuous employment with us or one of our affiliates for a period of time (not to exceed two years). No employee may purchase shares under the ESPP at a rate in excess of $25,000 worth of our common shares based on the fair market value per share of our common shares at the beginning of an offering for each calendar year such a purchase right is outstanding. Finally, no employee will be eligible for the grant of any purchase rights under the ESPP if immediately after such rights are granted, such employee has voting power over 5% or more of our outstanding capital shares measured by vote or value under Section 424(d) of the Code.

Changes to Capital Structure. In the event that there occurs a change in our capital structure through such actions as a share split, merger, amalgamation, arrangement, consolidation, reorganization, recapitalization, reincorporation, share dividend, dividend in property other than cash, large nonrecurring cash dividend, liquidating dividend, combination of shares, exchange of shares, change in corporate structure, or similar transaction, the board of directors will make appropriate adjustments to: (1) the class(es) and maximum number of shares reserved under the ESPP, (2) the class(es) and maximum number of shares by which the share reserve may increase automatically each year, (3) the class(es) and number of shares subject to and purchase price applicable to outstanding offerings and purchase rights and (4) the class(es) and number of shares that are subject to purchase limits under ongoing offerings.

Corporate Transactions. In the event of certain significant corporate transactions, any then-outstanding rights to purchase our shares under the ESPP may be assumed, continued, or substituted for by any surviving or acquiring entity (or its parent company). If the surviving or acquiring entity (or its parent company) elects not to assume, continue, or substitute for such purchase rights, then the participants' accumulated payroll contributions will be used to purchase shares of our share capital within 10 business days before such corporate transaction, and such purchase rights will terminate immediately.

Under the ESPP, a corporate transaction is generally the consummation of: (1) a sale of all or substantially all of our assets, (2) the sale or disposition of more than 50% of our outstanding securities, (3) a merger, amalgamation, arrangement or consolidation where we do not survive the transaction and (4) a merger, amalgamation, arrangement or consolidation where we do survive the transaction but the shares of our share capital outstanding immediately before such transaction are converted or exchanged into other property by virtue of the transaction.

Amendment or Termination. Our board of directors has the authority to amend or terminate our ESPP, provided that except in certain circumstances such amendment or termination may not materially impair any outstanding purchase rights without the holder's consent. We will obtain shareholder approval of any amendment to our ESPP as required by applicable law or listing requirements

Non-Employee Director Compensation

We have not historically had a formal compensation policy with respect to service on our board of directors, but we have reimbursed our non-employee directors for direct expenses incurred in connection with attending meetings of our board of directors or its committees, and occasionally granted share options.

In April 2019, our board of directors approved a non-employee director compensation policy that will be effective upon the effectiveness of the registration statement of which this prospectus is a part. Under this policy, we will pay each of our non-employee directors a cash retainer for service on the board of directors and for service on each committee on which the director is a member. The chairperson of each committee will receive a higher retainer for such service. These retainers are payable in arrears in four equal quarterly installments on the last day of each quarter, provided that the amount of such payment will be prorated for any portion of such quarter that the director is not serving on our board of directors or the applicable committee. No retainers will be paid in respect of any period prior to the completion of this offering. The retainers to be paid to non-employee directors for service on the board of directors and for service on each committee of the board of directors on which the director is a member are as follows:

Position	Annual Service Retainer	Chairperson Additional Annual Retainer
Board of directors	$ 35,000	$ 30,000
Audit committee	7,500	7,500
Compensation committee	6,000	6,000
Nominating and corporate governance committee	4,000	4,000

In addition, under our non-employee director compensation policy, each non-employee director elected to our board of directors after the completion of this offering will receive an option to purchase 19,000 shares of our common stock. The shares subject to each such stock option will vest annually over a three-year period, subject to the director's continued service as a director. Further, on the date of each annual meeting of stockholders held after the completion of this offering, each non-employee director that continues to serve as a non-employee member on our board of directors will receive an option to purchase 10,900 shares of our common stock. The shares subject to each such stock option will vest in full on the date that is 12 months after the grant date, subject to the director's continued service as a director. The exercise price per share of these options will equal the fair market value of our common stock on the date of grant.

This policy is intended to provide a total compensation package that enables us to attract and retain qualified and experienced individuals to serve as directors and to align our directors' interests with those of our stockholders.

Director Compensation Table

The following table sets forth information regarding the compensation earned for service on our board of directors by our non-employee directors and for their service as a consultant to us, if applicable, during the year ended December 31, 2018. Joseph Oliveto also served on our board of directors, but did not receive any additional compensation for his service as a director and therefore is not included in the table below. The compensation for Joseph Oliveto as a named executive officer is set forth above under "— Summary Compensation Table." Messrs. Edick and Tomsicek joined our board of directors in March 2019 and did not receive any compensation from us in the year ended December 31, 2018.

NAME	FEES EARNED OR PAID IN CASH ($)	OPTION AWARDS ($)[1][2]	TOTAL ($)
Marco Boorsma.	—	—	—
Nilesh Kumar	—	—	—
Debra K. Liebert	—	—	—
Dion Madsen[3]	—	—	—
Paul Truex	50,000	80,267	130,267
Scott Weiner[3]	—	—	—

(1) In accordance with SEC rules, this column reflects the aggregate grant date fair value of the option awards granted during fiscal year 2018 computed in accordance with ASC 718. Assumptions used in the calculation of these amounts are included in note 6 to our audited consolidated financial statements included elsewhere in this prospectus. These amounts do not reflect the actual economic value that will be realized by our non-employee directors upon the vesting of the share options, the exercise of the share options or the sale of the common shares underlying such share options.

(2) The following table provides information regarding the number of common shares underlying share options granted to our non-employee directors that were outstanding as of December 31, 2018:

NAME	OPTION AWARDS OUTSTANDING AT YEAR-END
Paul Truex	79,556

(3) Messrs. Madsen and Weiner resigned from our board of directors effective October 15, 2018.

CERTAIN RELATIONSHIPS AND RELATED PARTY TRANSACTIONS

The following includes a summary of transactions since January 1, 2016 and any currently proposed transactions, to which we were or are to be a participant, in which (1) the amount involved exceeds the lesser of $120,000 or 1% of the average of our total assets at year end for the last two completed fiscal years, and (2) any of our directors, executive officers or holders of more than 5% of our share capital, or any affiliate or member of the immediate family of the foregoing persons, had or will have a direct or indirect material interest, other than compensation and other arrangements that are described under the section titled "Executive and Director Compensation."

We believe the terms obtained or consideration that we paid or received, as applicable, in connection with the transactions described below were comparable to terms available or the amounts that we would pay or receive, as applicable, in arm's-length transactions.

Preferred Financings

Class B Preferred Share Financing

In various closings throughout 2016 and 2017, we issued an aggregate of 2,830,907 Class B preferred shares at a price per share of $6.1172 in a private placement to accredited investors, raising aggregate gross proceeds of approximately $10.0 million.

The table below sets forth the number of our Class B preferred shares purchased by our executive officers, directors, holders of more than 5% of our share capital and their affiliated entities or immediate family members. Each Class B preferred share in the table below will automatically convert into one common share upon the completion of this offering.

NAME	CLASS B PREFERRED SHARES (#)	AGGREGATE CASH PURCHASE PRICE ($)
Fonds de Solidarité des Travailleurs du Québec (F.T.Q.)	333,619	2,040,816
Entities affiliated with A.M. Pappas Life Science Ventures IV, LP[1]	235,496	1,440,576
Entities affiliated with BDC Capital, Inc.[2]	392,493	2,400,961
Domain Partners VIII, L.P.[3]	673,126	4,117,647

(1) Scott Weiner was a member of our board of directors and a partner at A.M. Pappas Life Science Ventures IV, L.P. at the time of the initial closing of our Class B preferred shares financing. Mr. Weiner resigned from our board of directors effective October 15, 2018.

(2) Ela Borenstein, who was a member of our board of directors at the initial closing of our Class B preferred shares financing, was a managing partner at BDC Capital, Inc.

(3) Debra K. Liebert, a member of our board of directors, is a managing director at Domain Associates, LLC, the manager of Domain Partners VIII, L.P., or Domain, and was designated to our board by Domain.

Class C Preferred Share Financing

In July 2017, we issued an aggregate of 3,786,878 Class C preferred shares at a price per share of $7.2619 in a private placement to accredited investors for aggregate gross cash proceeds of $27.5 million.

The table below sets forth the number of Class C preferred shares purchased by our executive officers, directors, holders of more than 5% of our share capital and their affiliated entities or immediate family

members. Each Class C preferred share in the table below will automatically convert into one common share upon the completion of this offering.

NAME	CLASS C PREFERRED SHARES (#)	AGGREGATE CASH PURCHASE PRICE ($)
Novo Holdings A/S[1]	1,377,048	10,000,000
Forbion Capital Fund III Cooperatief U.A.[2]	688,524	5,000,000
Fonds de Solidarité des Travailleurs du Québec	437,203	3,174,934
Entities affiliated with A.M. Pappas Life Science Ventures IV, L.P.[3]	203,664	1,478,994
Entities affiliated with BDC Capital, Inc.[4]	336,687	2,444,995
Domain Partners VIII, L.P.[5]	330,640	2,401,080

(1) Nilesh Kumar, a member of our board of directors, is a partner at Novo Ventures (US), Inc., which is wholly owned by, and provides consulting services to, Novo Holdings A/S. Dr. Kumar was designated to our board by Novo Holdings A/S.

(2) Marco Boorsma, a member of our board of directors, is a general partner at Forbion Capital Fund III Cooperatief U.A., or Forbion, and was designated to our board by Forbion.

(3) Scott Weiner was a then member of our board of directors and a partner at A.M. Pappas Life Science Ventures IV, L.P. Mr. Weiner resigned from our board of directors effective October 15, 2018.

(4) Dion Madsen, who was then a member of our board of directors and senior managing partner of BDC Capital, Inc., is now the co-founder and partner of Amplitude Ventures Capital Management Inc., or Amplitude. Investments by BDC Capital, Inc. are managed by Amplitude. Mr. Madsen resigned from our board of directors effective October 15, 2018.

(5) Debra K. Liebert, a member of our board of directors, is a managing director at Domain Associates, LLC, the manager of Domain and was designated to our board by Domain.

Class D Preferred Share Financing

In October 2018, we issued an aggregate of 8,116,892 Class D preferred shares at a price per share ranging from $9.4295 to $12.2583 in a private placement to accredited investors for aggregate gross cash proceeds of $80.0 million.

The table below sets forth the number of Class D preferred shares purchased by our executive officers, directors, holders of more than 5% of our share capital and their affiliated entities or immediate family

members. Each Class D preferred share in the table below will automatically convert into one common share upon the completion of this offering.

NAME	CLASS D PREFERRED SHARES (#)	AGGREGATE CASH PURCHASE PRICE ($)
Novo Holdings A/S[1]	964,089	9,090,907
Entities affiliated with RTW Master Fund Ltd.	2,855,189	27,500,000
Entities affiliated with Venrock Healthcare Capital Partners III, L.P.	1,815,089	20,000,000
Forbion Capital Fund III Cooperatief U.A.[2]	482,045	4,545,455
Fonds de Solidarité des Travailleurs du Québec	306,092	2,886,303
Entities affiliated with A.M. Pappas Life Science Ventures IV, L.P.[3]	142,588	1,344,540
Entities affiliated with BDC Capital, Inc.[4]	235,719	2,222,725
Domain Partners VIII, L.P.[5]	231,485	2,182,800

(1) Nilesh Kumar, a member of our board of directors, is a partner at Novo Ventures (US), Inc., which is wholly owned by, and provides consulting services to, Novo Holdings A/S. Dr. Kumar was designated to our board by Novo Holdings A/S.

(2) Marco Boorsma, a member of our board of directors, is a general partner at Forbion and was designated to our board by Forbion.

(3) Scott Weiner was a then member of our board of directors and a partner at A.M. Pappas Life Science Ventures IV, L.P. Mr. Weiner resigned from our board of directors effective October 15, 2018.

(4) Dion Madsen, who was then a member of our board of directors, is the co-founder and partner of Amplitude. Investments by BDC Capital, Inc. are managed by Amplitude. Mr. Madsen resigned from our board of directors effective October 15, 2018.

(5) Debra K. Liebert, a member of our board of directors, is a managing director at Domain Associates, LLC, the manager of Domain and was designated to our board by Domain.

Registration Rights Agreement

We are party to a third amended and restated registration rights agreement, dated October 15, 2018, with all holders of our preferred shares. This agreement provides that these holders are entitled to certain registration rights, including the right to demand that we file a registration statement or request that their shares be covered by a registration statement that we otherwise file. The registration rights will terminate upon the earliest of (i) the occurrence of certain mergers or consolidations of the company, (ii) the date on which the shares that are the subject to the agreement are publicly sold, or if they may be publicly sold: (x) pursuant to Rule 144 of the Securities Act and (y) Section 2.5 of Regulation 45-102 respecting Resale of Securities, as adopted by the Canadian Securities Administrators of and (iii) five years after the completion this offering. For a description of the registration rights, see the section titled "Description of Share Capital — Registration Rights."

Shareholders' Agreement

We are party to a fourth amended and restated shareholders' agreement, dated October 15, 2018, with the holders of our preferred shares and certain holders of our common shares. This agreement provides that these holders will vote in accordance with the terms of the agreement, including in matters related to the composition of our board of directors. In addition, this agreement provides for certain transfer restrictions, information rights and preemptive rights in favor of certain holders of our preferred shares with regard to certain issuances of our share capital. This agreement will terminate upon the completion of this offering.

Other Transactions

We have entered into various employment-related agreements with our executive officers that, among other things, provide for compensatory and certain change in control benefits. For a description of these agreements and arrangements, see the section titled "Executive and Director Compensation — Employment Arrangements."

We have also granted options to purchase shares of our common shares to our executive officers and directors. For a description of these options, see the section titled "Executive and Director Compensation."

Indemnity Agreements

We have entered or intend to enter, and intend to continue to enter, into separate indemnity agreements with some of our directors and executive officers, in addition to the indemnification provided for in our bylaws. These indemnity agreements provide our directors and executive officers with contractual rights to indemnification and, in some cases, expense advancement in any action or proceeding arising out of their services as one of our directors or executive officers or as a director or executive officer of any other company or enterprise to which the person provides services at our request. For more information regarding these indemnity agreements, see "Management — Limitation on Liability and Indemnification Matters."

Related Party Transaction Policy

In connection with this offering, we have adopted a written related party transaction policy that sets forth our procedures for the identification, review, consideration and approval or ratification of related party transactions. This policy became effective upon the effectiveness of the registration statement of which this prospectus is a part. For purposes of this policy only, a "related person transaction" is a transaction, arrangement or relationship (or any series of similar transactions, arrangements or relationships) in which we and any related person are participants involving an amount that exceeds the lesser of $120,000 or 1% of the average of our total assets at year end for the last two completed fiscal years. Transactions involving compensation for services provided to us as an employee, consultant or director are not considered related-person transactions under this policy. A "related person" is any executive officer, director, nominee to become a director or a holder of more than 5% of our share capital, or any affiliate or member of the immediate family of the foregoing.

Under the policy, where a transaction has been identified as a related-person transaction, management must present information regarding the proposed related-person transaction to our audit committee or, where review by our audit committee would be inappropriate due to a conflict of interest, to another independent body of our board of directors, for review. The presentation must include a description of, among other things, all of the parties, the direct and indirect interests of the related persons, the purpose of the transaction, the material facts, the benefits of the transaction to us and whether any alternative transactions are available, an assessment of whether the terms are comparable to the terms available from unrelated third parties and management's recommendation. To identify related-person transactions in advance, we rely on information supplied by our executive officers, directors and certain significant shareholders. In considering related-person transactions, our audit committee or another independent body of our board of directors takes into account the relevant available facts and circumstances including, but not limited to:

- the risks, costs and benefits to us;
- the impact on a director's independence in the event the related person is a director, immediate family member of a director or an entity with which a director is affiliated;
- the terms of the transaction;
- the availability of other sources for comparable services or products; and
- the terms available to or from, as the case may be, unrelated third parties under the same or similar circumstances.

All of the transactions described in this section were entered into prior to the adoption of this policy. Although we have not had a written policy for the review and approval of transactions with related persons, our board of directors has historically reviewed and approved any transaction where a director or officer had a financial interest, including the transactions described above. Prior to approving such a transaction, the material facts as to a director's or officer's relationship or interest in the agreement or transaction were disclosed to our board of directors. Our board of directors took this information into account when evaluating the transaction and in determining whether such transaction was fair to us and in the best interest of all our shareholders.

PRINCIPAL SHAREHOLDERS

The following table sets forth information regarding beneficial ownership of our share capital as of March 31, 2019 by:

- each person, or group of affiliated persons, known by us to beneficially own more than 5% of our common shares;
- each of our directors;
- each of our named executive officers; and
- all of our current executive officers and directors as a group.

The percentage ownership information under the column titled "Before Offering" is based on 18,165,742 common shares outstanding as of March 31, 2019, assuming the automatic conversion of all outstanding preferred shares into an aggregate of 17,550,802 common shares immediately prior to the completion of this offering. The percentage ownership information under the column titled "After Offering" is based on the sale of 5,500,000 common shares in this offering. The percentage ownership information assumes no exercise of the underwriters' option to purchase additional shares and no purchases of any common shares in this offering by the beneficial owners identified in the table below.

Information with respect to beneficial ownership has been furnished by each director, officer or beneficial owner of more than 5% of our common shares. We have determined beneficial ownership in accordance with the rules of the SEC. These rules generally attribute beneficial ownership of securities to persons who possess sole or shared voting power or investment power with respect to those securities. In addition, the rules include common shares issuable pursuant to the exercise of options that are either immediately exercisable or exercisable within 60 days of March 31, 2019. These shares are deemed to be outstanding and beneficially owned by the person holding those options for the purpose of computing the percentage ownership of that person, but they are not treated as outstanding for the purpose of computing the percentage ownership of any other person. Unless otherwise indicated, the persons or entities identified in this table have sole voting and investment power with respect to all shares shown as beneficially owned by them, subject to applicable community property laws.

