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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2019.

OR

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

For the transition period from to

Commission file number 001-38899

Milestone Pharmaceuticals Inc.

(Exact name of registrant as specified in its charter)

Quebec	**Not applicable**
(State or Other Jurisdiction of Incorporation or Organization)	(I.R.S. Employer Identification No.)
1111 Dr. Frederik-Phillips Boulevard, Suite 420 Montréal, Québec CA	**H4M 2X6**
(Address of Principal Executive Offices)	(Zip Code)

Registrant's telephone number, including area code **(514)-336-0444**

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

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

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☐ No ☒

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes ☐ No ☒

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

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

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

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

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

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

The aggregate market value (approximate) of the registrant's common equity held by non-affiliates based on the closing price of a share of the registrant's common share for The Nasdaq Stock Market on June 30, 2019 (the last business day of the registrant's most recently completed second fiscal quarter) was $217.5 million.

As of March 3, 2020, the total number of shares outstanding of the registrant's Common Shares was 24,559,470 shares, net of treasury shares.

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

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K 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 Annual Report on Form 10-K, 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 Annual Report on Form 10-K, 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;
- 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 Annual Report on Form 10-K may include additional factors that could harm our business and financial performance. Moreover, we operate in a very competitive and rapidly changing environment. New risk factors emerge from time to time, and it is not possible for our management to predict all risk factors nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in, or implied by, any forward-looking statements.

In light of the significant uncertainties in these forward-looking statements, you should not rely upon forward-looking statements as predictions of future events. Although we believe that we have a reasonable basis for each forward-looking statement contained in this Annual Report on Form 10-K, 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 Annual Report on Form 10-K.

PART I

ITEM 1. BUSINESS

Overview

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

PSVT is a rapid heart rate condition characterized by episodes of supraventricular tachycardia, or SVT, that start and stop without warning. Episodes of SVT are 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. Calcium channel blockers available in oral form are frequently used prophylactically to control the frequency and duration of future episodes of SVT. For treatment of episodes of SVT, approved calcium channel blockers are administered intravenously under medical supervision, usually in the emergency department. The combination of convenient nasal-spray delivery, rapid-onset and short duration of action of etripamil has the potential to shift the current treatment paradigm for episodes of SVT away from the burdensome and costly emergency department setting. If approved, we believe that etripamil will be the first self-administered therapy for the rapid termination of episodes of SVT wherever and whenever they occur.

Our development program for etripamil for the treatment of PSVT consists of three Phase 3 clinical trials, one Phase 2 trial, and Phase 1 trials. We believe this clinical trial program, if successful, will be sufficient to support approval in the United States and the European Union.

NODE-301 is our ongoing, placebo-controlled Phase 3 safety and efficacy trial, which is being conducted in North America. NODE-301 may serve as a single pivotal efficacy trial required for approval by the U.S. Food and Drug Administration, or FDA. The trial is being conducted in two parts. NODE-301A will continue until the trial's adjudication committee has evaluated data from the treatment of 150 SVT events with blinded study drug (etripamil or placebo). All pivotal efficacy analyses will be conducted on data from NODE-301A. NODE-301B will follow patients already enrolled in NODE-301 who did not take the study drug in NODE-301A. Data from NODE-301B will be analyzed as a pivotal safety and supportive efficacy data set, and will contribute to potentially valuable sub-population analyses and pharmaco-economic assessments. Following consultation with the FDA in 2019, we confirmed the two-part design, along with an increase in the sample size of NODE-301A from 100 to 150 adjudicated SVT events. The upsize of the trial satisfies a request from the European Medicines Agency, or EMA.

NODE-302 is our ongoing Phase 3 open-label safety extension trial. Patients who complete NODE-301 may enroll in NODE-302 and receive up to an additional 11 doses of etripamil. 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 SVT. All patients randomized in NODE-301 will be eligible for NODE-302. Patients who have successfully dosed with the study drug and completed a study closure visit will be eligible to enroll in NODE-302 to manage any subsequent episodes of SVT. 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 and the trial is ongoing. Trial safety results will contribute to the etripamil safety database.

NODE-303 is our ongoing Phase 3 open label safety trial, which is being conducted primarily in North America, Europe and Latin America. We designed NODE-303 to evaluate the safety of etripamil when self-administered without medical supervision, and to evaluate the treatment safety and efficacy of etripamil on multiple SVT episodes. The trial is designed to enroll up to 3,000 patients in order to collect data on approximately 1,000 patients taking etripamil in an at-home setting. A more accurate sizing of the trial will be determined once an overall size of the safety dataset is determined for NDA filing following future discussions with the FDA and other regulatory authorities. Based on a

review of the NODE-301 safety data available in June 2019, the FDA and multiple European and Latin American regulatory authorities have agreed to allow patient enrollment in NODE-303 without an in-office safety test dose, which is a safeguard required in the NODE-301 trial, and in a broad patient population including patients taking concomitant beta-blockers and calcium channel blockers.

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 episodes of SVT within 15 minutes at the dose selected for our Phase 3 trials versus a 35% termination rate for placebo. We have also completed two Phase 1 clinical trials in healthy volunteers, characterizing the pharmacokinetics and pharmacodynamic effect of etripamil.

We believe that PSVT is a large and under-recognized market that we estimate affects approximately two million Americans, with over 300,000 newly diagnosed patients per year, 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. PSVT patients experiencing an episode of SVT 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.

As with PSVT, calcium channel blockers are also approved for use in intravenous form for the treatment of some episodes of atrial fibrillation in which patients experience rapid ventricular rates. We plan to initiate in 2020 a Phase 2 proof-of-concept clinical trial in a controlled setting to evaluate the potential effectiveness of etripamil to reduce ventricular rate in atrial fibrillation patients who present to the clinic with rapid ventricular rate. The trial will enroll approximately 50 patients, randomized to etripamil 70 mg versus placebo, with a primary endpoint of reduction in ventricular rate.

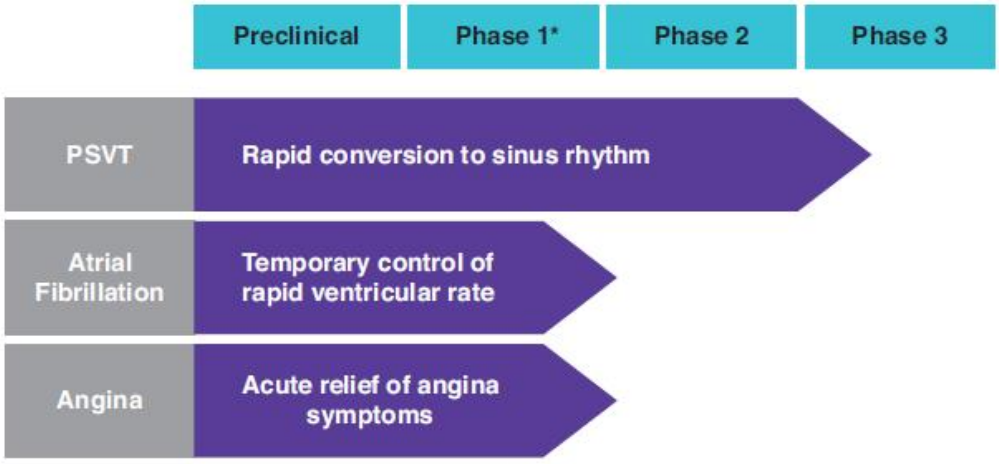
As we generate more data on the safety and efficacy profile of etripamil in PSVT and atrial fibrillation with rapid ventricular rate, we will continue to assess whether etripamil could be developed to potentially fulfill other areas of unmet medical need.

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.

Our Pipeline

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



* We are relying on our Phase 2 clinical trial of etripamil to support further clinical development of etripamil in PSVT, atrial fibrillation and angina.

Our Strategy

Our goal is to identify, develop and commercialize innovative cardiovascular medicines, including etripamil for the treatment of PSVT and other cardiovascular indications, and additional clinical-stage compounds for other cardiovascular 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 expect top-line data from our Phase 3 clinical trial of etripamil, which may serve as a single pivotal efficacy trial in the United States, in the middle of 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 proof-of-concept clinical trials with patients with atrial fibrillation and angina.

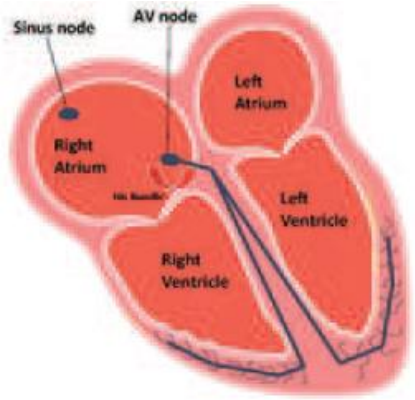
- ***Maximize the value of our programs by maintaining flexibility to commercialize our product candidates independently or through collaborative partnerships.*** We currently have exclusive development and commercialization rights for etripamil for our initial indications of PSVT, atrial fibrillation 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 novel treatments for cardiovascular conditions. 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

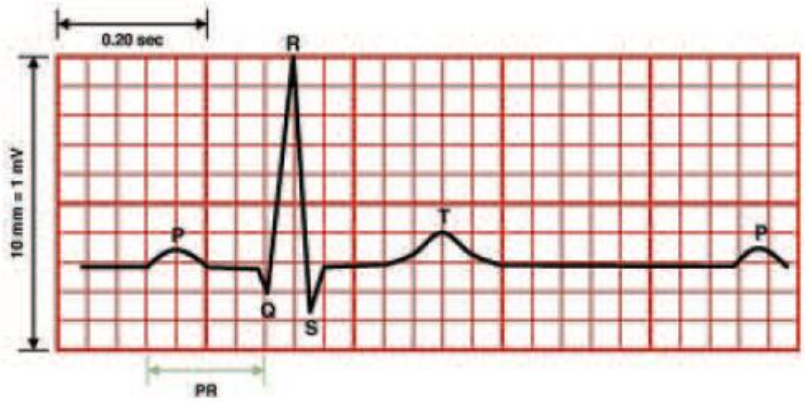
Normal Conduction

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 heartbeat 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 heartbeat 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 heartbeat 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 SVT. 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 relevant pharmacodynamic effect of approximately 30-45 minutes in humans, compared with other calcium channel blockers that have pharmacodynamic effects of several hours.