Except as otherwise noted below, the address for each person or entity listed in the table is c/o Milestone Pharmaceuticals Inc., 1111 Dr. Frederik-Philips Blvd., Suite 420, Montréal, Québec CA H4M 2X6.

	NUMBER OF SHARES BENEFICIALLY OWNED	PERCENTAGE OF SHARES BENEFICIALLY OWNED	
		BEFORE OFFERING	AFTER OFFERING
Greater than 5% Shareholders:			
RTW Investments, LP[1]	2,855,189	15.7%	12.1%
Novo Holdings A/S[2]	2,341,137	12.9%	9.9%
Fonds de solidarité des travailleurs du Québec (F.T.Q.)[3]	2,286,977	12.6%	9.7%
BDC Capital, Inc. and affiliates[4]	2,188,008	12.1%	9.2%
Entities affiliated with Venrock[5]	1,815,007	10.0%	7.7%
Domain Associates, L.L.C. and affiliates[6]	1,706,438	9.4%	7.2%
Pappas Capital, LLC and affiliates.[7]	1,315,610	7.3%	5.6%
Entities affiliated with Forbion[8]	1,170,569	6.5%	5.0%
Directors and Named Executive Officers:			
Joseph Oliveto[9]	477,618	2.6%	2.0%
Lorenz Muller[10]	55,456	*	*
Francis Plat[11]	99,342	*	*
Marco Boorsma	—	*	*
Paul Edick	—	*	*
Nilesh Kumar[12]	—	*	*
Debra K. Liebert	—	*	*
Michael Tomsicek	—	*	*
Paul Truex[13]	45,078	*	*
All current executive officers and directors as a group (11 persons)	936,943	5.0%	3.9%

* Represents beneficial ownership of less than 1%.

(1) Includes (i) 2,478,979 shares held directly by RTW Master Fund, Ltd. and (ii) 376,210 shares held directly by RTW Innovation Master Fund, Ltd. RTW Investments, LP is the investment manager of each of these funds, and has the power to vote and the power to direct the disposition of all such common shares held by the funds. Roderick Wong, M.D. is the Managing Partner and Chief Investment Officer of RTW Investments, LP and may be deemed to beneficially own such common shares. The address of RTW Investments, LP and Dr. Wong is 412 West 15th Street, Floor 9, New York, New York, 10011.

(2) The board of directors of Novo Holdings A/S, or Novo, currently consists of Viviane Monges, Jeppe Christiansen, Steen Riisgaard, Lars Rebien Sørensen, Jean-Luc Butel and Francis Cuss, who share investment and voting control with respect to the shares held by Novo and may exercise such control only with the support of a majority of the members of the Novo board of directors. No individual member of the Novo board of directors is deemed to hold any beneficial ownership or reportable pecuniary interest in the shares held by Novo. The principal business address of Novo is Tuborg Havnevej 19, DK-2900 Hellerup, Denmark.

(3) The address for this entity is 545 Cremazie Blvd. East, Suite 200, Montréal, Québec, H2M 2W4, Canada.

(4) Includes 1,094,004 shares held by BDC Capital, Inc., or BDC Capital, and 1,094,004 shares held by GO Capital, s.e.c., a fund for which BDC Capital is the general partner and investment manager. BDC Capital has the power to vote and the power to direct the disposition of all such shares held by itself and Go Capital, s.e.c. BDC Capital's investment in our company is managed by Amplitude Ventures Capital Management Inc., or Amplitude, of which Dion Madsen and Jean-François Pariseau serve as partners. Go Capital, s.e.c. is managed by Dominique Bélanger, Managing Partner, Co-Investments at BDC Capital. BDC Capital retains the right to approve of certain investment, voting or divestiture decisions proposed by Amplitude, such

decisions being approved, depending on their quantum and potential impact, by either senior management at BDC Capital or by BDC Capital's investment committee. The address for BDC Capital and its affiliates is 5 Place Ville-Marie, Suite 400, Montréal, Québec, H3B 5E7, Canada.

(5) Includes (i) 1,650,080 shares held directly by Venrock Healthcare Capital Partners III, LP and (ii) 165,007 shares held directly by VHCP Co-Investment Holdings III, LLC. VHCP Management III, LLC is the general partner of Venrock Healthcare Capital Partners III, LP and the manager of VHCP Co-Investment Holdings III, LLC and may be deemed to beneficially own such common shares. Bong Koh and Nimish Shah are the managing members of VHCP Management III, LLC and may be deemed to beneficially own such common shares. The address of the Venrock entities Drs. Koh and Shah is 7 Bryant Park, 23rd Floor, New York, New York 10018.

(6) Represents 1,706,438 shares held directly by Domain Partners VIII, L.P. ("DP VIII"). The principal business of DP VIII is that of a private investment partnership. The sole general partner of DP VIII is One Palmer Square Associates VIII, LLC, a Delaware limited liability company ("OPSA VIII"). The principal business of OPSA VIII is that of acting as the general partner of DP VIII. James C. Blair, Brian H. Dovey, Brian K. Halak, Jesse I. Treu, and Nicole Vitullo are the managing members of OPSA VIII and have shared voting and dispositive power over the shares beneficially owned by DP VIII. Domain Associates, L.L.C. is ("DA") is the Manager of DPVIII. Debra K. Liebert is a member of our board of directors, a member of OPSA VIII and an employee of DA. Ms. Liebert has no voting or investment control with respect to any of the above noted holdings. Ms. Liebert disclaims beneficial ownership of the shares reflected above as beneficially owned by DPVIII except to the extent of her pecuniary interest therein. The address of Domain Associates, L.L.C. and affiliated entities is 202 Carnegie Center, Suite 104, Princeton, New Jersey, 08540.

(7) Includes (i) 1,255,843 shares held directly by A.M. Pappas Life Science Ventures IV, L.P. ("Pappas Ventures IV") and (ii) 59,767 shares held directly by PV IV CEO Fund, L.P. ("PV IV" and together with Pappas Ventures IV, the "Pappas Funds"). The principal business of the Pappas Funds is investing in early-stage life science companies. AMP&A Management IV, LLC ("Management IV") is the general partner of each of the Pappas Funds and has a management agreement with Pappas Capital, LLC ("Pappas Capital") whereby Pappas Capital provides management services for the Pappas Funds. As a result, Pappas Capital's investment committee exercises sole dispositive and voting power over the securities owned by the Pappas Funds. Arthur Pappas is the sole managing member of Pappas Capital. By virtue of these relationships, Management IV, Pappas Capital and Mr. Pappas may be deemed to beneficially own the securities owned directly by the Pappas Funds. Each of Management IV, Pappas Capital and Mr. Pappas disclaims beneficial ownership of such securities except to the extent of its or his respective pecuniary interest therein. The address of each of the foregoing is 2520 Meridian Parkway, Suite 400, Durham, North Carolina 27713.

(8) Represents shares held by Forbion Capital Fund III Coöperatief U.A ("FCF III"). Forbion III Management B.V., the director of FCF III, may be deemed to have voting and dispositive power over the common shares held by FCF III. Investment decisions with respect to the common shares held by FCF III can be made by its investment committee which may delegate such powers to the authorized representatives of Forbion III Management B.V. Mssrs. Slootweg, van Osch, Mulder, van Houten, van Deventer, Reithinger and Boorsma ("Partners") are partners of FCPM II Services B.V., which acts as the investment advisor to the directors of FCF III. Each of the Partners disclaim beneficial ownership of such common shares, except to the extent of his pecuniary interest therein. The address of FCF III, Forbion III Management B.V. and FCPM III Services B.V. is Gooimeer 2-35, 1411 DC Naarden, The Netherlands.

(9) Includes 204,462 common shares issuable upon the exercise of options.

(10) Includes 5,838 common shares issuable upon the exercise of options.

(11) Includes 87,885 common shares issuable upon the exercise of options.

(12) Dr. Kumar, a member of our board of directors, is employed as a Partner at Novo Ventures (US) Inc., which provides certain consultancy services to Novo, and Dr. Kumar is not deemed to have beneficial ownership of the shares held by Novo.

(13) Includes 28,173 common shares issuable upon the exercise of options.

DESCRIPTION OF SHARE CAPITAL

The following is a description of the material terms of our common shares and preferred shares as will be set forth in our amended articles of incorporation as expected to be amended in connection with this offering. The following description of our share capital is intended as a summary only and is qualified in its entirety by reference to our articles of incorporation and amendments thereto, which are filed as exhibits to the registration statement of which this prospectus is a part, and to the applicable provisions of the BCA. The following also assumes the conversion of all of our preferred shares into common shares in accordance with their terms.

General

Following the completion of this offering, based upon shares outstanding as of December 31, 2018, our share capital will consist of an unlimited number of common shares, no par value per share, of which 23,647,589 shares will be issued and outstanding, and an unlimited number of preferred shares, no par value per share, none of which will be issued and outstanding.

Common Shares

Outstanding Shares

As of December 31, 2018, we had 18,147,589 common shares outstanding, which were held by approximately 42 shareholders of record, assuming the automatic conversion of all outstanding preferred shares into 17,550,802 common shares immediately prior to the completion of this offering.

Voting Rights

Under our amended articles of incorporation to be in effect following the completion of this offering, the holders of common shares will be entitled to one vote for each share held at any meeting of the shareholders.

Dividends

Subject to the prior rights of the holders of our preferred shares, the holders of common shares will be entitled to receive dividends as and when declared by our board of directors. See "Dividend Policy."

Liquidation

Subject to the prior payment to the holders of our preferred shares, in the event of our liquidation, dissolution or winding-up or other distribution of our assets among our shareholders, the holders of common shares will be entitled to share *pro rata* in the distribution of the balance of our assets.

Rights and Preferences

The holders of common shares will have no preemptive, conversion rights or other subscription rights. There will be no redemption or sinking fund provisions applicable to our common shares. There will be no provision in our amended articles of incorporation to be in effect following the closing of this offering requiring the holders of common shares to contribute additional capital or permitting or restricting the issuance of additional securities or any other material restrictions. The rights, preferences and privileges of the holders of common shares will be subject to and may be adversely affected by, the rights of the holders of any series of preferred shares that we may designate in the future.

Preferred Shares

We will not have any preferred shares outstanding following the completion of this offering. Under our amended articles of incorporation to be in effect following the completion of this offering, we will be authorized to issue, without shareholder approval, an unlimited number of preferred shares, issuable in one or more series, and, subject to the provisions of the BCA, having such designations, rights, privileges, restrictions and conditions, including dividend and voting rights, as our board of directors may determine,

and such rights and privileges, including dividend and voting rights, may be superior to those of the common shares. The issuance of preferred shares, while providing flexibility in connection with possible acquisitions and other corporate purposes, could, among other things, have the effect of delaying, deferring or preventing a change in control of our company and might adversely affect the market price of our common shares and the voting and other rights of the holders of common shares. We have no current plans to issue any preferred shares following the completion of this offering.

Options

As of December 31, 2018, 2,295,045 common shares were issuable upon the exercise of 2,295,045 outstanding share options, at a weighted-average exercise price of $1.7713 per common share. For additional information regarding terms of our equity incentive plans, see the section titled "Executive and Director Compensation — Equity Incentive Plans."

Registration Rights

Following the completion of this offering, holders of the common shares issued upon the conversion of our preferred shares, including any accrued dividends thereon upon the completion of this offering will be entitled to certain rights with respect to registration of any securities held by such investors, as well as any under the Securities Act. These shares are referred to as registrable securities. The holders of these registrable securities possess registration rights pursuant to the terms of our third amended and restated registration rights agreement and are described in additional detail below. The registration of common shares pursuant to the exercise of the registration rights described below would enable the holders to trade these shares without restriction under the Securities Act when the applicable registration statement is declared effective. We will pay the registration expenses, other than underwriting discounts, selling commissions and share transfer taxes for the shares registered pursuant to the demand, piggyback and Form S-3 registrations described below. Expenses relating to underwriting discounts, selling commissions and share transfer taxes for the shares registered will be borne by us and the participating holders in proportion to the number of common shares sold by each, or, as between the participating holders, as such participating holders may otherwise agree.

Generally, in an underwritten offering, the managing underwriter, if any, has the right, subject to specified conditions, to limit the number of shares the holders may include. The demand, piggyback and Form S-3 registration rights described below will expire upon the earliest of (i) the occurrence of certain mergers or consolidations of the company, (ii) the date on which the shares that are the subject to the agreement are publicly sold, or if they may be publicly sold: (x) pursuant to Rule 144 of the Securities Act and (y) Section 2.5 of Regulation 45-102 respecting Resale of Securities, as adopted by the Canadian Securities Administrators, and (iii) five years after the completion of this offering.

Demand Registration Rights

Upon the earlier of the one year anniversary of the completion of this offering, or October 15, 2021, holders of 17,632,003 common shares issuable upon conversion of all of our outstanding preferred shares, including the accrued dividends, if any, will be entitled to certain demand registration rights. At any time beginning on the earlier of the one year anniversary of the completion of this offering, or October 15, 2021, the holders of at least 25% of registrable securities then outstanding may, on not more than two occasions, request that we register all or a portion of their shares, subject to certain specified exceptions, pursuant to either the Securities Act, Regulation 41-101 respecting General Prospectus Requirements, as adopted by Canadian Securities Administrators or both.

Piggyback Registration Rights

Following the completion of this offering, holders of 17,632,003 common shares issuable upon conversion of all of our outstanding preferred shares, including the accrued dividends, will be entitled to include their shares of registrable securities in any registration statement we file in the event that we propose to register

any of our securities under the Securities Act in an offering, either for our own account or for the account of other security holders, subject to specified conditions and limitations.

S-3 Registration Rights

Following the completion of this offering, holders of 17,632,003 common shares issuable upon conversion of all of our outstanding preferred shares, including the accrued dividends, will initially be entitled to certain Form S-3 registration rights. The holders of at least 25% of registrable securities then outstanding may, on not more than two occasions within any 12-month period, request that we register all or a portion of their shares on Form S-3 or a form under the Canada-United States Multijurisdictional Disclosure System, or the MJDS, if we are qualified to file a registration statement on Form S-3 or the MJDS, as applicable, subject to specified exceptions. Such request for registration on Form S-3 must cover securities with an aggregate offering price which equals or exceeds $10.0 million. The right to have such shares registered on Form S-3 is further subject to other specified conditions and limitations.

Indemnification

The third amended and restated registration rights agreement contains customary cross-indemnification provisions, pursuant to which we are obligated to indemnify the selling shareholders in the event of material misstatements or omissions in the registration statement attributable to us, and they are obligated to indemnify us for material misstatements or omissions in the registration statement attributable to them.

Transfer Agent and Registrar

Our transfer agent and registrar for our common shares is Computershare Investor Services Inc., with an address of 1500 Robert-Bourassa Boulevard, 7th Floor, Montréal, Quebec H3A 3S8.

Nasdaq Global Market Listing

Our common shares have been approved for listing on The Nasdaq Global Select Market under the trading symbol "MIST."

Advance Notice Procedures and Shareholder Proposals

Under the BCA, shareholders may make proposals for matters to be considered at the annual general meeting of shareholders. Such proposals must be sent to us in advance of any proposed meeting by delivering a timely written notice in proper form to our registered office in accordance with the requirements of the BCA. The notice must include information on the business the shareholder intends to bring before the meeting.

In addition, our amended and restated bylaws are expected to require that shareholders provide us with advance notice of their intention to nominate any persons, other than those nominated by management, for election to our board of directors at a meeting of shareholders.

These provisions could have the effect of delaying the nomination of certain persons for director that are favored by the holders of a majority of our outstanding voting securities.

MATERIAL DIFFERENCES BETWEEN THE BUSINESS CORPORATIONS ACT (QUÉBEC) AND THE DELAWARE GENERAL CORPORATION LAW

We are governed by the Business Corporations Act (Québec), or the BCA, which is generally similar to laws applicable to U.S. corporations. Significant differences between the BCA and the Delaware General Corporation Law, or DGCL, which governs companies incorporated in the State of Delaware, include the differences summarized below. This summary is not an exhaustive review of the two statutes, and reference should be made to the full text of both statutes for particulars of the differences.

	Delaware	BCA
Number and Election of Directors	Under the DGCL, the board of directors must consist of at least one director. The number of directors shall be fixed by the bylaws of the corporation, unless the certificate of incorporation fixes the number of directors, in which case a change in the number of directors shall only be made by an amendment of the certificate of incorporation. Under the DGCL, directors are elected at annual stockholder meetings by plurality vote of the stockholders, unless a shareholder-adopted bylaw prescribes a different required vote.	Under the BCA, the board of directors of a corporation must consist of at least three members, at least two of whom must not be officers or employees of the corporation or an affiliate of the corporation, so long as the corporation remains a "reporting issuer" for purposes of the BCA, which includes a corporation that has made a distribution of securities to the public. Under the BCA, directors are elected by the shareholders, in the manner and for the term, not exceeding three years, set out in the corporation's bylaws. Our bylaws provide that our directors are elected at each annual meeting of shareholders at which such an election is required.
Removal of Directors	Under the DGCL, any director or the entire board of directors may be removed, with or without cause, by the holders of a majority of the shares then entitled to vote at an election of directors, except (i) unless the certificate of incorporation provides otherwise, in the case of a corporation whose board of directors is classified, stockholders may effect such removal only for cause, or (ii) in the case of a corporation having cumulative voting, if less than the entire board of directors is to be removed, no director may be removed without cause if the votes cast against his removal would be sufficient to elect him if then cumulatively voted at an election of the entire board of directors, or, if there are classes of directors, at an election of the class of directors of which he is a part.	Under the BCA, unless the articles of a corporation provide for cumulative voting (which is not the case for us), shareholders of the corporation may, by resolution passed by a majority of the vote cast thereon at a special meeting of shareholders, remove any or all directors from office and may elect any qualified person to fill the resulting vacancy.

	Delaware	BCA
Vacancies on the Board of Directors	Under the DGCL, vacancies and newly created directorships may be filled by a majority of the directors then in office (even though less than a quorum) or by a sole remaining director unless (i) otherwise provided in the certificate of incorporation or bylaws of the corporation or (ii) the certificate of incorporation directs that a particular class of stock is to elect such director, in which case a majority of the other directors elected by such class, or a sole remaining director elected by such class, will fill such vacancy.	Under the BCA, vacancies that exist on the board of directors may generally be filled by the board if the remaining directors constitute a quorum. In the absence of a quorum, the remaining directors shall call a meeting of shareholders to fill the vacancy.
Board of Director Quorum and Vote Requirements	Under the DGCL, a majority of the total number of directors shall constitute a quorum for the transaction of business unless the certificate of incorporation or bylaws require a greater number. The bylaws may lower the number required for a quorum to one-third the number of directors, but no less. Under the DGCL, the board of directors may take action by the majority vote of the directors present at a meeting at which a quorum is present unless the certificate of incorporation or bylaws require a greater vote.	Under the BCA, subject to the corporation's bylaws, a majority of the directors in office constitutes a quorum at any meeting of the board. Our bylaws also provide that a majority of the directors in office constitutes a quorum at any meeting of the board. Under the BCA, a quorum of directors may exercise all the powers of the directors despite any vacancy on the board.

	Delaware	BCA
Transactions with Directors and Officers	The DGCL generally provides that no transaction between a corporation and one or more of its directors or officers, or between a corporation and any other corporation or other organization in which one or more of its directors or officers, are directors or officers, or have a financial interest, shall be void or voidable solely for this reason, or solely because the director or officer is present at or participates in the meeting of the board or committee which authorizes the transaction, or solely because any such director's or officer's votes are counted for such purpose, if (i) the material facts as to the director's or officer's interest and as to the transaction are known to the board of directors or the committee, and the board or committee in good faith authorizes the transaction by the affirmative votes of a majority of the disinterested directors, even though the disinterested directors be less than a quorum (ii) the material facts as to the director's or officer's interest and as to the transaction are disclosed or are known to the stockholders entitled to vote thereon, and the transaction is specifically approved in good faith by vote of the stockholders; or (iii) the transaction is fair as to the corporation as of the time it is authorized, approved or ratified, by the board of directors, a committee or the stockholders.	Under the BCA, every director or officer of a corporation must disclose the nature and value of any interest he or she has in a contract or transaction to which the corporation is a party. For the purposes of this rule, "interest" means any financial stake in a contract or transaction that may reasonably be considered likely to influence decision-making. Furthermore, a proposed contract or a proposed transaction, including related negotiations, is considered a contract or transaction. In addition, a director or an officer must disclose any contract or transaction to which the corporation and any of the following are a party: (i) an associate of the director or officer; (ii) a group of which the director or officer is a director or officer; or (iii) a group in which the director or officer or an associate of the director or officer has an interest. Such disclosure is required even for a contract or transaction that does not require approval by the board of directors. If a director is required to disclose his or her interest in a contract or transaction, such director is not allowed to vote on any resolution to approve, amend or terminate the contract or transaction or be present during deliberations concerning the approval, amendment or termination of such contract or transaction, unless the contract or transaction (i) relates primarily to the remuneration of the director or an associate of the director as a director, officer, employee or mandatory of the corporation or an affiliate of the corporation, (ii) is for indemnity or liability insurance under the BCA, or (iii) is with an affiliate of the corporation, and the sole interest of the director is as a director or officer of the affiliate.

Delaware	BCA
	If a director or officer does not disclose his or her interest in accordance with the BCA, or (in the case of a director) votes in respect of a resolution on a contract or transaction in which he or she is interested contrary to the BCA, the corporation or a shareholder may ask the court to declare the contract or transaction null and to require the director or officer to account to the corporation for any profit or gain realized on it by the director or officer or the associates of the director or officer, and to remit the profit or gain to the corporation, according to the conditions the court considers appropriate. However, the contract or transaction may not be declared null if it was approved by the board of directors and the contract or transaction was in the interest of the corporation when it was approved, nor may the director or officer concerned, in such a case, be required to account for any profit or gain realized or to remit the profit or gain to the corporation. In addition, the contract or transaction may not be declared null if it was approved by ordinary resolution by the shareholders entitled to vote who do not have an interest in the contract or transaction, the required disclosure was made to the shareholders and the contract or transaction was in the best interests of the corporation when it was approved, and if the director or officer acted honestly and in good faith, he or she may not be required to account for the profit or gain realized and to remit the profit or gain to the corporation.

	Delaware	BCA
Limitation on Liability of Directors	Under the DGCL, a corporation's certificate of incorporation may include a provision eliminating or limiting the personal liability of a director to the corporation and its stockholders for damages arising from a breach of fiduciary duty as a director. However, no provision can limit the liability of a director for: § breach of the director's duty of loyalty to the corporation or its stockholders; § acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of the law; § intentional or negligent payment of unlawful dividends or stock purchases or redemptions; or § for any transaction from which the director derived an improper personal benefit.	The BCA does not permit the limitation of a director's liability as the DGCL does.
Indemnification of Directors and Officers	The DGCL permits indemnification for derivative suits only for expenses (including legal fees) and only if the person is not found liable, unless a court determines the person is fairly and reasonably entitled to the indemnification.	Under the BCA, a corporation may indemnify a director or officer, a former director or officer or a person who acts or acted at the corporation's request as a director or officer, or an individual acting in a similar capacity of another group (who is referred to in this document as an indemnifiable person) against all costs, charges and expenses, including an amount paid to settle an action or satisfy a judgment, reasonably incurred by the indemnifiable person on the exercise of the person's functions or arising from any investigative or other proceeding in which the person is involved if: § the person acted honestly and loyalty in the interest of the corporation or other group, and § in the case of a proceeding enforceable by a monetary penalty, the person had reasonable grounds for believing the person's conduct was lawful.

	Delaware	BCA
		An indemnifiable person is also entitled to indemnity for reasonable defense costs and expenses if the person fulfills the above-mentioned requirements and was not judged to have committed any fault or omitted to do anything the person ought to have done. In the case of a derivative action, indemnity may be made only with court approval.
Call and Notice of Shareholder Meetings	Under the DGCL, an annual or special stockholder meeting is held on such date, at such time and at such place as may be designated by the board of directors or any other person authorized to call such meeting under the corporation's certificate of incorporation or bylaws. If an annual meeting for election of directors is not held on the date designated or an action by written consent to elect directors in lieu of an annual meeting has not been taken within 30 days after the date designated for the annual meeting, or if no date has been designated, for a period of 13 months after the later of the last annual meeting or the last action by written consent to elect directors in lieu of an annual meeting, the Delaware Court of Chancery may summarily order a meeting to be held upon the application of any stockholder or director.	Under the BCA, an annual meeting of shareholders must be held no later than 15 months after holding the last preceding annual meeting. Under the BCA, the directors of a corporation may call a special meeting at any time. In addition, holders of not less than 10% of the issued shares of a corporation that carry the right to vote at a meeting sought to be held may requisition the directors to call a meeting of shareholders.
Shareholder Action by Written Consent	Under the DGCL, a majority of the stockholders of a corporation may act by written consent without a meeting unless such action is prohibited by the corporation's certificate of incorporation.	Under the BCA, a written resolution signed by all the shareholders of a corporation who would have been entitled to vote on the resolution at a meeting is effective to approve the resolution.

	Delaware	BCA
Shareholder Nominations and Proposals	Not applicable.	Under the BCA, a shareholder entitled to vote at a shareholders' meeting may submit a shareholder proposal relating to matters which the shareholder wishes to propose and discuss at an annual shareholders' meeting and, subject to such shareholder's compliance with the prescribed time periods and other requirements of the BCA pertaining to shareholder proposals, the corporation is required to include such proposal in the information circular pertaining to any annual meeting at which it solicits proxies, subject to certain exceptions. Notice of such a proposal must be provided to the corporation at least 90 days before the anniversary date of the notice of meeting for the last annual shareholders' meeting. In addition, 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 five per cent of the shares or five per cent 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. We also expect that our amended and restated bylaws to be adopted upon consummation of this offering will require shareholders wishing to nominate directors or propose business for a meeting of shareholders to give timely advance notice in writing, as described in our bylaws.

	Delaware	BCA
Shareholder Quorum and Vote Requirements	Under the DGCL, quorum for a stock corporation is a majority of the shares entitled to vote at the meeting unless the certificate of incorporation or bylaws specify a different quorum, but in no event may a quorum be less than one-third of the shares entitled to vote. Unless the DGCL, certificate of incorporation or bylaws provide for a greater vote, generally the required vote under the DGCL is a majority of the shares present in person or represented by proxy, except for the election of directors which requires a plurality of the votes cast.	Under the BCA, unless the bylaws otherwise provide, the holders of a majority of the shares of a corporation entitled to vote at a meeting of shareholders, whether present in person or represented by proxy, constitute a quorum.
Amendment of Certificate of Incorporation	Generally, under the DGCL, the affirmative vote of the holders of a majority of the outstanding stock entitled to vote is required to approve a proposed amendment to the certificate of incorporation, following the adoption of the amendment by the board of directors of the corporation, provided that the certificate of incorporation may provide for a greater vote. Under the DGCL, holders of outstanding shares of a class or series are entitled to vote separately on an amendment to the certificate of incorporation if the amendment would have certain consequences, including changes that adversely affect the rights and preferences of such class or series.	Under the BCA, amendments to the articles of incorporation generally require the approval of not less than two-thirds of the votes cast by shareholders entitled to vote on the resolution. Specified amendments may also require the approval of other classes of shares. If the amendment is of a nature affecting a particular class or series in a manner requiring a separate class or series vote, that class or series is entitled to vote on the amendment whether or not it otherwise carries the right to vote.

	Delaware	BCA
Amendment of Bylaws	Under the DGCL, after a corporation has received any payment for any of its stock, the power to adopt, amend or repeal bylaws shall be vested in the stockholders entitled to vote; provided, however, that any corporation nay, in its certificate of incorporation, provide that bylaws may be adopted, amended or repealed by the board of directors. The fact that such power has been conferred upon the board of directors shall not divest the stockholders of the power nor limit their power to adopt, amend or repeal the bylaws.	Under the BCA, the directors may, by resolution, make, amend or repeal any bylaws that regulates the business or affairs of the corporation. Where the directors make, amend or repeal a bylaw, they are required under the BCA to submit that action to the shareholders at the next meeting of shareholders and the shareholders may confirm, reject or amend that action by simple majority, or ordinary resolution. If the action is rejected by shareholders, or the directors of a corporation do not submit the action to the shareholders at the next meeting of shareholders, the action will cease to be effective, and no subsequent resolution of the directors to make, amend or repeal a bylaw having substantially the same purpose or effect will he effective until it is confirmed.
Votes on Mergers, Consolidations and Sales of Assets	The DGCL provides that, unless otherwise provided in the certificate of incorporation or bylaws, the adoption of a merger agreement requires the approval of a majority of the outstanding stock of the corporation entitled to vote thereon.	Under the BCA, certain extraordinary corporate actions, such as amalgamations (other than with certain affiliated corporations), continuances and sales, leases or exchanges of the property of a corporation if as a result of such alienation the corporation would be unable to retain a significant part of its business activities, and other extraordinary corporate actions such as liquidations, dissolutions and (if ordered by a court) arrangements, are required to be approved by "special resolution." A "special resolution" is a resolution passed by not less than two-thirds of the votes cast by the shareholders who voted in respect of the resolution or signed by all shareholders entitled to vote on the resolution. In specified cases, a special resolution to approve the extraordinary corporate action is also required to be approved separately by the holders of a class or series of shares, including in certain cases a class or series of shares not otherwise carrying voting rights.

	Delaware	BCA
Dissenter's Rights of Appraisal	Under the DGCL, a stockholder of a Delaware corporation generally has the right to dissent flume, merger or consolidation in which the Delaware corporation is participating, subject to specified procedural requirements, including that such dissenting stockholder does not vote in favor of the merger or consolidation. However, the DGCL does not confer appraisal rights, in certain circumstances, including if the dissenting stockholder owns shares traded on a national securities exchange and will receive publicly traded shares in the merger or consolidation. Under the DGCL, a stockholder asserting appraisal rights does not receive any payment for his or her shares until the court determines the fair value or the parties otherwise agree to a value. The costs of the proceeding may be determined by the court and assessed against the parties as the court deems equitable under the circumstances.	The BCA provides that shareholders of a corporation are entitled to exercise dissent rights (called "the right to demand the repurchase of shares") and to be paid the fair value of their shares in connection with specified matters, including: § any amalgamation with another corporation (other than with certain affiliated corporations); § an amendment to the corporation's articles to add, change or remove any provisions restricting or constraining the transfer of shares; § an amendment to the corporation's articles to add. change or remove any restriction upon the businesses or businesses that the corporation may carry on; § a continuance under the laws of another jurisdiction; § a sale, lease or exchange of the property of the corporation or of its subsidiaries if, as a result of such alienation, the corporation is unable to retain a significant part of its business activity; § a court order permitting a shareholder to exercise his right to demand the repurchase of his shares in connection with an application to the court for an order approving an arrangement proposed by the corporation; § the carrying out of a going-private transaction; and certain amendments to the articles of a corporation which require a separate class or series vote by a holder of shares of any class or series. However, a shareholder is not entitled to dissent if an amendment to the articles is effected by a court order approving reorganization or by a court order made in connection with an action for an oppression remedy.

	Delaware	BCA
Oppression Remedy	The DGCL does not provide for a similar remedy.	The BCA provides an oppression remedy (called "rectification of abuse of power or iniquity") that enables a court to make any order, whether interim or final, to rectify matters that are oppressive or unfairly prejudicial to the interests of any securityholder, director or officer of the corporation if an application is made to a court by an "applicant". An "applicant" with respect to a corporation means any of the following: § a present or former registered holder or beneficiary of securities of the corporation or any of its affiliates; § a present or former officer or director of the corporation or any of its affiliates; and § any other person who in the discretion of the court has the interest to make the application. The oppression remedy provides the court with very broad and flexible powers to intervene in corporate affairs to protect shareholders and other complainants. While conduct that is in breach of fiduciary duties of directors or that is contrary to the legal right of a complainant will normally trigger the court's jurisdiction under the oppression remedy, the exercise of that jurisdiction does not depend on a finding of a breach of those legal and equitable rights. Furthermore, the court may order a corporation to pay the interim expenses of an applicant seeking an oppression remedy, but the applicant may be held accountable for interim costs on final disposition of the complaint (as in the case of a derivative action as described in "Shareholder Derivative Actions" below).

	Delaware	BCA
Shareholder Derivative Actions	Under the DGCL, stockholders may bring derivative actions on behalf of, and for the benefit of the corporation. The plaintiff in a derivative action on behalf of the corporation either must be or have been a stockholder of the corporation at the time of the transaction or must be a stockholder who became a stockholder by operation of law in the transaction regarding which the stockholder complains. A stockholder may not sue derivatively on behalf of the corporation unless the stockholder first makes demand on the corporation that it bring suit and the demand is refused, unless it is shown that making the demand would have been a futile act.	Under the BCA, a shareholder of a corporation may apply to a Québec court for leave to bring an action in the name of, and on behalf of, the corporation or any subsidiary, or to intervene in an existing action to which the corporation or any of its subsidiaries is a party, for the purpose of prosecuting, defending or discontinuing an action on behalf of the corporation or its subsidiary. Under the BCA, no action may be brought and no intervention in an action may be made unless a court is satisfied that: § the shareholder has given the required 14-day notice to the directors of the corporation or the subsidiary of the shareholder's intention to apply to the court if the directors do not bring, diligently prosecute or defend or discontinue the action; § the shareholder is acting in good faith; and § it appears to be in the interests of the corporation or the relevant subsidiary that the action be brought. prosecuted, defended or discontinued. Under the BCA, the court in a derivative action may make any order it thinks fit. In addition, under the BCA, a court may order the corporation or its relevant subsidiary to pay the shareholder's interim costs, including reasonable legal fees and disbursements. Although the shareholder may he held accountable for the interim costs on final disposition of the complaint, the shareholder is not required to give security for costs in a derivative action.

	Delaware	BCA
Anti-Takeover and Ownership Provisions	Unless an issuer opts out of the provisions of Section 203 of the DGCL, Section 203 generally prohibits a public Delaware corporation from engaging in a "business combination" with a holder of 15% or more of the corporation's voting stock (as defined in Section 203), referred to as an interested stockholder, for a period of three years after the date of the transaction in which the interested stockholder became an interested stockholder, except as otherwise provided in Section 203. For these purposes, the term "business combination" includes mergers, assets sales and other similar transactions with an interested stockholder.	While the BCA does not contain specific anti- takeover provisions with respect to "business combinations," rules and policies of certain Canadian securities regulatory authorities, including Multilateral Instrument 61-101 — Protection of Minority Security Holders in Special Transactions, or Multilateral Instrument 61-101, contain requirements in connection with, among other things, 'related party transactions" and "business combinations", including, among other things, any transaction by which an issuer directly or indirectly engages in the following with a related party: acquires, sells, leases or transfers an asset, acquires the related party, acquires or issues treasury securities, amends the terms of a security if the security is owned by the related party or assumes or becomes subject to a liability or takes certain other actions with respect to debt. The term "related party" includes directors, senior officers and holders of more than 10% of the voting rights attached to all outstanding voting securities of the issuer or holders of a sufficient number of any securities of the issuer to materially affect control of the issuer. Multilateral Instrument 61-101 requires, subject to certain exceptions, the preparation of a formal valuation relating to certain aspects of the transaction and more detailed disclosure in the proxy material sent to security holders in connection with a related party transaction including related to the valuation. Multilateral Instrument 61-101 also requires, subject to certain exceptions, that an issuer not engage in a related party transaction unless the shareholders of the issuer, other than the related parties, approve the transaction by a simple majority of the votes cast.