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

- Action: Etripamil is designed to act upon the desired target for only 30 to 45 minutes, with the goal of reducing long-term side effects that may occur with chronic drug therapy.
- Absorption: Etripamil is designed to be absorbed into the bloodstream in less than 10 minutes through the inner lining of the nose.
- Administration: Etripamil is designed to be 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, cardiologists in the United States were exposed to a target product profile, or TPP, 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 SVT episodes and anticipated being able to avoid 50% to 75% of these emergency department visits per year by using etripamil. When asked to rank their receptivity to the etripamil TPP on a Likert scale of one to seven, where a rating of one equated to “not at all favorable” and a rating of seven equated to “extremely favorable”, the PSVT patients surveyed provided an average (mean) rating of 6.3. Furthermore, a majority of patients in this research expressed positive expectations for treatment with the etripamil TPP, including that it would provide peace of mind between episodes and a sense of control over the disease, by reducing anxiety in anticipation of future episodes and allowing them to perform activities that they perceived to be limited without a reliable at-home therapy. A minority of patients expressed negative expectations for the etripamil TPP, primarily as a result of an aversion to administering medications intranasally. When presented with hypothetical prices to the patient in the range of $30 to $60 per dose, PSVT patients in this market research also reported a desire to use etripamil for an average of approximately 50% of their SVT episodes.

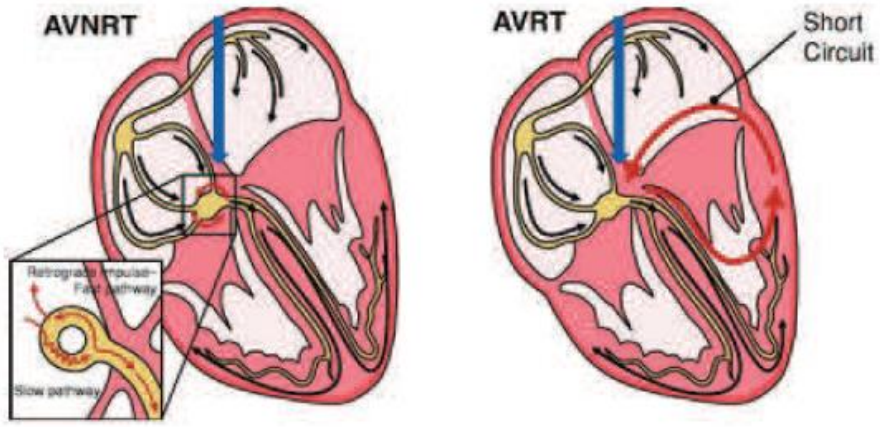
In this same research, 14 medical and pharmacy directors from both national and regional health plans in the United States were surveyed to assess the attractiveness of the etripamil TPP among payors. When asked their receptivity to the etripamil TPP, these payor representatives gave an average (mean) rating of 5.6 on the Likert scale. When presented with hypothetical wholesale acquisition costs to the payors of $1,000 and $500 per dose and then asked about the likelihood of coverage of etripamil by payors once it was approved, the representatives reported average (mean) Likert scores of 5.8 and 6.2, respectively. In this research, commonly reported drivers of the likelihood of covering etripamil were the lack of other approved treatment options, the potential for fast onset of action and high conversion, and the potential for effective health economic outcomes, in particular, the opportunity to offset the cost of emergency department visits and inpatient admissions.

We also commissioned a market research survey in 2018 and 2019 of 353 general cardiologists, electrophysiologists, and primary care physicians in the United States. We asked these healthcare providers to estimate the percentage of their PSVT patients that they would prescribe a product with the etripamil TPP, assuming these patients were not contraindicated to this product. In response, these providers reported expected prescription rates ranging from an average (mean) of 47% among electrophysiologists, or EPs, (n=50) to 58% among primary care physicians, or PCPs, (n=50), with cardiologists, or CCs, (n=253) reporting an average (mean) prescription rate of 54%. While the average prescription rates were similar across EPs and CCs, the typical expected use case for each physician group was different, with EP expected use cases typically being for shorter periods of time. The variability in prescription rates among all healthcare providers, including within each physician group, was high, especially among cardiologists, whose expected prescription rates ranged from 0% to 100%. Physicians in this market research also reported that a product with a fast onset of action and high conversion rates within 30-60 minutes of administration would be significantly better than current at-home treatment approaches and that they were familiar with and comfortable prescribing calcium channel blockers to their PSVT patients. However, physicians also noted that additional tests may be required prior to prescribing etripamil. Those additional tests included administering an ECG to rule out certain arrhythmias that would likely be

contraindicated with a product with the etripamil TPP. When asked about their receptivity to the profile of etripamil, physicians gave an average (mean) rating of 5.6 on a Likert scale.

PSVT

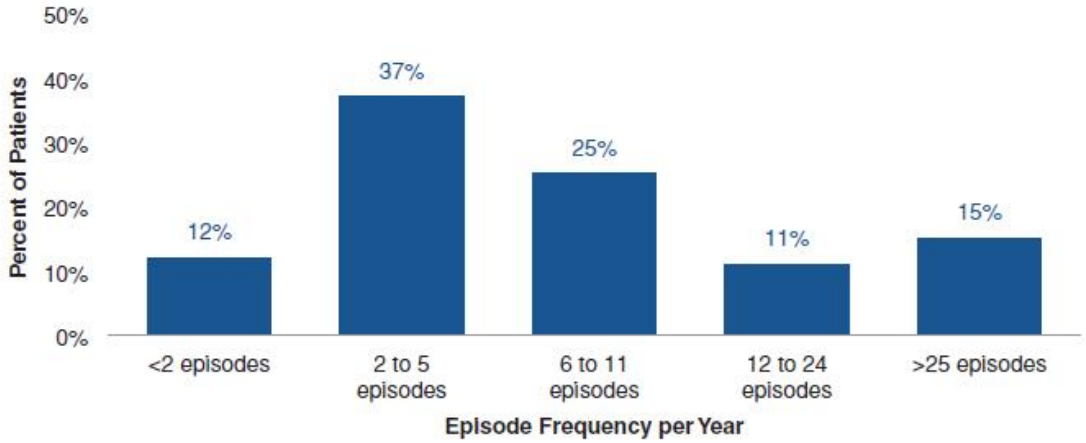
PSVT is a serious and recurring electrical disorder of the heart, which is caused by altered electrical conductivity over the AV node. PSVT refers to a rapid heart rate condition of the heart's upper chambers (atria) of abrupt onset and termination. In the most common form of PSVT called AV nodal reentrant 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 SVT 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. This survey indicated that it takes more than two years after first experiencing symptoms of PSVT for the average patient to receive a formal diagnosis. We believe this delay in diagnosis is primarily the result of the episodic nature of the disease and the requirement for an ECG when the patient is experiencing an SVT episode to confirm the diagnosis. 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 SVT episodes in the first 12 months after diagnosis.

Total Number of SVT 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 SVT 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 SVT, 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 SVT 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 SVT 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 SVT 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, lifestyle changes, 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 of SVT 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-arrhythmic 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 of SVT 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 an SVT 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 SVT includes IV administration of approved AV nodal-blocking agents in an acute care setting. The current standard of care for treatment of episodes of SVT is adenosine, but prior to its approval in 1990, episodes of SVT 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 SVT 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 SVT episodes that require visits to the emergency department may still occur, albeit for some patients 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 SVT 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. Furthermore, we estimate that approximately 300,000 new PSVT patients are diagnosed each year in the United States. We derive these estimates from the analysis of longitudinal claims data, which we believe is the most accurate method available to estimate the epidemiology of PSVT. In particular, we analyzed longitudinal Medicare claims data for patients age 65 and older and employer-based medical claims data for patients under age 65 with five or more years of continuous enrollment, for the years 2008 through 2016. We identified patients who, during this time period, had either two or more PSVT codes (ICD9 427.0 or ICD10 I47.1) in the outpatient setting or one or more of these codes in the emergency department or inpatient setting. Another prevalence analysis was published and presented at the 2018 International Academy of Cardiology’s Scientific Sessions. Using four years of longitudinal claims data in patients under age 65, this analysis arrived at similar conclusions regarding the number of PSVT patients in the United States. Both of these analyses were funded by us and included participation by our employees.

Other published sources that attempt to quantify the epidemiology of PSVT, such as the MESA study published in the Journal of the American College of Cardiology in 1998, and the PREEMPT study published in the Journal of the American Heart Association in 2018, provide important demographic and clinical characteristic data on patients with PSVT. For example, in the MESA study, fewer than 40% of the adjudicated incident cases of PSVT would have been detected had the investigators limited their screening to those patients identified by the PSVT ICD-9 Code (427.0). In

addition, 21% of the incident PSVT patients in the MESA study also had a diagnosis of atrial fibrillation (18%) or atrial flutter (6%). As an epidemiology tool, however, we believe these studies underestimate the incidence and prevalence of PSVT due to the episodic nature of the disease as well as the variability in the duration of the episodes, as the investigators in both studies relied only on data from patients presenting to healthcare settings acutely, with the episode confirmed on ECG during the encounter, to estimate the incidence and prevalence of PSVT.

From market research conducted in 2017 and 2018, we estimate a core target addressable market of approximately 40-65% of the prevalent population that we estimate has a higher burden of PSVT as measured by episode frequency and duration, emergency department visits and prophylactic use of chronic medications to reduce episode frequency. We define this core addressable market as patients who have been diagnosed with PSVT and who are engaging the healthcare system for treatment of PSVT, as identified by insurance claims, on an annual basis. Beyond this core addressable market, we believe that there is a significant opportunity for etripamil to help the estimated 1.4 million patients who have been diagnosed with PSVT but do not engage in the healthcare system on an annual basis. We believe many of these patients do not seek treatment for PSVT because they are not satisfied with the current options to manage an acute episode or because they have been told by their physician that their condition is not life threatening and episodes of SVT will eventually self-terminate. We believe that these untreated patients may re-engage the healthcare system if alternative treatment options are available to them. In addition, we believe that advances in digital health and wearable technology may lead to more rapid diagnosis of PSVT in the future, resulting in more patients seeking treatment for their symptoms.

Current treatment approaches for PSVT consume significant healthcare resources. One recently published longitudinal analysis in the American Journal of Cardiology has shown that mean annual total healthcare spending per PSVT patient in the year following diagnosis tripled for patients less than 65 years old (from $9,028 to $29,867) and nearly doubled for patients 65 years old and older (from $10,867 to $20,143) compared to the year prior to diagnosis. Spending for PSVT and related cardiac arrhythmia services accounted for 67% and 47%, respectively, of the increase in expenditures in these patient groups. A second analysis, presented at the 2018 International Academy of Cardiology's Scientific Sessions, concluded that rates of emergency department visits and hospitalizations were 1.8 and 3.0 times higher, respectively, following diagnosis in patients less than 65 years old compared with the prior, pre-diagnosis year. Expenditures for ablations in patients less than 65 years old averaged $4,700 per patient (23% of the overall spending increase), as compared to $451 per patient (5% of the overall spending increase) in patients 65 years old and older, which is consistent with lower rates of ablation overall in elderly patients. In total, we estimate from these claims data that approximately $3 billion is spent each year in the United States on treatments for PSVT, with 58% or $1.9 billion of annual costs being driven by ablation procedures, and 36% or $1.2 billion resulting from emergency department visits, hospitalizations and outpatient hospital visits 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 an SVT 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 at-home setting, and expect top-line data in the middle of first half of 2020. We have completed a second Phase 1 clinical trial, further characterizing the pharmacokinetics and pharmacodynamics of etripamil in Japanese and non-Japanese healthy volunteers. We are also conducting two open label Phase 3 safety trials. The FDA agreed that our Phase 3 clinical program could support an NDA filing in the United States.

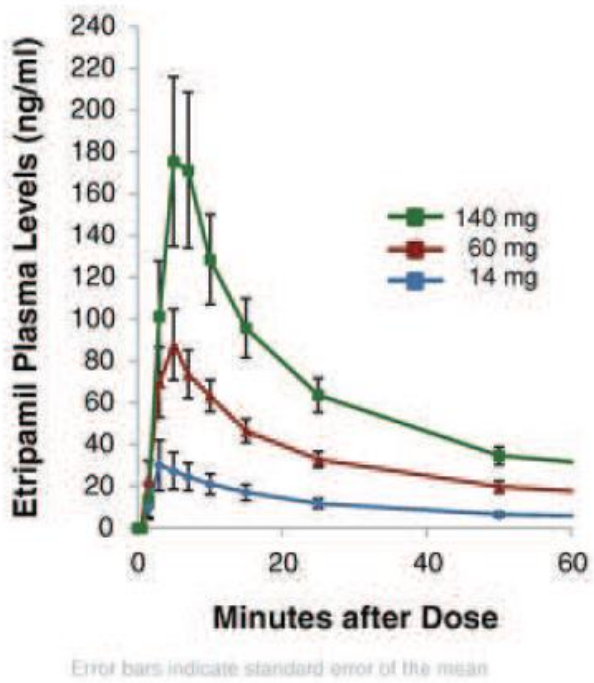
Phase 1 Clinical Data

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 formulations of etripamil administered via the nasal route in healthy, adult male subjects. All doses of etripamil were generally well tolerated, and there was no difference in the safety profile and PK between the two formulations of etripamil, 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.

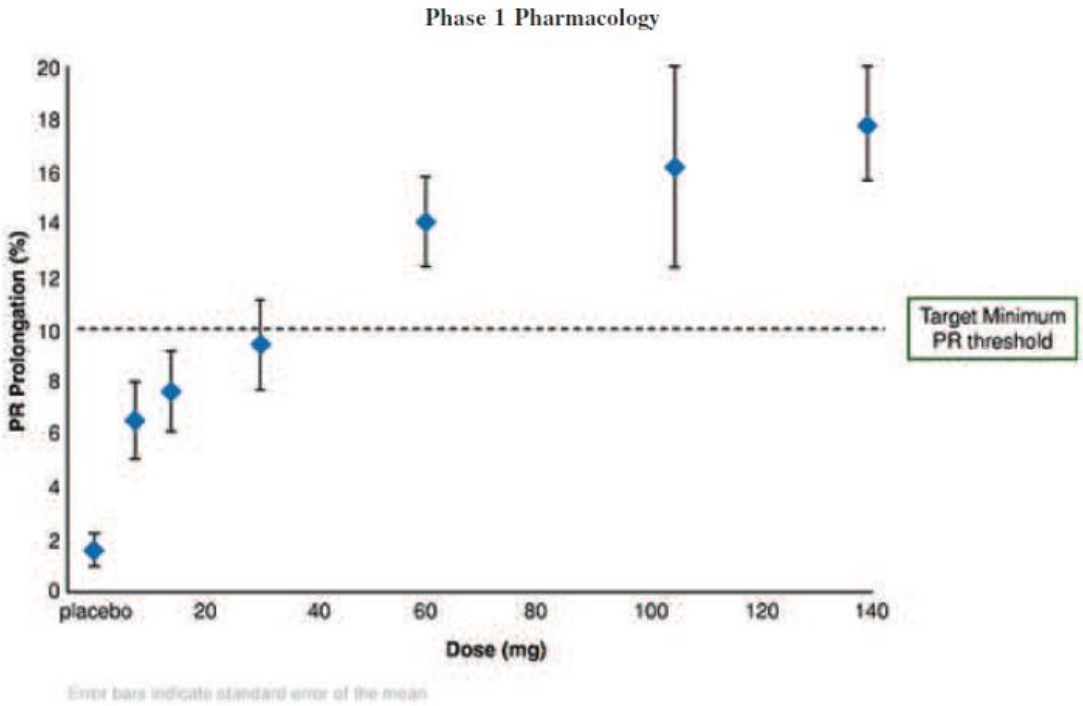
Following nasal administration of etripamil, PK analyses demonstrated rapid absorption and elimination, a dose-proportional systemic exposure, or area under the curve, and maximum plasma concentration for etripamil and its primary inactive metabolite. These findings were consistent across a range of 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 dose of etripamil 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 an SVT 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



We completed a second Phase 1 trial, NODE-102, comparing the pharmacokinetics and pharmacodynamics of etripamil 35 mg, 70 mg, and 105 mg versus placebo in Japanese and non-Japanese healthy volunteers. We believe this trial provides further justification for the selected 70 mg dose in our Phase 3 program, and may be used to support further clinical development of etripamil in Japan.

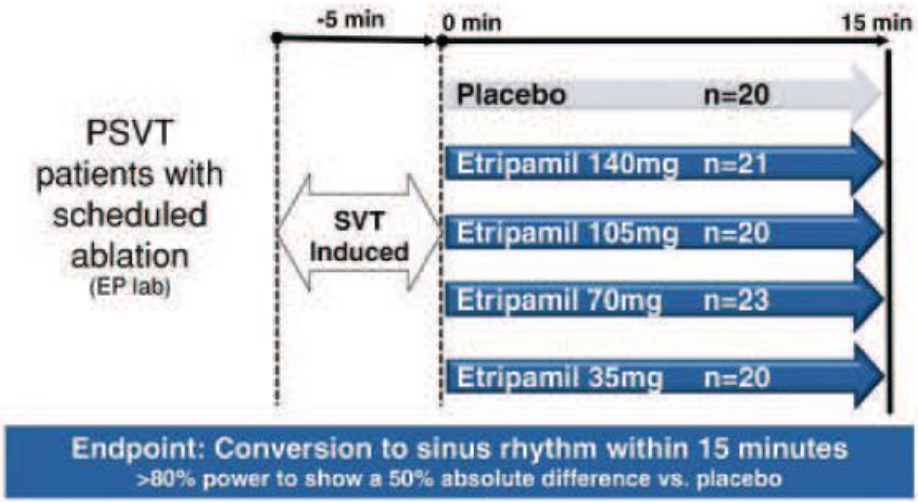
Phase 2 Clinical Data

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 SVT in a controlled setting, we conducted the study in the electrophysiology, or EP, laboratory setting, where the SVT 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 SVT. 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) SVT, 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, SVT was induced and sustained for 5 minutes in 104 patients, who were 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

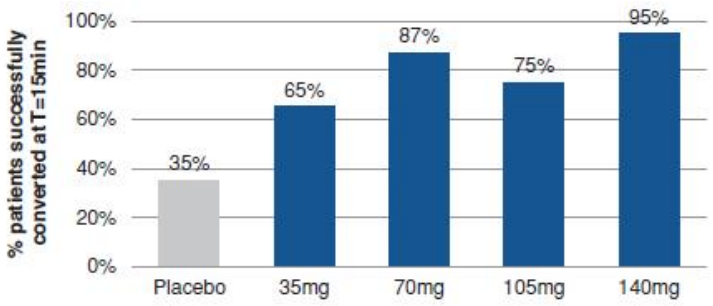
baseline characteristics across the five treatment groups. The mean heart rate in SVT at time 0 was 177 bpm in the placebo group and 168 bpm, 173 bpm, 180 bpm and 155 bpm in the etripamil 35 mg, 70 mg, 105 mg and 140 mg groups, respectively.