SHARES ELIGIBLE FOR FUTURE SALE

Prior to this offering, there has been no public market for our common shares, and a liquid trading market for our common shares may not develop or be sustained after this offering. Future sales of our common shares, including shares issued upon the exercise of outstanding options, in the public market after the completion of this offering, or the perception that those sales may occur, could adversely affect the prevailing market price for our common shares from time to time or impair our ability to raise equity capital in the future. As described below, only a limited number of our common shares will be available for sale in the public market for a period of several months after the completion of this offering due to contractual and legal restrictions on resale described below. Future sales of our common shares in the public market either before or after restrictions lapse, or the perception that those sales may occur, could adversely affect the prevailing market price of our common shares at such time and our ability to raise equity capital at a time and price we deem appropriate.

Sale of Restricted Shares

Based on the number of common shares outstanding as of December 31, 2018, upon the closing of this offering and assuming (i) the automatic conversion of our outstanding preferred shares into an aggregate of 17,550,802 common shares immediately prior to the completion of this offering, (ii) no exercise of the underwriters' option to purchase additional common shares, and (iii) no exercise of outstanding options, we will have outstanding an aggregate of approximately 23,647,589 common shares. Of these shares, all of the 5,500,000 common shares to be sold in this offering will be freely tradable in the public market without restriction or further registration under the Securities Act, unless the shares are held by any of our "affiliates" as such term is defined in Rule 144 of the Securities Act, or Rule 144 or subject to lock-up agreements. All remaining common shares held by existing shareholders immediately prior to the consummation of this offering will be "restricted securities," as such term is defined in Rule 144. These restricted securities were issued and sold by us in private transactions and are eligible for public sale only if registered under the Securities Act or if they qualify for an exemption from registration under the Securities Act, including the exemptions provided by Rule 144 or Rule 701 of the Securities Act, or Rule 701, which rules are summarized below.

As a result of the lock-up agreements referred to below and the provisions of Rule 144 and Rule 701 under the Securities Act, based on the number of our common shares outstanding as of December 31, 2018, the common shares (excluding the shares sold in this offering) that will be available for sale in the public market are as follows:

APPROXIMATE NUMBER OF SHARES	FIRST DATE AVAILABLE FOR SALE INTO PUBLIC MARKET
18,147,589 shares	181 days after the date of this prospectus, upon expiration of the lock-up agreements referred to below, subject in some cases to applicable volume, manner of sale and other limitations under Rule 144 and Rule 701.

We may issue common shares from time to time as consideration for future acquisitions, investments or other corporate purposes. In the event that any such acquisition, investment or other transaction is significant, the number of common shares that we may issue may in turn be significant. We may also grant registration rights covering those common shares issued in connection with any such acquisition and investment.

In addition, the common shares reserved for future issuance under our 2019 Plan will become eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules, the lock-up agreements, a registration statement under the Securities Act or an exemption from registration, including Rule 144 and Rule 701.

Rule 144

In general, persons who have beneficially owned restricted common shares for at least six months, and any affiliate of the company who owns common shares, are entitled to sell their securities without registration with the SEC under an exemption from registration provided by Rule 144.

Under Rule 144, as currently in effect, once we have been subject to the public company reporting requirements of the Exchange Act for at least 90 days, and we are current in our Exchange Act reporting at the time of sale, a person (or persons whose shares are required to be aggregated) who is not deemed to have been one of our "affiliates" for purposes of Rule 144 at any time during the 90 days preceding a sale and who has beneficially owned restricted securities within the meaning of Rule 144 for at least six months, including the holding period of any prior owner other than one of our "affiliates," is entitled to sell those shares in the public market (subject to the lock-up agreement referred to below, if applicable) without complying with the manner of sale, volume limitations or notice provisions of Rule 144, but subject to compliance with the public information requirements of Rule 144. If such a person has beneficially owned the shares proposed to be sold for at least one year, including the holding period of any prior owner other than "affiliates," then such person is entitled to sell such shares in the public market without complying with any of the requirements of Rule 144 (subject to the lock-up agreement referred to below, if applicable).

In general, under Rule 144, as currently in effect, once we have been subject to the public company reporting requirements of the Exchange Act for at least 90 days, our "affiliates," as defined in Rule 144, who have beneficially owned the shares proposed to be sold for at least six months, are entitled to sell in the public market, upon expiration of any applicable lock-up agreements and within any three-month period, a number of those common shares that does not exceed the greater of:

- 1% of the number of common shares then outstanding, which will equal approximately 236,476 common shares immediately upon the completion of this offering (calculated as of December 31, 2018 on the basis of the assumptions described above and assuming no exercise of the underwriter's option to purchase additional shares and no exercise of outstanding options); or

- the average weekly trading volume of our common shares on Nasdaq during the four calendar weeks preceding the filing of a notice on Form 144 with respect to such sale.

Such sales under Rule 144 by our "affiliates" or persons selling shares on behalf of our "affiliates" are also subject to certain manner of sale provisions, notice requirements and to the availability of current public information about us. Notwithstanding the availability of Rule 144, the holders of substantially all of our restricted securities have entered into lock-up agreements as referenced below and their restricted securities will become eligible for sale (subject to the above limitations under Rule 144) upon the expiration of the restrictions set forth in those agreements.

Rule 701

In general, under Rule 701 as currently in effect, any of our employees, directors, officers, consultants or advisors who acquired common shares from us in connection with a written compensatory share or option plan or other written agreement in compliance with Rule 701 before the effective date of the registration statement of which this prospectus is a part (to the extent such common shares are not subject to a lock-up agreement) and who are not our "affiliates" as defined in Rule 144 during the immediately preceding 90 days, is entitled to rely on Rule 701 to resell such shares beginning 90 days after the date of this prospectus in reliance on Rule 144, but without complying with the notice, manner of sale, public

information requirements or volume limitation provisions of Rule 144. Persons who are our "affiliates" may resell those shares beginning 90 days after the date of this prospectus without compliance with Rule 144's minimum holding period requirements (subject to the terms of the lock-up agreement referred to below, if applicable).

Lock-Up Agreements

In connection with this offering, we, our directors, our executive officers and holders of all of our other outstanding common shares or securities convertible into or exchangeable for common shares outstanding upon the completion of this offering, have agreed, subject to certain exceptions, with the underwriters not to directly or indirectly offer, sell, contract to sell, pledge, grant any option to purchase, make any short sale or otherwise dispose of or hedge any common shares or any options to purchase common shares, or any securities convertible into or exchangeable for common shares during the period from the date of the lock-up agreement continuing through the date 180 days after the date of this prospectus, except with the prior written consent of the representatives of the underwriters, and certain other exceptions. These agreements are described in the section titled "Underwriting."

In addition to the restrictions contained in the lock-up agreements described above, we have entered into agreements with certain security holders, including the third amended and restated registration rights agreement and our standard form of option agreement, that contain market stand-off provisions imposing restrictions on the ability of such security holders to offer, sell or transfer our equity securities for a period of 180 days following the date of this prospectus.

Prior to the completion of the offering, certain of our employees, including our executive officers, and/or directors, may enter into written trading plans that are intended to comply with Rule 10b5-1 under the Exchange Act. Sales under these trading plans would not be permitted until the expiration of the lock-up agreements relating to the offering described above.

Following the lock-up periods set forth in the agreements described above, and assuming that the representatives of the underwriters do not release any parties from these agreements and that there is no extension of the lock-up period, all of the common shares that are restricted securities or are held by our affiliates as of the date of this prospectus will be eligible for sale in the public market in compliance with Rule 144.

Registration Rights

Upon the completion of this offering, the holders of 17,632,003 common shares will be entitled to rights with respect to the registration of their shares under the Securities Act, subject to the lock-up agreements described under "— Lock-Up Agreements" above. Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act, except for shares purchased by affiliates, immediately upon the effectiveness of the registration statement of which this prospectus is a part. Any sales of securities by these shareholders could have a material adverse effect on the trading price of our common shares. See the section titled "Description of Share Capital — Registration Rights."

Equity Incentive Plans

We intend to file with the SEC a registration statement on Form S-8 under the Securities Act covering the common shares reserved for issuance under our equity incentive plans. The registration statement is expected to be filed and become effective as soon as practicable after the completion of this offering. Accordingly, shares registered under the registration statement will be available for sale in the open market following its effective date, subject to Rule 144 volume limitations and the lock-up agreements described above, if applicable.

MATERIAL U.S. FEDERAL INCOME TAX CONSIDERATIONS FOR U.S. HOLDERS

The following is a description of the material U.S. federal income tax consequences to the U.S. Holders described below of owning and disposing of our common shares. It is not a comprehensive description of all tax considerations that may be relevant to a particular U.S. Holder. This discussion applies only to a U.S. Holder that holds our common shares as a capital asset for U.S. federal tax purposes (generally, property held for investment). In addition, it does not describe all of the tax consequences that may be relevant in light of a U.S. Holder's particular circumstances, including state and local tax consequences, estate tax consequences, alternative minimum tax consequences, and tax consequences applicable to U.S. Holders subject to special rules, such as:

- banks, insurance companies, and certain other financial institutions;
- U.S. expatriates and certain former citizens or long-term residents of the United States;
- dealers or traders in securities who use a mark-to-market method of tax accounting;
- persons holding common shares as part of a hedging transaction, "straddle," wash sale, conversion transaction or integrated transaction or persons entering into a constructive sale with respect to common shares;
- persons whose "functional currency" for U.S. federal income tax purposes is not the U.S. dollar;
- brokers, dealers or traders in securities, commodities or currencies;
- tax-exempt entities or government organizations;
- S corporations, partnerships or other entities or arrangements classified as partnerships for U.S. federal income tax purposes, except to the limited extent set forth below;
- regulated investment companies or real estate investment trusts;
- persons who acquired our common shares pursuant to the exercise of any employee share option or otherwise as compensation;
- persons that own or are deemed to own 10% or more of the voting power or value of our shares; and
- persons holding our common shares in connection with a trade or business, permanent establishment or fixed base outside the United States.

If an entity that is classified as a partnership for U.S. federal income tax purposes holds common shares, the U.S. federal income tax treatment of a partner will generally depend on the status of the partner and the activities of the partnership. Partnerships holding common shares and partners in such partnerships are encouraged to consult their tax advisers as to the particular U.S. federal income tax consequences of holding and disposing of common shares.

U.S. Holders that own (directly, indirectly, or constructively) 10% or more of our total combined voting power or value could be subject to adverse U.S. federal income tax consequences pursuant to the controlled foreign corporation rules due to our ownership of a U.S. subsidiary. Such prospective U.S. Holders should consult with their tax advisors as to the tax consequences of acquiring, owning and disposing of our common shares.

The discussion is based on the Internal Revenue Code of 1986, as amended, or the Code, existing, proposed and temporary U.S. Treasury Regulations promulgated thereunder and administrative and judicial interpretations thereof and the income tax treaty between Canada and the United States, or the Canada-U.S. Tax Treaty, all as of the date hereof, changes to any of which may affect the tax consequences described herein — possibly with retroactive effect. There can be no assurances that the U.S. Internal Revenue Service, or the IRS, will not take a position concerning the tax consequences of the acquisition, ownership and disposition of our common shares or that such a position would not be sustained by a court.

A "U.S. Holder" is a holder who, for U.S. federal income tax purposes, is a beneficial owner of common shares who is eligible for the benefits of the Canada-U.S. Tax Treaty, including meeting the Limitation on Benefits article thereof, and is:

(i) an individual who is a citizen or resident of the United States;

(ii) a corporation, or another entity taxable as a corporation, created or organized in or under the laws of the United States, any state therein or the District of Columbia;

(iii) an estate the income of which is subject to U.S. federal income taxation regardless of its source; or

(iv) a trust if (1) a U.S. court is able to exercise primary supervision over the administration of the trust and one or more U.S. persons have authority to control all substantial decisions of the trust or (2) the trust has a valid election to be treated as a U.S. person under applicable U.S. Treasury Regulations.

U.S. Holders are encouraged to consult their tax advisers concerning the U.S. federal, state, local and foreign tax consequences of owning and disposing of our common shares in their particular circumstances.

THESE PARAGRAPHS ARE ONLY A SUMMARY OF CERTAIN U.S. FEDERAL INCOME TAX CONSIDERATIONS OF AN INVESTMENT IN OUR COMMON SHARES BY U.S. PERSONS, AND ARE INTENDED AS A GENERAL GUIDE ONLY. WE STRONGLY ENCOURAGE ALL POTENTIAL U.S. PERSONS WHO MAY PURCHASE OUR COMMON SHARES TO OBTAIN ADVICE IN ADVANCE OF DOING SO FROM THEIR OWN TAX ADVISERS AS TO THE U.S. FEDERAL, STATE AND LOCAL AND FOREIGN TAX CONSEQUENCES OF THEIR ACQUISITION, OWNERSHIP AND DISPOSITION OF OUR COMMON SHARES IN THEIR OWN SPECIFIC CIRCUMSTANCES.

Passive Foreign Investment Company Rules

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 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. The application of the PFIC rules is subject to uncertainty in several respects, and therefore, no assurances can be provided with respect to our PFIC status for our taxable year ending December 31, 2018 or with regard to our PFIC status in the past or in the future.

A separate determination must be made after the close of each taxable year as to whether we are a PFIC for that year. As a result, our PFIC status may change from year to year. The total value of our assets for purposes of the asset test generally may be determined in part by reference to the market price of the common shares, which may fluctuate considerably. Fluctuations in the market price of the common shares may result in our being a PFIC for any taxable year. Because of the uncertainties involved in establishing our PFIC status, our United States tax counsel expresses no opinion regarding our PFIC status.

If we are classified as a PFIC in any year with respect to which a U.S. Holder owns common shares, we will continue to be treated as a PFIC with respect to such U.S. Holder in all succeeding years during which the U.S. Holder owns the common shares, regardless of whether we continue to meet the tests described above unless (i) we cease to be a PFIC and the U.S. Holder has made a valid "deemed sale" election under the PFIC rules, (ii) we cease to be a PFIC and the U.S. Holder has a valid mark-to-market election in effect (as described below) or (iii) the U.S. Holder makes a valid QEF Election with respect to all taxable years during such U.S. Holders holding period in which we are a PFIC. However, a U.S. Holder may make a QEF Election with respect to our common shares only if we annually provide such U.S. Holder with certain tax information.

If we are a PFIC for our taxable year ending December 31, 2019, or any subsequent taxable years, we expect to provide U.S. Holders, upon request, a "PFIC Annual Information Statement", with the information required to allow U.S. Holders to make a QEF Election for United States federal income tax purposes.

If a U.S. Holder makes a QEF Election with respect to a PFIC, in lieu of the tax consequences described below, the U.S. Holder will be subject to current taxation on its pro rata share of the PFIC's ordinary earnings and net capital gain for each taxable year that the entity is classified as a PFIC. If a U.S. Holder makes a QEF Election with respect to us, any distributions paid by us out of our earnings and profits that were previously included in the U.S. Holder's income under the QEF Election would not be taxable to the holder. A U.S. Holder will increase its tax basis in its common shares by an amount equal to any income included under the QEF Election and will decrease its tax basis by any amount distributed on the common shares that is not included in the holder's income. In addition, a U.S. Holder will recognize capital gain or loss on the disposition of common shares in an amount equal to the difference between the amount realized and the holder's adjusted tax basis in the common shares. U.S. Holders should note that if they make QEF Elections with respect to us and lower-tier PFICs, they may be required to pay U.S. federal income tax with respect to their common shares for any taxable year significantly in excess of any cash distributions (which are expected to be zero) received on the common shares for such taxable year. U.S. Holders should consult their tax advisors regarding making QEF Elections in their particular circumstances. If a U.S. Holder does not make and maintain a QEF election for the U.S. Holder's entire holding period for our common shares by making the election for the first year in which the U.S. Holder owns our common shares pursuant to this offering, the U.S. Holder will be subject to the adverse PFIC rules discussed above unless the U.S. Holder can properly make a "purging election" with respect to our common shares in connection with the U.S. Shareholder's QEF Election. A purging election may require the U.S. Holder to recognize taxable gain on the U.S. Holder's shares. No purging election is necessary for a U.S. Holder that timely makes a QEF election for the first year in which the U.S. Holder acquired our common shares.

If the "deemed sale" election is made, a U.S. Holder will be deemed to have sold the common shares the U.S. Holder holds at their fair market value and any gain from such deemed sale would be subject to the rules described below. After the deemed sale election, so long as we do not become a PFIC in a subsequent taxable year, the U.S. Holder's common shares with respect to which such election was made will not be treated as shares in a PFIC and the U.S. Holder will not be subject to the rules described below with respect to any "excess distribution" the U.S. Holder receives from us or any gain from an actual sale or other disposition of the common shares. U.S. Holders should consult their tax advisors as to the possibility and consequences of making a deemed sale election if we cease to be a PFIC and such election becomes available.