Phase 2 Clinical Trial Design



The primary endpoint in this clinical trial was the conversion of SVT to sinus rhythm within 15 minutes after administration of etripamil or placebo. As shown in the figure below, the percentage of patients in whom SVT 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.

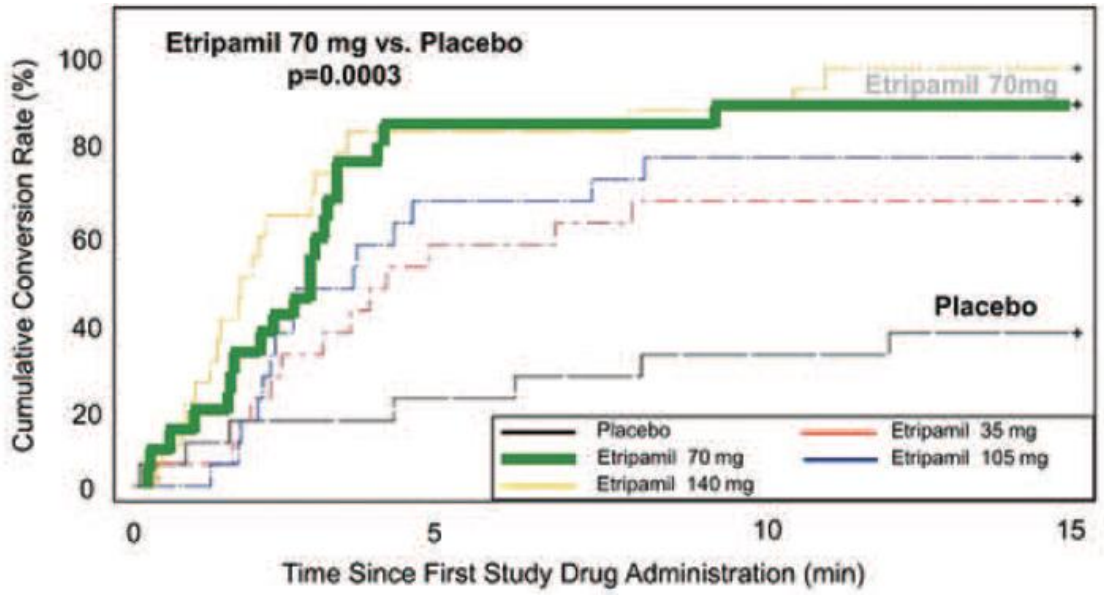
Etripamil Conversion Rates from SVT to Sinus Rhythm in Phase 2



# 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 doses of etripamil (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 SVT to Sinus Rhythm in Phase 2



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 105 mg dose group of etripamil 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 a 35mg dose of etripamil experienced facial flushing, shortness of breath, and chest discomfort. One patient who received a 105 mg dose of etripamil had nausea and vomiting, as well as a severe and serious cough. One patient who received a 140 mg dose of etripamil 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 SVT 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 SVT, the mean systolic blood pressure decreased at time 0 compared to the average at 20 and 10 minutes before SVT 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 of etripamil 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 at-home 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 SVT.

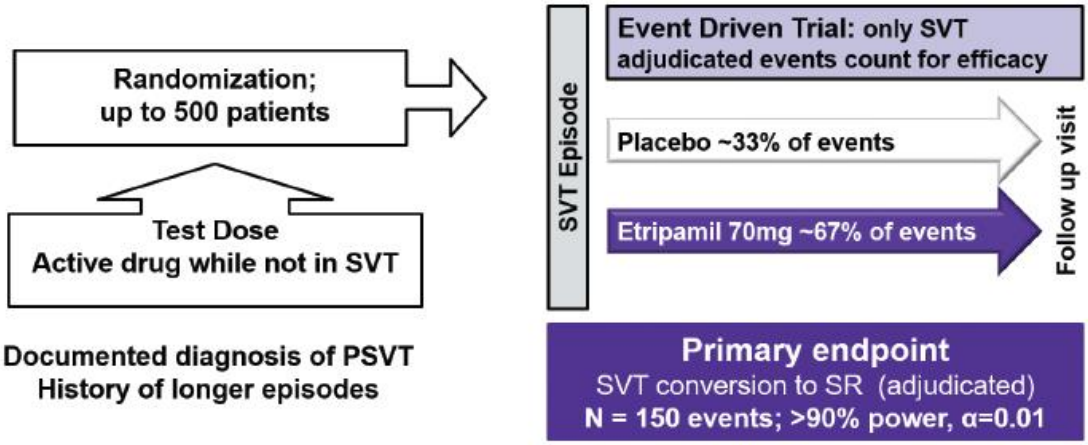
Based on our interactions with the regulatory agencies, our planned Phase 3 clinical program includes:

- NODE-301, a pivotal efficacy trial to assess the time to conversion of etripamil compared to placebo in at-home setting;
- 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 the at-home setting 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 70 mg of etripamil versus placebo in terminating an SVT episode in the at-home 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 of 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 SVT episode. Upon experiencing their next SVT 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 150 adjudicated SVT events are treated.

Phase 3 Clinical Trial Design



SR = Sinus Rhythm; PSVT = Paroxysmal Supraventricular Tachycardia; Study randomization scheme 2:1 etripamil : placebo

Each patient will stay in the NODE-301 trial until one episode of SVT 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 SVT with etripamil.

NODE-301 is being conducted in two parts. NODE-310A will continue until the trial's adjudication committee has evaluated data from the treatment of 150 patients with an episode confirmed to be SVT with etripamil or placebo. All pivotal efficacy analyses will be conducted on data from NODE-301A. NODE-301B will follow patients already enrolled in NODE-301 who did not take the study drug in NODE-301A. Data from NODE-301B will be analyzed for efficacy as a secondary data set and will contribute to potentially valuable sub-population analyses and pharmaco-economic assessments. In 2019, the FDA agreed to this two-part design, along with an increase in the sample size of NODE-301 pivotal analyses from 100 to 150 episodes confirmed to be SVT. The upsize of the trial satisfies a regulatory request from the EMA to eliminate the use of un-blinded, third-party data reviews, which would have directed us when to stop the study for purposes of safeguarding against potential randomization imbalances.

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 SVT.

Patients who have successfully dosed with the study drug in NODE-301 and completed a study closure visit are eligible to enroll in NODE-302 to manage any subsequent episodes of SVT. Eligibility is also 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 safety results will contribute to the etripamil safety database.

NODE-303. NODE-303 is an open-label global safety trial enrolling up to 3,000 patients who did not participate in NODE-301 or NODE-302 in order to collect data on approximately 1,000 patients taking etripamil in an at-home setting. 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 SVT episodes. The patients have the opportunity to manage up to four episodes of SVT in NODE-303.

NODE-303 was initiated in October 2019. Based on a review of the NODE-301 safety data available in June 2019, the FDA and multiple European and Latin American regulatory authorities agreed to allow patient enrollment in NODE-303 without an in-office safety test dose and in a broad patient population, including patients taking concomitant beta-blockers and calcium channel blockers.

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 at-home 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 plan to initiate a Phase 2 proof-of-concept clinical trial in 2020 to evaluate the potential effectiveness of etripamil to reduce ventricular rate in patients with atrial fibrillation with rapid ventricular rate for whom IV-administered calcium channel blockers have been used effectively. The trial will be conducted in Canada in collaboration with the Montreal Heart Institute and other research centers. The primary endpoint of the trial is reduction of ventricular rate in patients with symptomatic atrial fibrillation and elevated ventricular rate.

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 heartbeat. 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 could be used to rapidly reduce or relieve angina symptoms in the at-home 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 in the early stages of planning small pharmacodynamic and dose-ranging clinical trials to test the efficacy and safety of etripamil in various forms of angina. We expect to initiate a Phase 2 clinical trial in angina 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, NODE-302, and NODE-303 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 with PSVT to self-administer treatment to terminate SVT 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: InRhythm (flecainide), a sodium channel blocker in Phase II from InCarda Therapeutics, Inc., and 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 January 31, 2020, 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 a corresponding patent in Europe and 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, including the federal civil False Claims Act, which can be enforced by individuals through civil whistleblower and qui tam actions, and civil monetary penalties laws, 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, as defined by such law, 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.

There remain judicial and Congressional challenges to certain aspects of the PPACA, as well as 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, 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." In addition, the 2020 federal spending package permanently eliminates, effective January 1, 2020, the PPACA-mandated "Cadillac" tax on high-cost employer-sponsored health coverage and medical device tax and, effective January 1, 2021, also eliminates the health insurer tax. 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 December 2018, CMS published a new 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. Additionally, on December 18, 2019, the U.S. Court of Appeals for the 5th Circuit upheld the District Court ruling that the individual mandate was unconstitutional and remanded the case back to the District Court to determine whether the remaining provisions of the ACA are invalid as well. On March 2, 2020, the United States Supreme Court granted the petitions for writs of certiorari to review this case and has allotted one hour for oral arguments. It is unclear when such oral arguments are to be held and when a decision

is expected to be made. It is also unclear how such litigation 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 2029 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 2020 contains further drug price control measures that could be enacted during the 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 solicited feedback on some of these measures and has implemented others under its existing authority. For example, in May 2019, CMS issued a final rule to allow Medicare Advantage plans the option to use step therapy for Part B drugs beginning January 1, 2020. This final rule codified CMS's policy change that was effective January 1, 2019. Although a number of these and other measures may 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.

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 December 31, 2019, we had 30 full-time employees, 14 of whom were primarily engaged in research and development activities and 9 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 that occupies 5,116 square feet of leased office space under a lease that expires in September 2022. 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.

ITEM 1A. RISK FACTORS

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

Risks Related to Our Financial Position and Capital Needs

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

Since inception in 2003, we have incurred significant operating losses. Our net loss was $55.2 million and $23.2 million for the years ended December 31, 2019 and 2018, respectively. As of December 31, 2019, we had an accumulated deficit of $113.5 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, either directly or indirectly with third parties, to commercialize etripamil or any future product candidate for which we may obtain marketing approval;
- build a portfolio of product candidates through development, or the acquisition or in-license of drugs, product candidates or technologies;

- initiate preclinical studies and clinical trials for etripamil for any additional indications we may pursue, including the clinical trials for the treatment of atrial fibrillation with rapid ventricular rate 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 or a history of successful clinical development and commercialization of products.

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

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

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

Based on our research and development plans, we expect that our existing cash, cash equivalents and short-term investments, will be sufficient to fund our operations for at least the next 12 months. 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 ability of vendors who we rely on to accurately forecast expenses and deliver on expectations;
- the costs, timing and outcome of regulatory review of etripamil and any future product candidates;
- the costs and timing of future commercialization activities, including product manufacturing, marketing, sales and distribution, for etripamil and any future product candidates for which we receive marketing approval;
- the revenue, if any, received from commercial sales of etripamil and any future product candidates for which we receive marketing approval;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims;
- the extent to which we acquire or in-license other product candidates and technologies; and
- the costs of operating as a public company.

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

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

Until such time, if ever, as we can generate substantial product revenue, we expect to finance our cash needs through public or private equity or debt financings, third-party funding, marketing and distribution arrangements, as well as other collaborations, strategic alliances and licensing arrangements, or any combination of these approaches. We do not have any committed external source of funds. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest may be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a shareholder. Debt and equity financings, if

available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as redeeming our shares, making investments, incurring additional debt, making capital expenditures, declaring dividends or placing limitations on our ability to acquire, sell or license intellectual property rights.

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

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

In general, where control of a corporation has been acquired by a person or group of persons, subsection 111(5) of the Income Tax Act (Canada), or the Canadian Tax Act, and equivalent provincial income tax legislation restrict the corporation's ability to carry forward non-capital losses from preceding taxation years. We have not performed a detailed analysis to determine whether an acquisition of control for the purposes of subsection 111(5) of the Canadian Tax Act has occurred after each of our previous issuances of common shares or preferred shares. In addition, if we undergo an acquisition of control, our ability to utilize non-capital losses could be limited by subsection 111(5) of the Canadian Tax Act. As of December 31, 2019 we had Canadian federal and provincial non-capital loss carry forwards of $86.6 million and $86.1 million, respectively, which expire beginning in 2027 through 2039. In addition, we also have scientific research and experimental development expenditures of $9.4 million and $11.1 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.

Our subsidiary's ability to use our net operating loss carryforwards and certain other tax attributes for U.S. income tax purposes may be limited.

As of December 31, 2019, we had federal net operating loss carryforwards of $12.4 million as a result of expenses incurred in Milestone Pharmaceuticals USA, Inc., our wholly-owned subsidiary. Under U.S. federal income tax legislation enacted in 2017, informally titled the Tax Cuts and Jobs Act, or the Tax Act, federal NOLs incurred in taxable years ending after December 31, 2017, may be carried forward indefinitely, but the deductibility of federal NOLs generated in tax years beginning after December 31, 2017, is limited. In addition, under Sections 382 and 383 of the Code and corresponding provisions of state law, if a corporation undergoes an "ownership change," which is generally defined as a greater than 50% change (by value) in its equity ownership over a three-year period, the corporation's ability to use its pre-change NOL carryforwards, or NOLs, and other pre-change tax attributes (such as research tax credits) to offset its post-change income may be limited. It is possible that we have experienced one or more ownership changes in the past. In addition, we may also experience ownership changes in the future as a result of subsequent shifts in our share ownership some of which may be outside of our control. As a result, if we earn net taxable income, our ability to use our pre-ownership change NOL carryforwards to offset U.S. federal taxable income may be subject to limitations, which could potentially result in increased future tax liability to us. In addition, at the state level, there may be periods during which the use of NOLs is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed.

Risks Related to the Development of Our Product Candidates

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

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

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

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

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

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

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

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

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

The development of additional product candidates is risky and uncertain.

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

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

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

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

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

In addition, the design of a clinical trial can determine whether its results will support approval of a product, and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced. Clinical trial design flaws are more likely in therapy areas, such as PSVT, where there are limited previous trials from which to learn and model clinical trials. As an organization, we have limited experience designing clinical trials and may be unable to design and execute a clinical trial to support regulatory approval. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials even after achieving promising results in preclinical testing and earlier clinical trials. Data obtained from preclinical and clinical activities are subject to varying interpretations, which may delay, limit or prevent regulatory approval. In addition, we may experience regulatory delays or rejections as a result of many factors, including changes in regulatory policy during the period of our product candidate development. Any such delays could negatively impact our business, financial condition, results of operations and prospects.

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

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

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

- delays in reaching a consensus with regulatory authorities on design or implementation of our clinical trials;

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

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

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

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

- experience damage to our reputation.

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

Further, we, the FDA or an IRB may suspend our clinical trials at any time if it appears that we or our collaborators are failing to conduct a trial in accordance with regulatory requirements, including the FDA's current Good Clinical Practice, or GCP, regulations, that we are exposing participants to unacceptable health risks, or if the FDA finds deficiencies in our investigational new drug applications, or INDs, or the conduct of these trials. Therefore, we cannot predict with any certainty the schedule for commencement and completion of future clinical trials. If we experience delays in the commencement or completion of our clinical trials, or if we terminate a clinical trial prior to completion, the commercial prospects of our product candidates could be negatively impacted, and our ability to generate revenues from our product candidates may be delayed.

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

Our product candidates will require clinical testing before we are prepared to submit an NDA, or comparable application to foreign regulatory authorities, for regulatory approval. We cannot predict with any certainty if or when we might submit an application for regulatory approval for any of our product candidates or whether any such application will be approved by the FDA or foreign regulatory authority. 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 or foreign regulatory authority 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 trials, we are attempting to enroll elderly patients and patients taking concomitant medications that impact the heart, such as other calcium channel blockers and beta blockers. We are doing this in order to obtain efficacy and safety data on patients representing the subset of our intended population that is most vulnerable to safety concerns with the use of etripamil. 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 episodes of SVT 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 150 episodes confirmed to be SVT are treated. PSVT is episodic and unpredictable, and our Phase 3 trial design depends on patients experiencing and recognizing an episode of SVT, 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 SVT episodes for those patients that enroll in the trial. Conducting a Phase 3 clinical trial for a PSVT treatment in an at-home 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 an SVT 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 pharmacodynamic effect 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.

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 pandemics and public health emergencies, including those related to COVID-19 coronavirus, geopolitical actions, including war and terrorism or natural disasters including earthquakes, typhoons, floods and fires.

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

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

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

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

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

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

- decreased demand for any product candidate that we may develop;
- loss of revenue;
- substantial monetary awards to trial participants or patients;

- significant time and costs to defend the related litigation;
- withdrawal of clinical trial participants;
- increased insurance costs;
- the inability to commercialize any product candidate that we may develop; and injury to our reputation and significant negative media attention.

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

Risks Related to Regulatory Compliance

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

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

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

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

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

Such regulatory requirements may differ from country to country depending on where we have received regulatory approval.

In addition, drug manufacturers and their facilities are subject to payment of user fees and continual review and periodic inspections by the FDA and other regulatory authorities for compliance with cGMP requirements and adherence to commitments made in the NDA or foreign marketing application. If we, or a regulatory authority, discover previously unknown problems with a drug, such as adverse events of unanticipated severity or frequency, or problems with the facility where the drug is manufactured or if a regulatory authority disagrees with the promotion, marketing or labeling of that drug, a regulatory authority may impose restrictions relative to that drug, the manufacturing facility or us, including requesting a recall or requiring withdrawal of the drug from the market or suspension of manufacturing.

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

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

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

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

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

In addition, we cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. For example, certain policies of the Trump administration may impact our business and industry. Namely, the Trump administration has taken several

executive actions, including the issuance of a number of Executive Orders, that could impose significant burdens on, or otherwise materially delay, the FDA's ability to engage in routine regulatory and oversight activities such as implementing statutes through rulemaking, issuance of guidance, and review and approval of marketing applications. It is difficult to predict how these executive actions, including the Executive Orders, will be implemented and the extent to which they will affect the FDA's ability to exercise its regulatory authority. If these executive actions impose constraints on the FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted.

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

Healthcare providers, physicians and third-party payors in the United States and elsewhere will play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our current and future arrangements with healthcare professionals, principal investigators, consultants, customers and third-party payors subject us to various federal and state fraud and abuse laws, data privacy and security laws, transparency laws and other healthcare laws that may constrain the business or financial arrangements and relationships through which we research, sell, market, and distribute our products, if we obtain marketing approval.

The federal Anti-Kickback Statute prohibits the offer, receipt, or payment of remuneration in exchange for or to induce the referral of patients or the use of products or services that would be paid for in whole or part by Medicare, Medicaid or other federal healthcare programs. Remuneration has been broadly defined to include anything of value, including cash, improper discounts, and free or reduced price items and services. Additionally, the intent standard under the federal Anti-Kickback Statute was amended by the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively, PPACA, to a stricter standard such that a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. Further, PPACA codified case law 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 False Claims Act.