For each taxable year we are treated as a PFIC with respect to U.S. Holders, U.S. Holders will be subject to special tax rules with respect to any "excess distribution" such U.S. Holder receives and any gain such U.S. Holder recognizes from a sale or other disposition (including a pledge) of common shares, unless (i) such U.S. Holder makes a QEF Election with respect to all taxable years of a U.S. Holder's holding period during which we are a PFIC or makes a purging election to cause a deemed sale of the common shares at their fair market value in conjunction with a QEF election or (ii) our common shares constitute "marketable" securities, and such U.S. Holder makes a mark-to-market election as discussed below. Distributions a U.S. Holder receives in a taxable year that are greater than 125% of the average annual distributions a U.S. Holder received during the shorter of the three preceding taxable years or the U.S. Holder's holding period for the common shares will be treated as excess distributions; in addition, any gain recognized from the disposition of our common shares will constitute an excess distribution. Under these special tax rules:

- an excess distribution will be allocated ratably over a U.S. Holder's holding period for the common shares;
- the amount allocated to the current taxable year, and any taxable year prior to the first taxable year in which we became a PFIC, will be treated as ordinary income; and
- the amount allocated to each other year will be subject to the highest tax rate in effect for that year and the interest charge generally applicable to underpayments of tax will be imposed on the resulting tax attributable to each such year.

The tax liability for amounts allocated to years prior to the year of disposition or the year of an "excess distribution" cannot be offset by any net operating losses for such years, and gains (but not losses) realized on the sale of the common shares cannot be treated as capital, even if a U.S. Holder holds the common shares as capital assets.

If we are a PFIC, a U.S. Holder will generally be subject to similar rules with respect to distributions we receive from, and our dispositions of the shares of, any of our direct or indirect subsidiaries that also are PFICs, as if such distributions were indirectly received by, and/or dispositions were indirectly carried out by, such U.S. Holder.

If we are a PFIC, U.S. Holders can avoid the interest charge on excess distributions or gain relating to the common shares by making a mark-to-market election with respect to the common shares, provided that the common shares are "marketable." Common shares will be marketable if they are "regularly traded" on certain U.S. stock exchanges or on a foreign stock exchange that meets certain conditions. For these purposes, the common shares will be considered regularly traded during any calendar year during which they are traded, other than in de minimis quantities, on at least 15 days during each calendar quarter. Any trades that have as their principal purpose meeting this requirement will be disregarded. Our common shares will be listed on Nasdaq, which is a qualified exchange for these purposes. Consequently, if our common shares remain listed on Nasdaq and are regularly traded, and you are a U.S. Holder that holds our common shares, we expect the mark-to-market election would be available to you if we are a PFIC. Each U.S. Holder should consult its tax advisor as to whether a mark-to-market election is available or advisable with respect to the common shares.

A U.S. Holder that makes a mark-to-market election must include as ordinary income for each year an amount equal to the excess, if any, of the fair market value of the common shares at the close of the taxable year over the U.S. Holder's adjusted tax basis in the common shares. Accordingly, such mark-to-market election may accelerate the recognition of income without a corresponding receipt of cash. An electing holder may also claim an ordinary loss deduction for the excess, if any, of the U.S. Holder's adjusted basis in the common shares over the fair market value of the common shares at the close of the taxable year, but this deduction is allowable only to the extent of any net mark-to-market gains for prior years. Gains from an actual sale or other disposition of the common shares will be treated as ordinary income, and any losses incurred on a sale or other disposition of the common shares will be treated as an ordinary loss to the extent of any net mark-to-market gains for prior years. Once made, the election cannot be revoked without the consent of the IRS, unless the common shares cease to be marketable. However, a mark-to-market election generally cannot be made for equity interests in any lower-tier PFICs that we own, unless shares of such lower-tier PFIC are themselves "marketable." As a result, even if a U.S. Holder validly makes a mark-to-market election with respect to our common shares, the U.S. Holder may continue to be subject to the PFIC rules with respect to its indirect interest in any of our investments that are treated as an equity interest in a PFIC for U.S. federal income tax purposes. U.S. Holders should consult their tax advisors as to the availability and desirability of a mark-to-market election, as well as the impact of such election on interests in any lower-tier PFICs.

Unless otherwise provided by the U.S. Treasury, each U.S. Holder of a PFIC is required to file an annual report containing such information as the U.S. Treasury may require. A U.S. Holder's failure to file the annual report will cause the statute of limitations for such U.S. Holder's U.S. federal income tax return to remain open with regard to the items required to be included in such report until three years after the U.S. Holder files the annual report, and, unless such failure is due to reasonable cause and not willful neglect, the statute of limitations for the U.S. Holder's entire U.S. federal income tax return will remain open during such period.

WE STRONGLY URGE YOU TO CONSULT YOUR TAX ADVISOR REGARDING THE IMPACT OF OUR PFIC STATUS ON YOUR INVESTMENT IN THE COMMON SHARES AS WELL AS THE APPLICATION OF THE PFIC RULES TO YOUR INVESTMENT IN THE COMMON SHARES.

Taxation of Distributions

Subject to the discussion above under "Passive Foreign Investment Company Rules," to the extent the PFIC rules do not apply otherwise, distributions paid on common shares (including any amounts withheld in respect of foreign taxes), other than certain pro rata distributions of common shares, will generally be treated as dividends to the extent paid out of our current or accumulated earnings and profits (as determined under U.S. federal income tax principles). Because we may not calculate our earnings and profits under U.S. federal income tax principles, we expect that distributions generally will be reported to U.S. Holders as dividends. Subject to applicable limitations, dividends paid to certain non-corporate U.S. Holders may be taxable at preferential rates applicable to "qualified dividend income." However, the qualified dividend income treatment will not apply if we are treated as a PFIC with respect to the U.S. Holder for the taxable year in which a dividend is paid or the preceding year. The amount of the dividend will be treated as foreign-source dividend income to U.S. Holders and will not be eligible for the dividends-received deduction generally available to U.S. corporations under the Code. Dividends will generally be included in a U.S. Holder's income on the date of the U.S. Holder's receipt of the dividend. The amount of any dividend income paid in foreign currency will be the U.S. dollar amount calculated by reference to the exchange rate in effect on the date of actual or constructive receipt, regardless of whether the payment is in fact converted into U.S. dollars. If the dividend is converted into U.S. dollars on the date of receipt, a U.S. Holder should not be required to recognize foreign currency gain or loss in respect of the dividend income. A U.S. Holder may have foreign currency gain or loss if the dividend is converted into U.S. dollars after the date of receipt. Such gain or loss would generally be treated as U.S. source ordinary income or loss. The amount of any distribution of property other than cash (and other than certain pro rata distributions of common shares or rights to acquire common shares) will be the fair market value of such property on the date of distribution.

For foreign tax credit limitation purposes, our dividends will generally be treated as passive category income. A U.S. Holder generally may claim the amount of any Canadian withholding tax as either a deduction from gross income or a credit against its U.S. federal income tax liability. However, the foreign tax credit is subject to numerous complex limitations that must be determined and applied on an individual basis.. Each U.S. Holder should consult its own tax advisors regarding the foreign tax credit rules.

Sale or Other Taxable Disposition of Common Shares

Subject to the discussion above under "Passive Foreign Investment Company Rules," to the extent the PFIC rules do not apply otherwise, gain or loss realized on the sale or other taxable disposition of common shares will be capital gain or loss, and will be a long-term capital gain or loss if the U.S. Holder held the common shares for more than one year. The amount of the gain or loss will equal the difference between the U.S. Holder's adjusted tax basis in the common shares disposed of and the amount realized on the disposition, in each case as determined in U.S. dollars. This gain or loss will generally be U.S. source gain or loss for foreign tax credit purposes. The deductibility of capital losses is subject to limitations.

If the consideration received by a U.S. Holder is not paid in U.S. dollars, the amount realized will be the U.S. dollar value of the payment received determined by reference to the spot rate of exchange on the date of the sale or other disposition. However, if the common shares are treated as traded on an "established securities market" and a U.S. Holder is either a cash basis taxpayer or an accrual basis taxpayer that has made a special election (which must be applied consistently from year to year and cannot be changed without the consent of the IRS), such U.S. Holder will determine the U.S. dollar value of the amount realized in a non-U.S. dollar currency by translating the amount received at the spot rate of exchange on the settlement date of the sale. If a U.S. Holder is an accrual basis taxpayer that is not eligible to or does not elect to determine the amount realized using the spot rate on the settlement date, such U.S. Holder will recognize foreign currency gain or loss to the extent of any difference between the U.S. dollar amount

realized on the date of sale or disposition and the U.S. dollar value of the currency received at the spot rate on the settlement date.

Medicare Tax on Net Investment Income

Certain U.S. Holders who are individuals, estates or trusts are subject to an additional 3.8% U.S. federal income tax on all or a portion of their "net investment income," which generally includes dividends on the common shares and net gains from the disposition of the common shares. U.S. Holders that are individuals, estates or trusts should consult their tax advisors regarding the applicability of the Medicare tax to them.

Information Reporting and Backup Withholding

Payments of dividends and sales proceeds that are made within the United States or through certain U.S.-related financial intermediaries generally are subject to information reporting, and may be subject to backup withholding, unless (i) the U.S. Holder is a corporation or other exempt recipient or (ii) in the case of backup withholding, the U.S. Holder provides a correct taxpayer identification number and certifies that it is not subject to backup withholding (generally, by providing an IRS Form W-9).

Backup withholding is not an additional tax. The amount of any backup withholding from a payment to a U.S. Holder will be allowed as a credit against the holder's U.S. federal income tax liability and may entitle it to a refund, provided that the required information is timely furnished to the IRS.

Information with Respect to Foreign Financial Assets

Certain U.S. Holders who are individuals (and, under regulations, certain entities) may be required to report information relating to the common shares, subject to certain exceptions (including an exception for common shares held in accounts maintained by certain U.S. financial institutions). Such U.S. Holders who fail to timely furnish the required information may be subject to a penalty. Additionally, if a U.S. Holder does not file the required information, the statute of limitations with respect to tax returns of the U.S. Holder to which the information relates may not close until three years after such information is filed.

Certain U.S. Holders who are individuals (and, under regulations, certain entities) may be required to report information relating to the common shares, subject to certain exceptions (including an exception for common shares held in accounts maintained by certain U.S. financial institutions). Such U.S. Holders who fail to timely furnish the required information may be subject to a penalty. Additionally, if a U.S. Holder does not file the required information, the statute of limitations with respect to tax returns of the U.S. Holder to which the information relates may not close until three years after such information is filed. U.S. Holders should consult their tax advisers regarding their reporting obligations with respect to their ownership and disposition of the common shares.

MATERIAL CANADIAN FEDERAL INCOME TAX CONSIDERATIONS

The following is, as of the date hereof, a summary of the principal Canadian federal income tax considerations generally applicable under the Income Tax Act (Canada) and the regulations promulgated thereunder, collectively the Tax Act, to a purchaser who acquires, as beneficial owner, the common shares under this offering, and who, for purposes of the Tax Act and at all relevant times, (i) is not, and is not deemed to be, resident in Canada, (ii) holds the common shares as capital property, (iii) deals at arm's length with, and is not affiliated with, the company or the underwriters, and (iv) does not use or hold and will not be deemed to use or hold, the common shares in a business carried on in Canada, hereinafter, a Non-Resident Holder. Special rules, which are not discussed in this summary, may apply to a Non-Resident Holder that is an "authorized foreign bank" within the meaning of the Tax Act or an insurer carrying on an insurance business in Canada and elsewhere. Any such Non-Resident Holder should consult its own tax advisor.

This summary is based upon the provisions of the Tax Act in force as of the date hereof, all specific proposals to amend the Tax Act that have been publicly announced by or on behalf of the Minister of Finance (Canada) prior to the date hereof, or the Proposed Amendments, the Canada-U.S. Tax Treaty, or the Treaty, and an understanding of the current administrative policies and assessing practices of the Canada Revenue Agency, or the CRA, published in writing by it prior to the date hereof. This summary assumes the Proposed Amendments will be enacted in the form proposed. However, no assurance can be given that the Proposed Amendments will be enacted in their current form, or at all. This summary is not exhaustive of all possible Canadian federal income tax considerations and, except for the Proposed Amendments, does not take into account or anticipate any changes in the law or any changes in the CRA's administrative policies or assessing practices, whether by legislative, governmental or judicial action or decision, nor does it take into account or anticipate any other federal or any provincial, territorial or foreign tax considerations, which may differ significantly from those discussed herein.

This summary is not applicable to a Non-Resident Holder who makes or has made a "functional currency" reporting election; or that has entered or enters into a "derivative forward agreement" with respect to the common shares (each as defined in the Tax Act). Any such Non-Resident Holder should consult its own tax advisor with respect to an investment in the common shares.

This summary is of a general nature only and is not intended to be, nor should it be construed to be, legal or tax advice to any prospective purchaser or holder of the common shares, and no representations with respect to the income tax consequences to any prospective purchaser or holder are made. Consequently, prospective purchasers or holders of the common shares should consult their own tax advisors with respect to their particular circumstances.

A Non-Resident Holder who acquires the common shares will be required to allocate the purchase price between the common shares on a reasonable basis in order to determine their respective costs for purposes of the Tax Act. Non-Resident Holders should consult their own tax advisers in this regard.

Currency Conversion

Generally, for purposes of the Tax Act, all amounts relating to the acquisition, holding or disposition of the common shares must be converted into Canadian dollars based on the exchange rates as determined in accordance with the Tax Act. The amounts subject to withholding tax and any capital gains or capital losses realized by a Non-Resident Holder may be affected by fluctuations in the Canadian-U.S. dollar exchange rate.

Dispositions

A Non-Resident Holder generally will not be subject to tax under the Tax Act in respect of a capital gain realized on the disposition or deemed disposition of a common share, unless the common share constitutes "taxable Canadian property" (as defined in the Tax Act) of the Non-Resident Holder at the time of

disposition and the Non-Resident Holder is not entitled to relief under an applicable income tax treaty or convention. In addition, capital losses arising on the disposition or deemed disposition of a common share will not be recognized under the Tax Act, unless the common share constitutes "taxable Canadian property" to the Non-Resident Holder thereof for purposes of the Tax Act.

Provided the common shares are listed on a "designated stock exchange," as defined in the Tax Act (which currently includes the Nasdaq Stock Market), at the time of disposition, the common shares will generally not constitute taxable Canadian property of a Non-Resident Holder at that time, unless at any time during the 60-month period immediately preceding the disposition the following two conditions are satisfied concurrently: (i) (a) the Non-Resident Holder; (b) persons with whom the Non-Resident Holder did not deal at arm's length; (c) partnerships in which the Non-Resident Holder or a person described in (b) holds a membership interest directly or indirectly through one or more partnerships; or (d) any combination of the persons and partnerships described in (a) through (c), owned 25% or more of the issued shares of any class or series of the shares of the company; and (ii) more than 50% of the fair market value of the shares of the company was derived directly or indirectly from one or any combination of: real or immovable property situated in Canada, "Canadian resource properties", "timber resource properties" (each as defined in the Tax Act), and options in respect of, or interests in or for civil law rights in, such properties, whether or not such properties exist. Notwithstanding the foregoing, in certain circumstances set out in the Tax Act, the common shares could be deemed to be taxable Canadian property. Even if the common shares are taxable Canadian property to a Non-Resident Holder, such Non-Resident Holder may be exempt from tax under the Tax Act on the disposition of such common shares by virtue of an applicable income tax treaty or convention. **A Non-Resident Holder contemplating a disposition of common shares that may constitute taxable Canadian property should consult a tax advisor prior to such disposition.**

Dividends

Dividends paid or credited on the common shares or deemed to be paid or credited on the common shares to a Non-Resident Holder by the Company are subject to Canadian withholding tax under the Tax Act at the rate of 25%, although such rate may be reduced under the provisions of an applicable income tax convention between Canada and the Non-Resident Holder's country of residence. For example, under the Treaty, the rate of withholding tax on dividends paid or credited or deemed to be paid or credited to a beneficially entitled Non-Resident Holder who is resident in the U.S. for purposes of the Treaty and who is fully entitled to the benefits of the Treaty (a "**U.S. Holder**") is generally limited to 15% of the gross amount of the dividend (or 5% in the case of a U.S. Holder that is a corporation beneficially owning at least 10% of the Company's voting shares). Non-Resident Holders are urged to consult their own tax advisors to determine their entitlement to relief under an applicable income tax treaty.

UNDERWRITING

Subject to the terms and conditions set forth in the underwriting agreement, dated May 8, 2019, among us and Jefferies LLC, Cowen and Company, LLC and Piper Jaffray & Co., as the representatives of the underwriters named below and the joint book-running managers of this offering, we have agreed to sell to the underwriters, and each of the underwriters has agreed, severally and not jointly, to purchase from us, the respective number of common shares shown opposite its name below:

Underwriter	Number of Shares
Jefferies LLC	2,145,000
Cowen and Company, LLC	1,595,000
Piper Jaffray & Co.	1,320,000
Oppenheimer & Co. Inc.	440,000
Total	5,500,000

The underwriting agreement provides that the obligations of the several underwriters are subject to certain conditions precedent such as the receipt by the underwriters of officers' certificates and legal opinions and approval of certain legal matters by their counsel. The underwriting agreement provides that the underwriters will purchase all of the common shares if any of them are purchased. If an underwriter defaults, the underwriting agreement provides that the purchase commitments of the nondefaulting underwriters may be increased or the underwriting agreement may be terminated. We have agreed to indemnify the underwriters and certain of their controlling persons against certain liabilities, including liabilities under the Securities Act, and to contribute to payments that the underwriters may be required to make in respect of those liabilities.

The underwriters have advised us that, following the completion of this offering, they currently intend to make a market in the common shares as permitted by applicable laws and regulations. However, the underwriters are not obligated to do so, and the underwriters may discontinue any market-making activities at any time without notice in their sole discretion. Accordingly, no assurance can be given as to the liquidity of the trading market for the common shares, that you will be able to sell any of the common shares held by you at a particular time or that the prices that you receive when you sell will be favorable.

The underwriters are offering the common shares subject to their acceptance of the common shares from us and subject to prior sale. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part. In addition, the underwriters have advised us that they do not intend to confirm sales to any account over which they exercise discretionary authority.