The federal false claims, including the False Claims Act, and civil monetary penalties laws, which prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, false or fraudulent claims for payment of federal funds, and knowingly making, or causing to be made, a false record or statement material to a false or fraudulent claim to avoid, decrease or conceal an obligation to pay money to the federal government.

The federal Health Information Insurance Portability and Accountability Act of 1996, or HIPAA, prohibits, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement, in connection with the delivery of, or payment for, healthcare benefits, items or services. Similar to the U.S. federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, also imposes, among other things, certain standards and obligations on covered entities including certain healthcare providers, health plans and healthcare clearinghouses, as well as their respective business associates that create, receive, maintain, or transmit individually identifiable health information for or on behalf of a covered entity relating to the privacy, security, transmission and breach reporting of individually identifiable health information.

The federal Physician Payments Sunshine Act, and its implementing regulations, require certain manufacturers of drugs, devices, biologics and medical supplies that are reimbursable under Medicare, Medicaid, or the Children's Health Insurance Program to report annually to Centers for Medicare & Medicaid Services information related to certain payments and other transfers of value to physicians, as defined by such law, and teaching hospitals, as well as ownership and investment interests held by the physicians described above and their immediate family members.

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.

Analogous state and foreign anti-kickback and false claims laws that may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third party payors, including private insurers, or that apply regardless of payor; 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 and local 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 the reporting of information related to drug pricing; state and local laws requiring the registration of pharmaceutical sales representatives; and state and foreign laws governing the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

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 PPACA, was passed, which substantially changed the way healthcare is financed by both governmental and private payors in the United States. There remain judicial and Congressional challenges to certain aspects of the PPACA as well as efforts by the Trump administration to repeal or replace certain aspects of the PPACA. 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." In addition, the 2020 federal spending package permanently eliminates, effective January 1, 2020, the PPACA-mandated "Cadillac" tax on high-cost employer-sponsored health coverage and medical device tax and, effective January 1, 2021, also eliminates the health insurer tax. 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. Additionally, on December 18, 2019, the U.S. Court of Appeals for the 5th Circuit upheld the District Court ruling that the individual mandate was unconstitutional and remanded the case back to the District Court to determine whether the remaining provisions of the PPACA are invalid as well. On March 2, 2020, the United States Supreme Court granted the petitions for writs of certiorari to review this case and has allotted one hour for oral arguments. It is unclear when such oral arguments are to be held and when a decision is expected to be made. It is unclear when such oral arguments are to be held and when a decision is expected to be made. It is also unclear how such litigation 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. At the federal level, the Trump administration's budget proposal for fiscal year 2020 contains further drug price control measures that could be enacted during the budget process or in other future legislation. In addition, 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 Department of Health and Human Services has solicited feedback on some of these measures and has implemented others under its existing authority. While some of these measures may 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. 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. We expect that additional U.S. healthcare reform measures will be adopted in the future, any of which could limit the amounts that the U.S. federal government will pay for healthcare products and services, which could result in reduced demand for etripamil or any future product candidates or additional pricing pressures.

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

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

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

Risks Related to Our Dependence on Third Parties

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

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

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

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

- inability to meet our product specifications and quality requirements consistently;
- delay or inability to procure or expand sufficient manufacturing capacity;
- issues related to scale-up of manufacturing;
- costs and validation of new equipment and facilities required for scale-up;
- our third-party manufacturers may not be able to execute our manufacturing procedures and other logistical support requirements appropriately;
- our third-party manufacturers may fail to comply with cGMP-compliance and other inspections by the FDA or other comparable regulatory authorities;
- our inability to negotiate manufacturing agreements with third parties under commercially reasonable terms, if at all;

- breach, termination or nonrenewal of manufacturing agreements with third parties in a manner or at a time that is costly or damaging to us;
- reliance on a single source for the nasal spray device;
- our third-party manufacturers may not devote sufficient resources to our product candidates;
- we may not own, or may have to share, the intellectual property rights to any improvements made by our third-party manufacturers in the manufacturing process for our product candidates;
- operations of our third-party manufacturers or suppliers could be disrupted by conditions unrelated to our business or operations, including the bankruptcy of the manufacturer or supplier; and carrier disruptions or increased costs that are beyond our control.

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

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

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

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

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

Our reliance on third parties to conduct clinical trials will result in less direct control over the management of data developed through clinical trials than would be the case if we were relying entirely upon our own staff. Any failure by third parties to prevent unauthorized access, use or disclosure of data, 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.

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.

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

Etripamil is administered through a nasal-spray device that we obtain from a single source supplier, and that supplier is relying on multiple component suppliers, 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 intra-nasal delivery system will be regulated as a drug/device combination product. 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 would 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. Further, failure to successfully develop or supply the device, or to gain or maintain its approval, could adversely affect sales of etripamil.

Risks Related to Our Intellectual Property

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

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

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

We may not be aware of all third-party intellectual property rights potentially relating to etripamil or any future product candidates. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in

some cases not at all. For example, U.S. applications filed before November 28, 2000 and certain U.S. applications filed after that date that will not be filed outside the United States remain confidential until a patent 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 pre-issuance 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 Chief Medical Officer, Francis Plat, our Chief Commercial Officer, Lorenz Muller and our Chief Financial Officer, Amit Hasija. Each of them may currently terminate their employment with us at any time. The loss of the services of any of these persons could impede the achievement of our research, development and commercialization objectives. We do not currently maintain "key person" life insurance on the lives of our executives or any of our employees other than on our President and Chief Executive Officer, Joseph Oliveto.

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

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

As of December 31, 2019, we had 30 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 are conducting clinical trial activities in Europe, which will subject us to European data protection laws, including GDPR. The GDPR, which came into effect on May 25, 2018, establishes new requirements applicable to the processing of personal data (i.e., data which identifies an individual or from which an individual is identifiable), affords new data protection rights to individuals (e.g., the right to erasure of personal data) and imposes penalties for serious breaches of up to 4% annual worldwide turnover or €20 million, whichever is greater. Individuals (e.g., study subjects) also have a right to compensation for financial or non-financial losses (e.g., distress). There may be circumstances under which a failure to comply with GDPR, or the exercise of individual rights under the GDPR, would limit our ability to utilize clinical trial data collected on certain subjects. The GDPR will likely impose additional responsibility and liability in relation to our processing of personal data. This may be onerous and materially adversely affect our business, financial condition, results of operations and prospects.

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

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

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

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

We actively search for and continually evaluate various acquisition and strategic collaboration opportunities, including licensing or acquiring complementary drugs, intellectual property rights, technologies or businesses, as deemed appropriate to carry out our business plan. Any potential acquisition or strategic partnership may entail numerous risks, including:

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

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

Risks Related to Ownership of Our Common Shares

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

The market price of our common shares has been and may continue to be highly volatile and could be subject to wide fluctuations in price in response to various factors, many of which are beyond our control. Since our initial public offering which occurred in May 2019, through March 1, 2020, the price of our common shares has ranged from $15.00 per share to $27.95 per share. The stock market in general and the market for biopharmaceutical and pharmaceutical companies in particular, has experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, you may not be able to sell your common shares at or above the price paid for the shares. In addition to the factors discussed in this "Risk Factors" section and elsewhere in this Annual Report on Form 10-K, 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.

Our common shares are thinly traded and our shareholders may be unable to sell their shares quickly or at market price.

Although we have had periods of high volume daily trading in our common shares, generally our shares are thinly traded. As a consequence of this lack of liquidity, the trading of relatively small quantities of shares by our shareholders may disproportionately influence the price of those shares in either direction. The price for our shares could, for example, decline significantly in the event that a large number of our common shares are sold on the market without commensurate demand, as compared to a seasoned issuer that could better absorb those sales without adverse impact on its share price.

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, 2019, our executive officers, directors and shareholders who owned more than 5% of our outstanding common shares, in the aggregate, beneficially owned shares representing 81.0% of our outstanding common shares. If our executive officers, directors and shareholders who owned more than 5% of our outstanding common shares acted together, they may be able to significantly influence all matters requiring shareholder approval, including the election and removal of directors and approval of any merger, consolidation or sale of all or substantially all of our assets. The concentration of voting power and transfer restrictions could delay or prevent an acquisition of our company on terms that other shareholders may desire or result in the management of our company in ways with which other shareholders disagree.

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

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

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

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

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

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

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

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 have been 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 expect that we may have been classified as a PFIC for our taxable year ending December 31, 2019. We have not yet made any determination as to our expected PFIC status for our taxable year ending December 31, 2020. If we are a PFIC for the current taxable year, 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. As a result, our PFIC status may change from year to year and we have not yet made any determination as to our expected PFIC status for the current year. Under the income test, our status as a PFIC depends on the composition of our income which will depend on the transactions we enter into in the future and our corporate structure. The composition of our income and assets is also affected by how, and how quickly, we spend the cash we raise in any offering.

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

A "U.S. Holder" is a holder who, for U.S. federal income tax purposes, 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.

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

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

year for which reporting was due. U.S. Holders should consult their tax advisors regarding the potential application of these rules to their investment in our common shares.

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

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

For example, the Tax Act enacted many significant changes to the U.S. tax laws. Future guidance from the Internal Revenue Service and other tax authorities with respect to the Tax Act may affect us, and certain aspects of the Tax Act could be repealed or modified in future legislation. In addition, it is uncertain if and to what extent various states will conform to the Tax Act or any newly enacted federal tax legislation. Changes in corporate tax rates, the realization of net deferred tax assets relating to our operations, the taxation of foreign earnings, and the deductibility of expenses under the Tax Act or future reform legislation could have a material impact on the value of our deferred tax assets, could result in significant one-time charges, and could increase our future U.S. tax expense. We urge you to consult with your legal and tax advisors with respect to this legislation and the potential tax consequences of investing in or holding our common shares.