Commission and Expenses

The underwriters have advised us that they propose to offer the common shares to the public at the initial public offering price set forth on the cover page of this prospectus and to certain dealers, which may include the underwriters, at that price less a concession not in excess of $0.63 per common share. After the offering, the initial public offering price, concession and reallowance to dealers may be reduced by the representatives. No such reduction will change the amount of proceeds to be received by us as set forth on the cover page of this prospectus.

The following table shows the public offering price, the underwriting discounts and commissions that we are to pay the underwriters and the proceeds, before expenses, to us in connection with this offering. Such amounts are shown assuming both no exercise and full exercise of certain of the underwriters' option to purchase additional shares.

	Per Share		Total	
	Without Option to Purchase Additional Shares	With Option to Purchase Additional Shares	Without Option to Purchase Additional Shares	With Option to Purchase Additional Shares
Public offering price	$ 15.00	$ 15.00	$ 82,500,000	$ 94,875,000
Underwriting discounts and commissions paid by us	$ 1.05	$ 1.05	$ 5,775,000	$ 6,641,250
Proceeds to us, before expenses	$ 13.95	$ 13.95	$ 76,725,000	$ 88,233,750

We estimate expenses payable by us in connection with this offering, other than the underwriting discounts and commissions referred to above, will be approximately $2.7 million. We have also agreed to pay the filing fees incident to, and the fees and disbursements of counsel for the underwriters in connection with, the required review by the Financial Industry Regulatory Authority, Inc. up to a maximum aggregate amount of $35,000.

Determination of Offering Price

Prior to this offering, there has not been a public market for our common shares. Consequently, the initial public offering price for our common shares will be determined by negotiations between us and the representatives. Among the factors to be considered in these negotiations will be prevailing market conditions, our financial information, market valuations of other companies that we and the underwriters believe to be comparable to us, estimates of our business potential, the present state of our development and other factors deemed relevant.

We offer no assurances that the initial public offering price will correspond to the price at which the common shares will trade in the public market subsequent to the offering or that an active trading market for the common shares will develop and continue after the offering.

Listing

Our common shares have been approved for listing on The Nasdaq Global Select Market under the trading symbol "MIST."

Option to Purchase Additional Shares

We have granted to certain of the underwriters an option, exercisable for 30 days from the date of this prospectus, to purchase, from time to time, in whole or in part, up to an aggregate of 825,000 shares from us at the public offering price set forth on the cover page of this prospectus, less underwriting discounts and commissions. If these underwriters exercise this option, each such underwriter will be obligated, subject to specified conditions, to purchase a number of additional shares approximately proportionate to that underwriter's initial purchase commitment as indicated in the table above. This option may be exercised only if the underwriters sell more shares than the total number set forth on the cover page of this prospectus.

No Sales of Similar Securities

We, our officers, directors and holders of our outstanding share capital and other securities have agreed, subject to specified exceptions, not to directly or indirectly:

- sell, offer, contract or grant any option to sell (including any short sale), pledge, transfer, establish an open "put equivalent position" within the meaning of Rule 16a-l(h) under the Exchange Act, or
- otherwise dispose of any shares of common shares, options or warrants to acquire common shares, or securities exchangeable or exercisable for or convertible into common shares currently or hereafter owned either of record or beneficially, or
- publicly announce an intention to do any of the foregoing for a period of 180 days after the date of this prospectus without the prior written consent of the representatives.

This restriction terminates after the close of trading of the common shares on and including the 180th day after the date of this prospectus.

The representatives may, in their sole discretion and at any time or from time to time before the termination of the 180-day period release all or any portion of the securities subject to lock-up agreements. There are no existing agreements between the underwriters and any of our shareholders who will execute a lock-up agreement, providing consent to the sale of shares prior to the expiration of the lock-up period.

Stabilization

The underwriters have advised us that they, pursuant to Regulation M under the Exchange Act, certain persons participating in the offering may engage in short sale transactions, stabilizing transactions, syndicate covering transactions or the imposition of penalty bids in connection with this offering. These activities may have the effect of stabilizing or maintaining the market price of the common shares at a level above that which might otherwise prevail in the open market. Establishing short sales positions may involve either "covered" short sales or "naked" short sales.

"Covered" short sales are sales made in an amount not greater than the underwriters' option to purchase additional common shares in this offering. The underwriters may close out any covered short position by either exercising their option to purchase additional common shares or purchasing common shares in the open market. In determining the source of shares to close out the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the option to purchase additional shares.

"Naked" short sales are sales in excess of the option to purchase additional common shares. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common shares in the open market after pricing that could adversely affect investors who purchase in this offering.

A stabilizing bid is a bid for the purchase of common shares on behalf of the underwriters for the purpose of fixing or maintaining the price of the common shares. A syndicate covering transaction is the bid for or the purchase of common shares on behalf of the underwriters to reduce a short position incurred by the underwriters in connection with the offering. Similar to other purchase transactions, the underwriter's purchases to cover the syndicate short sales may have the effect of raising or maintaining the market price of our common shares or preventing or retarding a decline in the market price of our common shares. As a result, the price of our common shares may be higher than the price that might otherwise exist in the open market. A penalty bid is an arrangement permitting the underwriters to reclaim the selling concession otherwise accruing to a syndicate member in connection with the offering if the common shares originally sold by such syndicate member are purchased in a syndicate covering transaction and therefore have not been effectively placed by such syndicate member.

Neither we nor any of the underwriters make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of our common shares. The underwriters are not obligated to engage in these activities and, if commenced, any of the activities may be discontinued at any time.

The underwriters may also engage in passive market making transactions in our common shares on The Nasdaq Global Select Market in accordance with Rule 103 of Regulation M during a period before the commencement of offers or sales of common shares in this offering and extending through the completion of distribution. A passive market maker must display its bid at a price not in excess of the highest independent bid of that security. However, if all independent bids are lowered below the passive market maker's bid, that bid must then be lowered when specified purchase limits are exceeded.

Electronic Distribution

A prospectus in electronic format may be made available by e-mail or on the web sites or through online services maintained by one or more of the underwriters or their affiliates. In those cases, prospective investors may view offering terms online and may be allowed to place orders online. The underwriters may agree with us to allocate a specific number of common shares for sale to online brokerage account holders. Any such allocation for online distributions will be made by the underwriters on the same basis as other allocations. Other than the prospectus in electronic format, the information on the underwriters' web sites and any information contained in any other web site maintained by any of the underwriters is not part of this prospectus, has not been approved and/or endorsed by us or the underwriters and should not be relied upon by investors.

Other Activities and Relationships

The underwriters and certain of their affiliates are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, investment research, principal investment, hedging, financing and brokerage activities. The underwriters and certain of their affiliates have, from time to time, performed, and may in the future perform, various commercial and investment banking and financial advisory services for us and our affiliates, for which they received or will receive customary fees and expenses.

In the ordinary course of their various business activities, the underwriters and certain of their affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers, and such investment and securities activities may involve securities and/or instruments issued by us and our affiliates. If the underwriters or their respective affiliates have a lending relationship with us, they routinely hedge their credit exposure to us consistent with their customary risk management policies. The underwriters and their respective affiliates may hedge such exposure by entering into transactions which consist of either the purchase of credit default swaps or the creation of short positions in our securities or the securities of our affiliates, including potentially the common shares offered hereby. Any such short positions could adversely affect future trading prices of the common shares offered hereby. The underwriters and certain of their respective affiliates may also communicate independent investment recommendations, market color or trading ideas and/or publish or express independent research views in respect of such securities or instruments and may at any time hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

Selling Restrictions

Canada

The common shares offered by this prospectus have not been qualified by prospectus for distribution in Canada, and may not be, directly or indirectly, offered or sold in Canada or to any residents of Canada, except in compliance with an exemption from Canadian prospectus requirements. Any sales of our common

shares in any province of Canada will only be made by a securities dealer appropriately registered in that province to make such sales, which may include a Canadian affiliate of one of the underwriters using a separate Canadian Offering Memorandum that will include a copy of this prospectus. Any common shares acquired may not be sold in Canada, except in compliance with Canadian prospectus requirements or an exemption therefrom.

Australia

This prospectus is not a disclosure document for the purposes of Australia's Corporations Act 2001 (Cth) of Australia, or Corporations Act, has not been lodged with the Australian Securities & Investments Commission and is only directed to the categories of exempt persons set out below. Accordingly, if you receive this prospectus in Australia:

You confirm and warrant that you are either:

- a "sophisticated investor" under section 708(8)(a) or (b) of the Corporations Act;
- a "sophisticated investor" under section 708(8)(c) or (d) of the Corporations Act and that you have provided an accountant's certificate to the company which complies with the requirements of section 708(8)(c)(i) or (ii) of the Corporations Act and related regulations before the offer has been made; or
- a "professional investor" within the meaning of section 708(11)(a) or (b) of the Corporations Act.

To the extent that you are unable to confirm or warrant that you are an exempt sophisticated investor or professional investor under the Corporations Act any offer made to you under this prospectus is void and incapable of acceptance.

You warrant and agree that you will not offer any of the shares issued to you pursuant to this prospectus for resale in Australia within 12 months of those securities being issued unless any such resale offer is exempt from the requirement to issue a disclosure document under section 708 of the Corporations Act.

European Economic Area

In relation to each member state of the European Economic Area which has implemented the Prospectus Directive, each referred to herein as a Relevant Member State, with effect from and including the date on which the Prospectus Directive is implemented in that Relevant Member State, referred to herein as the Relevant Implementation Date, no offer of any securities which are the subject of the offering contemplated by this prospectus has been or will be made to the public in that Relevant Member State other than any offer where a prospectus has been or will be published in relation to such securities that has been approved by the competent authority in that Relevant Member State or, where appropriate, approved in another Relevant Member State and notified to the relevant competent authority in that Relevant Member State in accordance with the Prospectus

Directive, except that with effect from and including the Relevant Implementation Date, an offer of such securities may be made to the public in that Relevant Member State:

- to any legal entity which is a "qualified investor" as defined in the Prospectus Directive;
- to fewer than 100 or, if the Relevant Member State has implemented the relevant provision of the 2010 PD Amending Directive, 150, natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the representatives of the underwriters for any such offer; or
- in any other circumstances falling within Article 3(2) of the Prospectus Directive,

provided that no such offer of securities shall require the company or any of the underwriters to publish a prospectus pursuant to Article 3 of the Prospectus Directive or supplement a prospectus pursuant to Article 16 of the Prospectus Directive.

For the purposes of this provision, the expression an "offer to the public" in relation to any securities in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and the securities to be offered so as to enable an investor to decide to purchase or subscribe the securities, as the same may be varied in that Relevant Member State by any measure implementing the Prospectus Directive in that Relevant Member State and the expression "Prospectus Directive" means Directive 2003/71/EC (and amendments thereto, including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member State), and includes any relevant implementing measure in the Relevant Member State and the expression "2010 PD Amending Directive" means Directive 2010/73/EU.

Hong Kong

No securities have been offered or sold, and no securities may be offered or sold, in Hong Kong, by means of any document, other than to persons whose ordinary business is to buy or sell shares or debentures, whether as principal or agent; or to "professional investors" as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong, or SFO, and any rules made under that Ordinance; or in other circumstances which do not result in the document being a "prospectus" as defined in the Companies Ordinance (Cap. 32) of Hong Kong, or CO, or which do not constitute an offer to the public for the purpose of the CO or the SFO. No document, invitation or advertisement relating to the securities has been issued or may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere), which is directed at, or the contents of which are likely to be accessed or read by, the public of Hong Kong (except if permitted under the securities laws of Hong Kong) other than with respect to securities which are or are intended to be disposed of only to persons outside Hong Kong or only to "professional investors" as defined in the SFO and any rules made under that Ordinance.

This prospectus has not been registered with the Registrar of Companies in Hong Kong. Accordingly, this prospectus may not be issued, circulated or distributed in Hong Kong, and the securities may not be offered for subscription to members of the public in Hong Kong. Each person acquiring the securities will be required, and is deemed by the acquisition of the securities, to confirm that he is aware of the restriction on offers of the securities described in this prospectus and the relevant offering documents and that he is not acquiring, and has not been offered any securities in circumstances that contravene any such restrictions.

Israel

This document does not constitute a prospectus under the Israeli Securities Law, 5728-1968, or the Securities Law, and has not been filed with or approved by the Israel Securities Authority. In the State of Israel, this document is being distributed only to, and is directed only at, and any offer of the shares is directed only at, (i) a limited number of persons in accordance with section 15A of the Securities Law and (ii) investors listed in the first addendum, or the Addendum, to the Israeli Securities Law, consisting primarily of joint investment in trust funds, provident funds, insurance companies, banks, portfolio managers, investment advisors, members of the Tel Aviv Stock Exchange, underwriters, venture capital funds, entities with equity in excess of NIS 50 million and "qualified individuals", each as defined in the Addendum (as it may be amended from time to time), collectively referred to as qualified investors (in each case purchasing for their own account or, where permitted under the Addendum, for the accounts of their clients who are investors listed in the Addendum). Qualified investors will be required to submit written confirmation that they fall within the scope of the Addendum, are aware of the meaning of same and agree to it.

Japan

The offering has not been and will not be registered under the Financial Instruments and Exchange Law of Japan (Law No. 25 of 1948 of Japan, as amended), or FIEL, and the Initial Purchaser will not offer or sell any securities, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan (which term as used herein means, unless otherwise provided herein, any person resident in Japan, including any corporation or other entity organized under the laws of Japan), or to others for re-offering or resale, directly

or indirectly, in Japan or to a resident of Japan, except pursuant to an exemption from the registration requirements of, and otherwise in compliance with, the FIEL and any other applicable laws, regulations and ministerial guidelines of Japan.

Singapore

This prospectus has not been and will not be lodged or registered with the Monetary Authority of Singapore. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or the invitation for subscription or purchase of the securities may not be issued, circulated or distributed, nor may the securities be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to the public or any member of the public in Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore, or the SFA, (ii) to a relevant person as defined under Section 275(2), or any person pursuant to Section 275(1A) of the SFA, and in accordance with the conditions, specified in Section 275 of the SFA, or (iii) otherwise pursuant to, and in accordance with the conditions of any other applicable provision of the SFA.

Where the securities are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

- a corporation (which is not an accredited investor as defined under Section 4A of the SFA) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or
- a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary is an accredited investor,

securities (as defined in Section 239(1) of the SFA) of that corporation or the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the common shares pursuant to an offer made under Section 275 of the SFA except:

- to an institutional investor or to a relevant person defined in Section 275(2) of the SFA, or to any person arising from an offer referred to in Section 275(1A) or Section 276(4)(i)(B) of the SFA;
- where no consideration is or will be given for the transfer;
- where the transfer is by operation of law;
- as specified in Section 276(7) of the SFA; or
- as specified in Regulation 32 of the Securities and Futures (Offers of Investments) (Shares and Debentures) Regulations 2005 of Singapore.

Switzerland

The securities may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange, or SIX, or on any other stock exchange or regulated trading facility in Switzerland. This prospectus has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this prospectus nor any other offering or marketing material relating to the securities or the offering may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this prospectus nor any other offering or marketing material relating to the offering, the company or the securities have been or will be filed with or approved by any Swiss regulatory authority. In particular, this prospectus will not be filed with, and the offer of securities will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA, or FINMA, and the offer of securities has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes, or CISA. The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of securities.

United Kingdom

This prospectus is only being distributed to, and is only directed at, persons in the United Kingdom that are qualified investors within the meaning of Article 2(1)(e) of the Prospectus Directive that are also (i) investment professionals falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended, referred to herein as the Order, and/or (ii) high net worth entities falling within Article 49(2)(a) to (d) of the Order and other persons to whom it may lawfully be communicated. Each such person is referred to herein as a Relevant Person.

This prospectus and its contents are confidential and should not be distributed, published or reproduced (in whole or in part) or disclosed by recipients to any other persons in the United Kingdom. Any person in the United Kingdom that is not a Relevant Person should not act or rely on this document or any of its contents.

LEGAL MATTERS

Certain legal matters in connection with this offering relating to U.S. law will be passed upon for us by Cooley LLP. The validity of the issuance of our common shares offered in this prospectus will be passed upon for us by Osler, Hoskin & Harcourt LLP, Montréal, Canada. Certain legal matters in connection with this offering will be passed upon for the underwriters by Wilmer Cutler Pickering Hale and Dorr LLP, New York, New York, with respect to U.S. law, and by McCarthy Tétrault LLP, with respect to Canadian law.

EXPERTS

The consolidated financial statements as of December 31, 2018 and 2017, and for each of the two years in the period ended December 31, 2018 included in this registration statement have been so included in reliance on the report of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in accounting and auditing.

SERVICE OF PROCESS AND ENFORCEMENT OF LIABILITIES

We are incorporated under the laws of Canada. Substantially all of our assets are located outside the United States. In addition, several of our directors and officers are nationals and/or residents of countries other than the United States, and all or a substantial portion of such persons' assets may be located outside the United States. As a result, it may be difficult for investors to effect service of process within the United States upon us or such persons or to enforce against them or against us, judgments obtained in United States courts, including judgments predicated upon the civil liability provisions of the securities laws of the United States or any state thereof. In addition, investors should not assume that the courts of Canada (i) would enforce judgments of U.S. courts obtained in actions against us, our officers or directors, or other said persons, predicated upon the civil liability provisions of the U.S. federal securities laws or other laws of the United States or (ii) would enforce, in original actions, liabilities against us or such directors, officers or experts predicated upon the United States federal securities laws or any securities or other laws of any state or jurisdiction of the United States.

In addition, there is doubt as to the applicability of the civil liability provisions of U.S. federal securities law to original actions instituted in Canada. It may be difficult for an investor, or any other person or entity, to assert U.S. securities laws claims in original actions instituted in Canada.

WHERE YOU CAN FIND ADDITIONAL INFORMATION

We have filed with the SEC a registration statement on Form S-1, including exhibits and schedules, under the Securities Act, with respect to the common shares being offered by this prospectus. This prospectus, which constitutes part of the registration statement, does not contain all of the information in the registration statement and its exhibits. For further information with respect to us and the common shares offered by this prospectus, we refer you to the registration statement and its exhibits. Statements contained in this prospectus as to the contents of any contract or any other document referred to are not necessarily complete, and in each instance, we refer you to the copy of the contract or other document filed as an exhibit to the registration statement. Each of these statements is qualified in all respects by this reference.

You may read our SEC filings, including this registration statement, over the Internet at the SEC's website at www.sec.gov. Upon the completion of this offering, we will be subject to the information reporting requirements of the Exchange Act and we will file reports, proxy statements and other information with the SEC. These reports, proxy statements and other information will be available on the website of the SEC referred to above. We also maintain a website at www.milestonepharmaceuticals.com, at which, following the completion of this offering, you may access these materials free of charge as soon as reasonably practicable after they are electronically filed with, or furnished to, the SEC. Information contained on or accessible through our website is not a part of this prospectus, and the inclusion of our website address in this prospectus is an inactive textual reference only.

MILESTONE PHARMACEUTICALS INC.
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Report of Independent Registered Public Accounting Firm

To the Board of Directors and Shareholders of
Milestone Pharmaceuticals Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheet of Milestone Pharmaceuticals Inc. and its subsidiary (the "Company") as of December 31, 2018 and 2017 and the related consolidated statements of loss, comprehensive loss, shareholders' deficit and convertible preferred shares and cash flows for the years then ended, including the related notes (collectively referred to as the "consolidated financial statements").

In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of 2018 and 2017 and its results of operations and its cash flows for the years then ended in conformity with accounting principles generally accepted in the United States of America.

Basis for Opinion

These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's consolidated financial statements based on our audit. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits of these consolidated financial statements in accordance with the standards of the PCAOB and in accordance with auditing standards generally accepted in the United States of America. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud.

The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits, we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/PricewaterhouseCoopers LLP[(1)]
Montréal, Québec, Canada
February 18, 2019, except for the effects of the reverse share split described in Note 1, as to which the date is April 29, 2019.

We have served as the Company's auditor since 2016.

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(1) CPA auditor, CA, public accountancy permit No. A113048

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

	Years Ended December 31,	
	2017	2018
Assets		
Current assets		
Cash and cash equivalents	$ 10,880	$ 85,947
Short-term investments (note 13)	16,032	29
Research and development tax credits receivable	427	290
Prepaid expenses	100	1,398
Other receivables (note 3)	116	387
Total current assets	27,555	88,051
Property and equipment (note 4)	35	30
Total assets	$ 27,590	$ 88,081
Liabilities		
Current liabilities		
Accounts payable and accrued liabilities (note 5)	$ 1,601	$ 4,477
Income taxes payable	4	56
	1,605	4,533
Convertible Preferred Shares (note 6)		
Class A1 preferred shares, no par value, unlimited shares authorized, 372,211 shares issued	2,027	2,027
Class A2 preferred shares, no par value, unlimited shares authorized, 2,443,914 shares issued	12,643	12,643
Class B preferred shares, no par value, unlimited shares authorized, 2,830,907 shares issued	17,198	17,198
Class C preferred shares, no par value, unlimited shares authorized, 3,786,878 shares issued	27,236	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	59,104	138,758
Shareholders' Deficit (note 7)		
Share capital		
Common shares, no par value, unlimited shares authorized, 239,990 shares issued and outstanding as of December 31, 2017, 596,787 shares issued and outstanding as of December 31, 2018	1,228	2,039
Additional paid-in capital	2,372	2,655
Cumulative translation adjustment	(1,634)	(1,634)
Accumulated deficit	(35,085)	(58,270)
Total shareholders' deficit	(33,119)	(55,210)
Total liabilities, convertible preferred shares and shareholders' deficit	$ (27,590)	$ 88,081
Commitments (note 11)		

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

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

	Years Ended December 31,	
	2017	2018
Operating expenses		
Research and development, net of tax credits (note 10)	$ 5,636	$ 16,849
General and administrative	1,502	3,052
Commercial activities	1,130	3,921
Loss from operations	(8,268)	(23,822)
Interest income, net of bank charges	186	711
Loss and comprehensive loss before income taxes	(8,082)	(23,111)
Income tax expense (note 9)	4	74
Net loss and comprehensive loss for the year	$ (8,086)	$ (23,185)
Weighted average number of shares outstanding, basic and diluted	236,750	319,202
Net loss per share, basic and diluted (note 8)	$ 34.15	$ 72.63

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

Milestone Pharmaceuticals Inc.
Consolidated Statements of Shareholders' Deficit and Convertible Preferred Shares
(in thousands of US dollars, except 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	To
Balance as of December 31, 2016	221,247	$ 1,191	372,211	$ 2,027	2,443,914	$ 12,643	2,258,753	$ 13,732	—	—	—	—	—	—	$ 2,199	$ (1,634)	$ (26,999)	$
Net loss and comprehensive loss	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	(8,086)	(
Issuance of Class B preferred shares, net of share issuance costs (note 5)	—	—	—	—	—	—	572,154	3,466	—	—	—	—	—	—	—	—	—	
Issuance of Class C preferred shares, net of share issuance costs (note 5)	—	—	—	—	—	—	—	—	3,786,878	$ 27,236	—	—	—	—	—	—	—	2
Exercise of stock options (note 6)	18,743	37	—	—	—	—	—	—	—	—	—	—	—	—	(17)	—	—	
Share-based compensation (note 6)	—	—	—	—	—	—	—	—	—	—	—	—	—	—	190	—	—	
Balance as of 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)	$ 2
Transactions in 2018																		
Net loss and comprehensive loss	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	(23,185)	(2
Issuance of Class C preferred shares, net of share issuance costs (note 6)	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	
Issuance of Class D1 preferred shares, net of share issuance costs (note 6)	—	—	—	—	—	—	—	—	—	—	6,893,236	$ 64,719	—	—	—	—	—	6
Issuance of Class D2 preferred shares, net of share issuance costs (note 6)	—	—	—	—	—	—	—	—	—	—	—	—	1,223,656	$ 14,935	—	—	—	1
Exercise of stock options (note 7)	356,797	811	—	—	—	—	—	—	—	—	—	—	—	—	(350)	—	—	
Share-based compensation (note 7)	—	—	—	—	—	—	—	—	—	—	—	—	—	—	633	—	—	
Balance as of 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)	$ 8

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

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

	Years Ended December 31,	
	2017	2018
Cash flows from		
Operating activities		
Net loss for the year	$ (8,086)	$ (23,185)
Adjustments to reconcile net loss to net cash used in operating activities:		
Amortization of property and equipment	8	10
Share-based compensation expense (note 7)	190	633
Changes in operating assets and liabilities:		
Other receivables	(86)	(271)
Research and development tax credits receivable	233	137
Prepaid expenses	(93)	(1,298)
Accounts payable and accrued liabilities	(222)	2,876
Income taxes payable	4	52
Net cash used in operating activities	(8,052)	(21,046)
Investing activities		
Acquisition of property and equipment	(36)	(5)
Redemption of short-term investments	45	19,032
Acquisition of short-term investments	(16,032)	(3,029)
Net cash (used in) provided by investing activities	(16,023)	15,998
Financing activities		
Issuance of Class B preferred shares (note 6)	3,500	—
Issuance of Class C preferred shares (note 6)	27,500	—
Issuance of Class D1 preferred shares (note 6)	—	65,000
Issuance of Class D2 preferred shares (note 6)	—	15,000
Issuance of common shares on exercise of share options (note 7)	20	461
Share issuance costs (note 6)	(298)	(346)
Net cash provided by financing activities	30,722	80,115
Net increase in cash and cash equivalents during the year	6,647	75,067
Cash and cash equivalents — Beginning of year	4,233	10,880
Cash and cash equivalents — End of year	$ 10,880	$ 85,947

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

Milestone Pharmaceuticals Inc.
Notes to Consolidated Financial Statements
(in thousands of US dollars, except 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 Québec. 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 Share 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 share 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 the consolidated financial statements have been retroactively adjusted for all periods presented to give effect to the reverse share split. The reverse share split was effected on April 26, 2019.

2 Summary of significant accounting policies

Basis of consolidation

The consolidated financial statements include the accounts of the Company and Milestone Pharmaceuticals USA, Inc. Milestone Pharmaceuticals USA, Inc. was incorporated on March 3, 2017. All intercompany transactions and balances have been eliminated.

Basis of presentation and use of accounting estimates

These consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America (US GAAP).

The preparation of consolidated financial statements in conformity with US GAAP requires the Company to make estimates and judgments that affect certain reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the consolidated financial statements and the reported amounts of revenue and expenses during the year. 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.

Reclassifications

Certain prior period amounts in the accompanying consolidated financial statements have been reclassified to conform to the current year presentation. For the year ended December 31, 2017, we reclassified $1,130 of expenses to commercial activities that had previously been classified as general and administrative expenses for comparative purposes. These reclassifications had no effect on previously reported net income or shareholders' deficit.

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

2 Summary of significant accounting policies (Continued)

Segment information

The Company manages its operations as a single operating segment for the purposes of assessing performance and making operating decisions. As of December 31, 2018, all of the Company's long-lived assets were domiciled in Canada.

Cash and cash equivalents

Cash and cash equivalents consist of cash and highly liquid investments that are readily convertible into cash with original maturities of three months or less at acquisition date.

Short-term investments

Short-term investments are recorded at fair value and are comprised of guaranteed investment certificates with a maturity greater than 90 days but less than one year and, as such, are classified as current assets. It is the Company's intent to hold these investments to maturity.

Concentration of credit risk

Financial instruments which potentially subject the Company to concentration of credit risk consist primarily of cash and cash equivalents and investment securities classified as held to maturity. The Company maintains deposits in federal financial institutions. Management believes that the Company is not exposed to significant credit risk due to the financial position of the depository institutions in which those deposits are held. Additionally, the Company has adopted an investment policy that includes guidelines relative to credit quality, diversification of maturities and liquidity.

Currency Risk

The Company is exposed to currency risk due to financial instruments denominated in foreign currencies. The Company is exposed to the Canadian dollar currency risk and does not enter into arrangements to hedge its currency risk exposure.

Property and equipment

Property and equipment is stated at historical cost less accumulated amortization. Expenditures for maintenance and repairs are recorded to expense as incurred. The Company reviews its property and equipment whenever events or changes in circumstances indicate that the carrying value of certain assets might not be recoverable and recognizes an impairment loss when it is probable that an asset's realizable value is less than the carrying value. To date, no such impairment losses have been recorded. Amortization is calculated using the straight-line method over the following estimated useful lives of the assets:

Computer hardware and software	3 years
Office equipment	5 years
Furniture and fixtures	5 years
Leasehold improvements	3 years

Share issuance costs

Share issuance costs applicable to the issuance of equity instruments are recorded as a reduction of the financing equity proceeds.

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

2 Summary of significant accounting policies (Continued)

Research and development and investment tax credits

Research and development costs are charged against income in the period of expenditure. The Company's research and development costs consist primarily of salaries and fees paid to contract research organizations (CROs) and to contract manufacturing organizations (CMOs).

Clinical trial expenses include direct costs associated with CROs, direct CMO costs for the formulation and packaging of clinical trial material, as well as investigator and patient-related costs at sites at which the Company's trials are being conducted. Direct costs associated with the Company's CROs and CMOs are generally payable on a time-and-materials basis, or when milestones are achieved. The invoicing from clinical trial sites can lag several months. The Company records expenses for its clinical trial activities performed by third parties based upon estimates of the percentage of work completed of the total work over the life of the individual study in accordance with agreements established with CROs and clinical trial sites. The Company determines the estimates through discussions with internal clinical personnel, CROs and CMOs as to the progress or stage of completion of trials or services and the agreed-upon fee to be paid for such services based on facts and circumstances known to the Company as of each consolidated balance sheet date. The actual costs and timing of clinical trials are highly uncertain, subject of risks and may change depending upon a number of factors, including the Company's clinical development plan. If the actual timing of the performance of services of the level of effort varies from the estimate, the Company will adjust the accrual accordingly. Adjustments to prior period estimates have not been material.

The Company recognizes the benefit of Canadian research and development tax credits as a reduction of research and development costs for fully refundable investment tax credits and as a reduction of income taxes for investment tax credits that can only be claimed against income taxes payable when there is reasonable assurance that the claim will be recovered.

Income taxes

The provision for income taxes is computed using the liability method. Under this method, deferred tax assets and liabilities are determined based on differences between financial reporting and tax bases of assets and liabilities. Deferred tax assets and liabilities are measured using enacted tax rates and laws that will be in effect when the differences are expected to reverse. A valuation allowance is recorded to reduce the carrying amount of deferred income tax assets when it is more likely than not that these assets will not be realized. Tax benefits related to tax positions not deemed to meet the "more-likely-than-not" threshold are not permitted to be recognized in the consolidated financial statements.

Foreign currency translations

The functional currency of the Company is the US dollar. Accordingly, transactions denominated in currencies other than the functional currency are measured and recorded in the functional currency at the exchange rate in effect on the date of the transactions. At each consolidated balance sheet date, monetary assets and liabilities denominated in currencies other than the functional currency are remeasured using the exchange rate in effect at that date. Non-monetary assets and liabilities and revenue and expense items denominated in foreign currencies are translated into the functional currency using the exchange rate prevailing at the dates of the respective transactions. Any gains or losses arising on remeasurement are included in the consolidated statement of operations.

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

2 Summary of significant accounting policies (Continued)

Share-based compensation

The Company has a share-based compensation plan which is described in detail in note 6 and records all share-based payments, including grants of employee share options, at their fair values. The fair value of share options granted to employees and non-employees is estimated at the date of grant using the Black-Scholes option pricing model. The Company recognizes share-based compensation expense over the requisite service period of the individual grants, which equals the vesting period, using the straight-line method. Forfeitures, if any, are recorded as they occur. Any consideration paid by employees on exercising share options and the corresponding portion previously credited to contributed surplus are credited to share capital. The Black-Scholes option pricing model used by the Company to calculate option values was developed to estimate fair value.

Redeemable convertible preferred shares

The Company classifies shares that are redeemable at a fixed or determinable price on a fixed or determinable date outside of permanent equity. The redeemable convertible preferred shares are classified outside of shareholders' deficit because the shares contain certain redemption features that are not solely within the control of the Company. The Company records convertible preferred shares at fair value upon issuance, net of any issuance costs or discounts.

Recently issued accounting pronouncements

From time to time, new accounting pronouncements are issued by the Financial Accounting Standards Board (FASB) or other standards-setting bodies, and they are adopted by the Company as of the specified effective date.

In February 2016, the FASB issued Accounting Standards Update (ASU) No. 2016-02, Leases. Under the new standard, lessees will need to recognize a right-of-use asset and a lease liability for virtually all of their leases (other than leases that meet the definition of a short-term lease). The liability will be equal to the present value of lease payments. The asset will be based on the liability, subject to adjustment, such as for initial direct costs.

For income statement purposes, the FASB retained a dual model, requiring leases to be classified as either operating or finance.

Operating leases will result in straight-line expense (similar to current operating leases) while finance leases will result in a front-loaded expense pattern (similar to current capital leases). Classification will be based on criteria that are largely similar to those applied in current lease accounting. Extensive quantitative and qualitative disclosures, including significant judgments made by management, will be required to provide greater insight into the extent of revenue and expense recognized and expected to be recognized from existing contracts. The standard is effective for fiscal years beginning after December 15, 2018. The new standard must be adopted using a modified retrospective transition and provides for certain practical expedients. Transition will require application of the new guidance at the beginning of the earliest comparative period presented. The Company is currently evaluating the impact of this standard on its consolidated financial statements.

In June 2018, the FASB amended the accounting for share-based payment awards issued to non-employees. Under the revised guidance, the accounting for awards issued to non-employees will be similar to the accounting for employee awards. This includes allowing for the measurement of awards at the

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

2 Summary of significant accounting policies (Continued)

Recently issued accounting pronouncements (Continued)

grant date and recognition of awards with performance conditions when those conditions are probable — both of which are earlier than under current guidance for non-employee awards. The new standard maintains or establishes certain specific guidance for non-employee awards on attribution of cost, requiring that an asset or expense be recognized in the same period and in the same manner as if the grantor had paid cash equal to the value of the award; and inputs to the option pricing model, providing an entity a policy choice to use the contractual term of an award as the expected term assumptions. The changes should reduce complexity and may also reduce volatility in the recognition of compensation cost for non-employee awards. The new guidance is effective for public business entities for fiscal years beginning after December 15, 2018. The Company is currently evaluating the impact that this standard will have on its consolidated financial statements.

3 Other receivables

Other receivables at December 31 are comprised of:

	2017	2018
Interest receivable	$ 44	$ 178
Sales tax receivable	72	209
	$ 116	$ 387

4 Property and equipment

Property and equipment consist of the following at December 31:

	2017	2018
Computer hardware and software	$ 4	$ 9
Office equipment	28	28
Leasehold improvements	4	4
Total	$ 36	$ 41
Less accumulated depreciation and amortization	1	11
Property and equipment, net	$ 35	$ 30

During the year ended December 31, 2018, the Company did not record any write off (in 2017, the Company wrote off fully amortized assets with a cost of $35). For the year ended December 31, 2018, amortization expense was $10 (in 2017, amortization expense was $8) and was included in research and development expense.