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

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

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

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

- not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting;
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;

- reduced disclosure obligations regarding executive compensation; and
- not being required to hold a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved.

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

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

We are incurring, and expect to continue to incur additional 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 are incurring, and expect to continue to 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 need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations have increased, and will continue to increase, our legal and financial compliance costs and make some activities more time-consuming and costly.

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

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

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

In addition, it may be difficult to assert U.S. securities law claims in original actions instituted in Canada. Canadian courts may refuse to hear a claim based on an alleged violation of U.S. securities laws against us or these persons on the grounds that Canada is not the most appropriate forum in which to bring such a claim. Even if a Canadian court agrees to hear a claim, it may determine that Canadian law and not U.S. law is applicable to the claim. If U.S. law is found to be applicable, the content of applicable U.S. law must be proved as a fact, which can be a time-consuming and costly process. Certain matters of procedure will also be governed by Canadian law. Furthermore, it may not be possible to subject foreign persons or entities to the jurisdiction of the courts in Canada. Similarly, to the extent that our assets are located in Canada, investors may have difficulty collecting from us any judgments obtained in the U.S. courts and predicated on the civil liability provisions of U.S. securities provisions.

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

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

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

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

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

The *Investment Canada Act* requires that a non-Canadian must file an application for review with the Minister responsible for the *Investment Canada Act* and obtain approval of the Minister prior to acquiring control of a "Canadian business" within the meaning of the *Investment Canada Act*, where prescribed financial thresholds are exceeded. Furthermore, limitations on the ability to acquire and hold our common shares may be imposed by the *Competition Act* (Canada). This legislation permits the Commissioner of Competition, or Commissioner, to review any acquisition or establishment, directly or indirectly, including through the acquisition of shares, of control over or of a significant interest in our company. Otherwise, there are no limitations either under the laws of Canada or Quebec, or in our articles on the rights of non-Canadians to hold or vote our common shares.

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

ITEM 1B. UNRESOLVED STAFF COMMENTS.

None.

ITEM 2. PROPERTIES.

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.

ITEM 3. LEGAL PROCEEDINGS.

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

ITEM 4. MINE SAFETY DISCLOSURES.

Not applicable.

PART II

ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES.

MARKET INFORMATION

Our common stock began trading on The Nasdaq Global Select Market on May 9, 2019. Our common stock trades under the symbol "MIST". Prior to the commencement of trading on the Nasdaq Global Select Market on May 9, 2019, there was no public market for our common stock.

HOLDERS OF RECORD

As of December 31, 2019, there were 30 holders of record of our common shares, including Cede & Co., a nominee for The Depository Trust Company, or DTC, which holds shares of our common shares on behalf of an indeterminate number of beneficial owners. All of the common shares held by brokerage firms, banks and other financial institutions as nominees for beneficial owners are deposited into participant accounts at DTC, and are considered to be held of record by Cede & Co. as one shareholder. Because many of our shares are held by brokers and other institutions on behalf of stockholders, we are unable to estimate the total number of shareholders represented by these record holders.

Recent Sales of Unregistered Securities

From January 1, 2019 through May 9, 2019, the date of the filing of our registration statement on Form S-8 (File No. 333-231347), we issued and sold an aggregate of 18,150 common shares to our service providers and former service providers upon the exercise of stock option awards under our Stock Option Plan, or the 2011 Plan, at exercise prices ranging from $1.12 to $1.54 per share, for aggregate proceeds of $25 thousand.

From January 1, 2019 through May 9, 2019, the date of the filing of our registration statement on Form S-8 (File No. 333-231347), and pursuant the terms of the 2011 Plan, we granted to our service providers stock option awards to purchase an aggregate of 116,742 common shares, at an exercise price of $9.42 per share.

The offers, sales and issuances of the securities described in the preceding paragraphs were deemed to be exempt from registration under Rule 701 promulgated under the Securities Act, or Rule 701, in that the transactions were by an issuer not involving any public offering or under Section 4(a)(2) of the Securities Act or under compensatory benefit plans and contracts relating to compensation as provided under Rule 701. The recipients of such securities were our employees, directors or consultants and received the securities under our 2011 Plan. Appropriate legends were affixed to the securities issued in these transactions.

Use of Proceeds from Initial Public Offering of Common Stock

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

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

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

Purchase of Equity Securities by the Issuer and Affiliated Purchasers

None.

Securities Authorized for Issuance Under Equity Compensation Plans

Information about securities authorized for issuance under our equity compensation plan is incorporated herein by reference to Item 12 of Part III of this Annual Report on Form 10-K.

ITEM 6. SELECTED FINANCIAL DATA.

Not Applicable.

ITEM 7. 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 Annual Report on Form 10-K. 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 Annual Report on Form 10-K.

Overview

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

PSVT is a rapid heart rate condition characterized by episodes of supraventricular tachycardia, or SVT, that start and stop without warning. Episodes of SVT are 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. Calcium channel blockers available in oral form are frequently used prophylactically to control the frequency and duration of future episodes of SVT. For treatment of episodes of SVT, approved calcium channel blockers are administered intravenously under medical supervision, usually in the emergency department. The combination of convenient nasal-spray delivery, rapid-onset and short duration of action of etripamil has the potential to shift the current treatment paradigm for episodes of SVT away from the burdensome and costly emergency department setting. If approved, we believe that etripamil will be the first self-administered therapy for the rapid termination of episodes of SVT wherever and whenever they occur.

Our development program for etripamil for the treatment of PSVT consists of three Phase 3 clinical trials, one Phase 2 trial, and Phase 1 trials. We believe this clinical trial program, if successful, will be sufficient to support approval in the United States and the European Union.

NODE-301 is our ongoing, placebo-controlled Phase 3 safety and efficacy trial, which is being conducted in North America. NODE-301 may serve as a single pivotal efficacy trial required for approval by the US Food and Drug Administration, or FDA. The trial is being conducted in two parts. NODE-301A will continue until the trial's adjudication committee has evaluated data from the treatment of 150 SVT events with blinded study drug (etripamil or placebo). All pivotal efficacy analyses will be conducted on data from NODE-301A. NODE-301B will follow patients already enrolled in NODE-301 who did not take the study drug in NODE-301A. Data from NODE-301B will be analyzed as a pivotal safety and supportive efficacy data set, and will contribute to potentially valuable sub-population analyses and pharmaco-economic assessments. Following consultation with the FDA in 2019, we confirmed the two-part design, along with an increase in the sample size of NODE-301A from 100 to 150 adjudicated SVT events. The upsize of the trial satisfies a request from the European Medicines Agency, or EMA.

NODE-302 is our ongoing Phase 3 open-label safety extension trial. Patients who complete NODE-301 may enroll in NODE-302 and receive up to an additional 11 doses of etripamil. 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 SVT. All patients randomized in NODE-301 will be eligible for NODE-302. Patients who have successfully dosed with the study drug and completed a study closure visit will be eligible to enroll in NODE-302 to manage any subsequent episodes of SVT. 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 and the trial is ongoing. Trial safety results will contribute to the etripamil safety database.

NODE-303 is our ongoing Phase 3 open label safety trial, which is being conducted primarily in North America, Europe and Latin America. We designed NODE-303 to evaluate the safety of etripamil when self-administered without medical supervision, and to evaluate the treatment safety and efficacy of etripamil on multiple SVT episodes. The trial is designed to enroll up to 3,000 patients in order to collect data on approximately 1,000 patients taking etripamil in an at-home setting. A more accurate sizing of the trial will be determined once an overall size of the safety dataset is determined for NDA filing following future discussions with the FDA and other regulatory authorities. Based on a review of the NODE-301 safety data available in June 2019, the FDA and multiple European and Latin American regulatory authorities have agreed to allow patient enrollment in NODE-303 without an in-office safety test dose, which is a safeguard required in the NODE-301 trial, and in a broad patient population including patients taking concomitant beta-blockers and calcium channel blockers.

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 episodes of SVT within 15 minutes at the dose selected for our Phase 3 trials versus a 35% termination rate for placebo. We have also completed two Phase 1 clinical trials in healthy volunteers, characterizing the pharmacokinetics and pharmacodynamic effect of etripamil.

As with PSVT, calcium channel blockers are also approved for use in intravenous form for the treatment of some episodes of atrial fibrillation in which patients experience rapid ventricular rates. We plan to initiate in 2020 a Phase 2 proof-of-concept clinical trial in a controlled setting to evaluate the potential effectiveness of etripamil to reduce ventricular rate in atrial fibrillation patients who present to the clinic with rapid ventricular rate. The trial will enroll approximately 50 patients, randomized to etripamil 70 mg versus placebo, with a primary endpoint of reduction in ventricular rate.

As we generate more data on the safety and efficacy profile of etripamil in PSVT and atrial fibrillation with rapid ventricular rate, we will continue to assess whether etripamil could be developed to potentially fulfill other areas of unmet medical need.

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

Since inception, we have incurred significant operating losses. For the years ended December 31, 2019 and 2018, we recorded net losses of $53.7 million and $23.2 million, respectively. As of December 31, 2019, we had an accumulated deficit of $111.8 million. We expect to continue to incur significant losses for the foreseeable future. We anticipate that a substantial portion of our capital resources and efforts in the foreseeable future will be focused on completing the necessary development activities required for obtaining regulatory approval and preparing for potential commercialization of our product candidates.