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

5 Accounts payable and accrued liabilities

Accounts payable and accrued liabilities comprised the following as of December 31:

	2017	2018
Trade accounts payable	$ 819	$ 2,603
Accrued research and development liabilities	132	1,012
Other accrued liabilities	156	164
Accrued compensation and benefits payable	494	698
	$ 1,601	$ 4,477

6 Convertible preferred shares

The Company's Class A1, A2, B, C, D1 and D2 redeemable convertible preferred shares (collectively known as "Convertible Preferred Shares") allow the holders to redeem their shares upon a change in control in the Company. As a result, the Company classifies its Convertible Preferred Shares as mezzanine equity. The Company charges specific incremental issuance costs incurred in the offering of Convertible Preferred Shares against the gross proceeds of the Convertible Preferred Shares.

Authorized

An unlimited number of Class A1 preferred shares, voting based on the number of common shares into which they could be converted, annual non-cumulative dividend of 8% in preference to the holders of common shares calculated on their issue price. In addition, the Class A1 preferred shares are eligible to their pro rata shares, on an as-converted basis, to any dividend paid on common shares. The Class A1 preferred shares are subject to a weighted average antidilution adjustment in the event of a common share issuance at a price per share lower than C$5.3193

An unlimited number of Class A2 preferred shares, voting based on the number of common shares into which they could be converted, preferential non-cumulative dividend of 8% *pari passu* with the Class B preferred shares and in preference to the holders of Class A1 preferred shares calculated on their issue price. In addition, the Class A2 preferred shares are eligible to their pro rata shares, on an as-converted basis, to any dividend paid on common shares. The Class A2 preferred shares are subject to a weighted average antidilution adjustment in the event of a common share issuance at a price per share lower than C$5.3193

An unlimited number of Class B preferred shares, voting based on the number of common shares into which they could be converted, preferential non-cumulative dividend of 8% *pari passu* with the Class A2 preferred shares and in preference to the holders of Class A1 preferred shares calculated on their issue price. In addition, the Class B preferred shares are eligible to their pro rata shares, on an as-converted basis, to any dividend paid on common shares. The Class B preferred shares are subject to

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

6 Convertible preferred shares (Continued)

a weighted average antidilution adjustment in the event of a common share issuance at a price per share lower than $6.1172

An unlimited number of Class C preferred shares, voting based on the number of common shares into which they could be converted, preferential non-cumulative dividend of 8% to the Class B and A2 preferred shares and in preference to the holders of Class A1 preferred shares calculated on their issue price. In addition, the Class B preferred shares are eligible to their pro rata shares, on an as-converted basis, to any dividend paid on common shares. The Class C preferred shares are subject to a weighted average antidilution adjustment in the event of a common share issuance at a price per share lower than $7.2619

An unlimited number of Class D1 preferred shares, voting based on the number of common shares into which they could be converted, preferential non -cumulative dividend of 8% pari passu with the Class D2 preferred shares, and in preference to the holders of the Class C, Class B, Class A2 and Class A1 preferred shares calculated on their issue price. In addition, the Class D1 preferred shares are eligible to their pro rata shares, on an as-converted basis, to any non-cumulative dividend paid on common shares. The Class D1 preferred shares are subject to a weighted average antidilution adjustment in the event of a common share issuance at a price per share lower than $9.4295.

An unlimited number of Class D2 preferred shares, voting based on the number of common shares into which they could be converted, preferential non-cumulative dividend of 8% pari passu with the Class D1 preferred shares, and in preference to the holders of the Class C, Class B, Class A2 and Class A1 preferred shares calculated on their issue price. In addition, the Class D2 preferred shares are eligible to their pro rata shares, on an as-converted basis, to any non-cumulative dividend paid on common shares. The Class D2 preferred shares are subject to a weighted average antidilution adjustment in the event of a common share issuance at a price per share lower than $12.2583.

The Company has early adopted the guidance on down round features from ASU 2017-11 with respect to the antidilution adjustments for the Class A1, Class A2, Class B, Class C, Class D1 and D2 preferred shares.

The Class A1, A2, B, C, D1 and D2 preferred shares are automatically converted into common shares at the applicable conversion price upon (i) closing of a qualified initial public offering at a price per share based on a pre-money valuation of the Company of at least $250,000 and resulting in gross proceeds of at least $60,000, whereby the shares would be listed on one or more Recognized Stock Exchanges; and (ii) the election to convert by a majority of the Class A1, A2, B, C, D1 and D2 preferred shares. The current conversion rate of Class A1, A2, B, C, D1 and D2 preferred shares into common shares is 1:1.

The holders of the Company's Convertible Preferred Shares will be entitled to receive non-cumulative dividends at the rate of 8% of the purchase price per annum in preference to any dividends to the holders of the common shares, payable as and if when declared by the Board of Directors. The Board has not declared any dividends as of December 31, 2018. The holders of the Convertible Preferred Shares also will be entitled to participate pro rata in any dividends paid to the holders of the common shares on an as-converted basis.

Upon the liquidation of the Company, the holders of Convertible Preferred Stock will be entitled to receive, as of December 31, 2018, in preference to the holders of the common stock and in order of priority, an

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

6 Convertible preferred shares (Continued)

amount equal to $12.4472 per share for Series D2 Convertible Preferred Stock, $9.5747 per share for Series D1 Convertible Preferred Stock, $7.9258 per share for Series C Convertible Preferred Stock, $7.3406 per share for Series B Convertible Preferred Stock, $7.713 per share for Series A2 Convertible Preferred Stock and $8.83 per share for Series A1 Convertible Preferred Stock (the "Liquidation Preference"). Following payment in full to the holders of preferred shares of all amounts distributable to them, the remaining assets of the Company available for distribution to holders of the Company's share capital shall be distributed on a pro rata basis among (i) the holders of any preferred shares convertible into common shares of the Company on an as if converted basis; and (ii) the holders of the common shares.

The holders of 70% of Class A1, A2, B, C, D1 and D2 preferred shares, voting as a single class, may require that the Company redeem the preferred shared at the earlier of a sale or an exclusive license of all or substantially all intellectual property of the Company or all of the assets and the fifth anniversary of the closing date of the Class D preferred shares. The redemption price will be the higher of the liquidation preference or the fair market value of such preferred shares. Class A1 preferred shares may only be redeemed once Class A2, B, C, D1 and D2 preferred shares are fully redeemed.

For the years ended December 31, 2017 and 2018, the Company issued the following Convertible Preferred Shares:

a) On March 15, 2017, the Company issued 572,154 Class B preferred shares for gross proceeds of $3,500. The costs related with this share issuance were $34.

b) On July 21, 2017, the Company entered into a share subscription under which it is committed to issue 7,573,766 new Class C preferred shares to its Class C preferred shareholders for a total consideration of $55,000. The shares were to be issued in two separate tranches based on the achievement of milestones as specified in the subscription agreement.

c) On July 21, 2017, the Company issued the first tranche of 3,786,878 Class C preferred shares for gross proceeds of $27,500. The costs related with this share issuance were $264.

d) On October 17, 2018, the Company issued 6,893,236 Class D1 preferred shares for gross proceeds of $65,000. The costs related with this share issuance were $281.

e) On October 17, 2018, the Company issued 1,223,656 Class D2 preferred shares for gross proceeds of $15,000. The costs related with this share issuance were $65.

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

6 Convertible preferred shares (Continued)

	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	Total
Balance as of December 31, 2016	372,211	$ 2,027	2,443,914	$ 12,643	2,258,753	$ 13,732	—	—	—	—	—	—	$ 28,402
Issuance of Class B preferred shares, net of share issuance costs	—	—	—	—	572,154	3,466	—	—	—	—	—	—	3,466
Issuance of Class C preferred shares, net of share issuance costs	—	—	—	—	—	—	3,786,878	$ 27,236	—	—	—	—	27,236
Balance as of December 31, 2017	372,211	$ 2,027	2,443,914	$ 12,643	2,830,907	$ 17,198	3,786,878	$ 27,236	—	—	—	—	$ 59,104
Issuances in 2018													
Issuance of Class D1 preferred shares, net of share issuance costs	—	—	—	—	—	—	—	—	6,893,236	$ 64,719	—	—	64,719
Issuance of Class D2 preferred shares, net of share issuance costs	—	—	—	—	—	—	—	—	—	—	1,223,656	$ 14,935	14,935
Balance as of December 31, 2018	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	138,758

7 Shareholders' deficit

Authorized share capital

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

During the year ended December 31, 2018, the Company issued a total of 356,797 common shares (in 2017, 18,743) for a total cash consideration of $461 (in 2017, $20) pursuant to the exercise of 356,797 stock options (in 2017, 18,743) at an average exercise price of $1.2873 per option (in 2017, $1.0639 per option). As a result, an amount of $350 (in 2017, $17) 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.

Additional paid-in capital

	2017	2018
Opening balance	$ 2,199	$ 2,372
Share-based compensation expense	190	633
Exercise of stock options	(17)	(350)
Closing balance	$ 2,372	$ 2,655

Share-based compensation

On October 15, 2018, the Company amended for a third time and restated the share option plan (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 is administered by the Board of Directors. The Board of Directors determines the number of options to be granted, the vesting period and the exercise price of new options. It is the Company's policy to establish the

Milestone Pharmaceuticals Inc.
Notes to Consolidated Financial Statements (Continued)
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7 Shareholders' deficit (Continued)

Share-based compensation (Continued)

exercise price at an amount that approximates 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.

As of December 31, 2018, there were 2,924,917 options available for awards under the 2011 Plan, of which 2,295,045 options were granted, leaving 629,797 available for future grant. The outstanding and exercisable options at December 31 were as follows:

	2017		2018	
	Number of shares	Weighted average exercise price	Number of shares	Weighted average exercise price
Outstanding at beginning of period	708,770	$ 1.0692	968,782	$ 1.1330
Forfeited/expired	—	—	(12,198)	1.0958
Granted	278,755	1.5160	1,695,258	2.0373
Exercised	(18,743)	1.0639	(356,797)	1.2873
Outstanding at end of period	968,782	$ 1.1330	2,295,045	$ 1.7713
Exercisable at end of period	517,757	$ 1.0107	588,817	$ 1.3139

As of December 31, 2018, the weighted average remaining contractual life was 8.6 years (for 2017, 7.9 years). The weighted average remaining contractual life was 6.6 years for vested options (for 2017, 7.0 years). 12,198 options were forfeited for the year ended December 31, 2018 (for 2017, zero).

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' deficit. The weighted average fair values of options granted in 2018 was $1.4628 per share (for 2017, $1.0479). Share-based compensation expense recognized for the year ended December 31, 2018 was $633 (in 2017, $190).

As of December 31, 2018, there was $2,402 (for 2017, $651) 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 3.1 years (for 2017, 2.5 years).

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Notes to Consolidated Financial Statements (Continued)
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7 Shareholders' deficit (Continued)

Share-based compensation (Continued)

	2017		2018	
	Number of options	Weighted average fair value	Number of options	Weighted average fair value
Non-vested share options at beginning of period	416,790	$ 0.9468	451,113	$ 1.0266
Forfeited/expired	—	—	(12,198)	1.0639
Granted	278,755	1.0479	1,695,258	1.4628
Vested, outstanding	(244,432)	$ 0.9202	(427,870)	$ 1.4788
Non-vested share options at end of period	451,113	$ 1.0266	1,706,303	$ 1.3458

The following table summarizes information with respect to share options outstanding as of December 31, 2018:

	Options outstanding			Options exercisable		
Exercise price	Number of options	Weighted average remaining contractual life (years)	Weighted average exercise price	Number of options	Weighted average remaining contractual life (years)	Weighted average exercise price
C$0.96	240,620	4.2	$ 0.702	240,620	4.2	$ 0.702
$1.12	271,310	7.3	$ 1.117	124,218	6.9	$ 1.117
$1.54	975,336	9.1	$ 1.543	116,271	8.6	$ 1.543
$1.91	82,771	9.6	$ 1.915	—	—	$ —
$2.66	725,008	9.9	$ 2.660	107,708	9.8	$ 2.660
Total	**2,295,045**	**8.6**	**$ 1.771**	**588,817**	**6.6**	**$ 1.314**

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.

Milestone Pharmaceuticals Inc.
Notes to Consolidated Financial Statements (Continued)
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7 Shareholders' deficit (Continued)

Share-based compensation (Continued)

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 years ended December 31, 2017 and 2018:

	2017	2018
Exercise price	$ 1.5160	$ 2.0373
Share price	$ 1.5160	$ 2.0373
Volatility	82%	82%
Risk-free interest rate	1.90%	2.84%
Expected life	5.72 years	6.25 years
Dividend	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 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.

Share-based payment awards with performance targets attainable after the requisite service period are treated as performance conditions that affect vesting. No compensation expense is recorded related to an award for which the transfer to the employee is contingent on the attainment of a performance target until it becomes probable that the performance target will be met.

The Company recognized share-based compensation expense as follows at December 31, 2017 and 2018:

	2017	2018
Administration	$ 83	$ 209
Research and development	107	371
Commercial activities	—	53
	$ 190	$ 633

8 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 during the period. The outstanding convertible preferred shares and share-based compensation have been excluded from the calculation

Milestone Pharmaceuticals Inc.
Notes to Consolidated Financial Statements (Continued)
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8 Net loss per share (Continued)

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 December 31, 2017 and 2018, as they would be anti-dilutive:

	2017	2018
Redeemable convertible preferred shares	9,433,910	17,550,802
Share options and unvested restricted share awards	968,782	2,295,045
	10,402,692	19,845,847

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

9 Income taxes

A reconciliation between tax expense and the product of accounting income multiplied by the basic income tax rate for the years ended December 31, 2017 and 2018 is as follows:

	2017	2018
Loss before income taxes	$ (8,082)	$ (23,111)
Basic income tax rate	26.79%	26.67%
Computed income tax recovery	(2,165)	(6,164)
Effect on income tax rate resulting from		
Accounting charges not deductible for tax purposes	10	12
Non-deductible share-based compensation	51	169
Unrecorded potential tax benefits of current period losses and other tax assets	2,103	6,183
Non-refundable investment tax credit used (earned) in the year	17	(145)
Other	(12)	19
Income tax expense reported in the consolidated statements of loss and comprehensive loss	$ 4	$ 74

The Company has incurred Canadian federal and provincial net operating losses (NOL) from inception. As of December 31, 2018, the Company has NOL carry-forwards of approximately $46,355 and $45,704, respectively, for Canadian federal and Québec purposes, available to reduce future taxable income, which expire beginning in 2027 through 2038. The Company has no NOLs for U.S. tax purposes. The Company also has scientific research and experimental development expenditures of approximately $5,828 and $7,972, respectively, for Canadian federal and Québec income tax purposes, which have not been deducted. These expenditures are available to reduce future taxable income and have an unlimited carry-

Milestone Pharmaceuticals Inc.
Notes to Consolidated Financial Statements (Continued)
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9 Income taxes (Continued)

forward period. Research and development tax credits and expenditures are subject to verification by the tax authorities, and, accordingly, these amounts may vary.

Deferred income taxes reflect the net tax effects of temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. The net deferred tax assets have not been recognized in these financial statements because the criteria for recognition of these assets were not met.

The Company's deferred tax assets consist of the following for the years ended December 31, 2017 and 2018:

	2017	2018
Net operating loss carry-forwards	6,621	12,209
Tax basis of property and equipment in excess of carrying values	91	93
Federal SR&ED investment tax credits	128	273
Taxation of federal SR&ED investment tax credits	(33)	(72)
Research and development expenditures	1,378	1,791
Financing costs	82	138
Others	3	21
Total gross deferred tax assets	8,270	14,453
Valuation allowance	(8,270)	(14,453)
Net deferred tax assets	—	—

The Company files income tax returns in Canada and the United States. The Company is subject to Canada Revenue Agency and Revenu Québec examination for fiscal years 2014 to 2018 due to unexpired statute of limitation periods and is subject to US Federal and state income tax examination for fiscal years 2017 and 2018.

10 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 (expressed in thousands of US dollars) have been recorded as a reduction of research and development expenditures for an amount of $257 for the year ended December 31, 2018 (for 2017, $523).

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11 Commitments

Facility lease

The Company has 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 for the next two years are as follows:

	Lease operating expenses	Lease base rent expenses
2019	$ 86	$ 130
2020	79	85
	$ 165	$ 215

Total rental expense under operating leases for the year ended December 31, 2018 was $232 (for 2017, $77).

12 Currency risk

The Company is exposed to the financial risk related to the fluctuation of foreign exchange rates and the degree of volatility of those rates. The foreign currency risk is limited to the portion of the Company's business transactions denominated in currency other than US dollars. The following table provides an indication of the Company's exposure to the Canadian dollar, which is expressed in US dollars as of December 31:

	2017	2018
Cash	$ 149	$ 246
Short-term investments	32	29
Accounts payable and accrued liabilities	470	538
Net financial position exposure	$ 651	$ 813

The Company does not enter into arrangements to hedge its currency risk exposure.

13 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

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Notes to Consolidated Financial Statements (Continued)
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13 Fair value of financial instruments (Continued)

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 following tables present the Company's fair value hierarchy for all its financial assets (by major security type measured at fair value on a recurring basis) for the years ending December 31, 2017 and 2018:

December 31, 2018	Estimated fair value $	Level 1 $	Level 2 $	Level 3 $
Assets				
Guaranteed investment certificates	29	29	—	—

December 31, 2017	Estimated fair value $	Level 1 $	Level 2 $	Level 3 $
Assets				
Guaranteed investment certificates	16,032	16,032	—	—

5,500,000 Common Shares

PROSPECTUS

Joint Book-Running Managers

Jefferies

Cowen

Piper Jaffray

Lead Manager

Oppenheimer & Co.

May 8, 2019

Through and including June 2, 2019 (the 25th day after the commencement of this offering), all dealers that buy, sell or trade common shares, whether or not participating in this offering, may be required to deliver a prospectus. This delivery requirement is in addition to the dealers' obligation to deliver a prospectus when acting as underwriters and with respect to their unsold allotments or subscriptions.