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

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

- establish a sales, marketing, manufacturing and distribution capability, either directly or indirectly through third parties, to commercialize etripamil or any future product candidate for which we may obtain marketing approval;
- build a portfolio of product candidates through development, or the acquisition or in-license of drugs, product candidates or technologies;
- initiate preclinical studies and clinical trials for etripamil for any additional indications we may pursue, including the clinical trials for the treatment of atrial fibrillation with rapid ventricular rate 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.

Reverse Share Split

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

Initial Public Offering

On May 13, 2019, we completed our IPO, whereby we issued 5,500,000 common shares at a public offering price of $15.00 per share. The shares began trading on The Nasdaq Global Select Market on May 9, 2019. On May 15, 2019, the underwriters fully exercised their option to purchase an additional 825,000 common shares at the public offering price of $15.00 per share. We received net proceeds from the IPO and the over-allotment exercise of $85.4 million, after deducting underwriting discounts and commissions and other offering expenses. Upon the closing of the IPO, 24,490,742 common shares were outstanding, which included all outstanding shares of our preferred shares that converted into 17,550,802 common shares.

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 with rapid ventricular rate 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, 2019 and 2018.

(in thousands)	Year Ended December 31, 2019	2018
Clinical and pre-clinical	$ 34,360	$ 12,546
Drug manufacturing and formulation	5,950	3,320
Regulatory and other costs	2,067	1,240
Less: investment tax credits	(392)	(257)
Total research and development expenses	$ 41,985	$ 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. 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 increase our administrative headcount significantly as we advance etripamil and any future product candidates through clinical development, which will also increase our general and administrative expenses.

Commercial Expenses

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

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

Interest Income

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

Results of Operations

Comparison of the Years Ended December 31, 2019 and 2018

The following table summarizes our results of operations:

(in thousands)	Year ended December 31, 2019	2018	$Change	% Change
Operating expenses				
Research and development, net of tax credits	41,985	16,849	25,136	149 %
General and administrative	7,004	3,052	3,952	129 %
Commercial	8,892	3,921	4,971	127 %
Total operating expenses	57,881	23,822	34,059	143 %
Loss from operations	(57,881)	(23,822)	(34,059)	143 %
Interest income, net of bank charges	2,596	711	1,885	265 %
Loss and comprehensive loss before income taxes	(55,285)	(23,111)	(32,174)	139 %
Income tax (recovery) expense	(56)	74	(130)	(176)%
Net loss and comprehensive loss	(55,229)	(23,185)	(32,044)	138 %

Research and Development Expenses

Research and development,or R&D expenses increased by $25.1 million, or 149%, for the year ended December 31, 2019 compared to the year ended December 31, 2018. Spending during 2019 was primarily related to advancing our Phase 3 efficacy and safety trials in etripamil for the treatment of PSVT and increases in headcount related expenses to support the trials and activities important for regulatory approvals. We spent $28.8 million on these programs in 2019 and $9.1 million in 2018. We recorded personnel and related R&D costs of $13.5 million for 2019 and $8.0 million in 2018. We also recognized $0.4 million and $0.3 million of R&D investment tax credits provided by the provincial government of Québec for the years ended December 31, 2019 and December 31, 2018, respectively. Tax credits are recorded as a reduction of our R&D expenses.

General and Administrative Expenses

General and administrative expenses increased by $4.0 million, or 129% for the year ended December 31, 2019 compared to the year ended December 31, 2018. During 2019, we increased our administrative headcount and, as a result, compensation and related personnel costs increased when compared to 2018. In addition, we incurred increased spending for consulting fees, recruiting fees and professional fees, including legal and accounting services incurred to support our IPO. Following the IPO, insurance costs increased in the second quarter of 2019 to support risk management activities as a public company.

Commercial Expenses

Commercial expenses increased by $5.0 million, or 127%, for the year ended December 31, 2019 when compared to 2018. During this period, commercial expenses reflect increased commercial headcount and related costs, increase in additional commercial and market research, increases in the scope of our patient engagement activities, and costs of a medical affairs team focused on engaging key opinion leaders' and raising disease awareness.

Interest Income, Net

Interest income, net of bank charges was $2.6 million and $0.7 million for the years ended December 31, 2019 and 2018, respectively. The increase in 2019 reflects increased earnings on cash and cash equivalents to the proceeds from the October 2018 Series D preferred share financing and the net cash proceeds from the IPO and over-allotment exercised in May 2019.

Net Loss

For the foregoing reasons, we had net losses of $55.2 million and $23.2 million for the years ended December 31, 2019 and 2018, respectively.

Liquidity and Capital Resources

Sources of Liquidity

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

We have incurred operating losses and experienced negative operating cash flows since our inception and anticipate that we will continue to incur losses for at least the next several years. As of December 31, 2019, we had $119.8 million cash & cash equivalents and short-term investments of NIL and an accumulated deficit of $113.5 million.

Based on our current operating plan, we expect our existing cash, cash equivalents and short-term investments will be sufficient to fund our operations for at least the next 12 months based on our most recent forecast.

Funding Requirements

We use our cash primarily to fund research and development expenditures. We expect to incur an increase in research and development expenses as well as general and administrative expenses and commercial activities as our R&D progresses. We expect to incur increasing operating losses for the foreseeable future as we continue the clinical development of our product candidate. At this time, due to the inherently unpredictable nature of clinical development, we cannot reasonably estimate the costs we will incur and the timelines that will be required to complete development, obtain marketing approval, and commercialize etripamil or any future product candidates, if at all. For the same reasons, we are also unable to predict when, if ever, we will generate revenue from product sales or whether, or when, if ever, we may achieve profitability. Clinical and preclinical development timelines, the probability of success, and development costs can differ materially from expectations.

In addition, we have exclusive development and commercialization rights for etripamil for all indications that we may pursue and as such have the potential to license development and or commercialization rights for etripamil to a potential partner. We plan to establish commercialization and marketing capabilities using a direct sales force to commercialize etripamil in the United States. Outside of the United States, we are considering commercialization strategies that may include collaborations with other companies. For other new product candidates, our efforts are focused on licensing development and/or commercialization rights from potential partners. In the case of either in-licensing or out-licensing, we cannot forecast when such arrangements will be secured, if at all, and to what degree such arrangements would affect our development and commercialization plans and capital requirements.

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

- the timing, progress and results of our ongoing and planned clinical trials and other development activities of etripamil in PSVT and in other cardiovascular indications;
- the scope, progress, results and costs of preclinical development, laboratory testing and clinical trials of etripamil for additional indications or any future product candidates that we may pursue;
- our ability to establish collaborations on favorable terms, if at all;
- the ability of vendors and third-party service providers to accurately forecast expenses and deliver on expectations;

- the costs, timing and outcome of regulatory review of etripamil and any future product candidates;
- the costs and timing of future commercialization activities, including product manufacturing, marketing, sales and distribution, for etripamil and any future product candidates for which we receive marketing approval;
- the revenue, if any, received from commercial sales of etripamil and any future product candidates for which we receive marketing approval;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims; and
- the extent to which we acquire or in-license other product candidates and technologies.

Until such time, if ever, as we can generate substantial revenue from product sales, we expect to fund our operations and capital funding needs through equity and/or debt financing. We may also consider entering into collaboration arrangements 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)	**2019**	**2018**	**$ Change**	**% Change**
Net cash (used in) provided by:				
Operating activities	(51,152)	(21,046)	(30,106)	143.05 %
Investing activities	(384)	15,998	(16,382)	(102.40)%
Financing activities	85,407	80,115	5,292	6.61 %
Net increase (decrease) in cash and cash equivalents during the period	33,871	75,067	(41,196)	

Operating Activities

In 2019, we used $51.2 million of cash in operating activities, which consisted of a net loss of $55.2 million offset by a net change of $2.9 million in our net operating assets and non-cash charges of $1.2 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 increase of $3.5 million for accounts payable, a net decrease of $0.2 million for research and development tax credits, interest and sales tax receivable and offset by an increase of $0.5 million for prepaid expenses.

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.

Investing Activities

For the year ended December 31, 2019, there was a net use of cash of $0.4 million mainly related to cash used for the acquisition of property and equipment. Short-term investment acquisitions used $35.0 million in cash and provided the same amount of redemptions leaving a balance of nil in short-term investments.

For the year ended December 31, 2018, our investing activities provided $16.0 million of cash due to the redemption of approximately net $16.0 million of short-term investments that we had acquired during the year ended December 31, 2017.

Financing Activities

In 2019, the IPO and the exercise by the underwriters of their option to purchase additional common shares provided a net cash consideration of $85.4 million. 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. Additionally, in the years ended December 31, 2019 and 2018, exercise of share options provided $44 thousand and $461 thousand, respectively.

Off-Balance Sheet Arrangements

We have not entered into any off-balance sheet arrangements, as defined in the rules and regulations of the Securities and Exchange Commission.

Contractual Obligations

We enter into contracts in the normal course of business with clinical research organizations (CRO), contract manufacturing organizations (CMO) 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 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 audited consolidated financial statements as at December 31, 2019, which have been prepared in accordance with United States generally accepted accounting principles, or U.S. GAAP and on a basis consistent with those accounting principles followed by us. The preparation of these audited consolidated financial statements requires our management to make judgments and estimates that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements, as well as the reported revenue generated and expenses incurred during the reporting periods. Our estimates are based on our historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Significant estimates and judgments include, but are not limited to, research and development tax credits recoverable, research and development expenses, and share-based compensation. Accordingly, actual results may differ from these judgments and estimates under different assumptions or conditions and any such differences may be material. We believe that the accounting policies discussed below are critical to understanding our historical and future performance, as these policies relate to the more significant areas involving management's judgments and estimates.

Effective January 1, 2019, the company adopted ASC Topic 842, and changed the manner in which it accounts for leases under the new standard. For a description of this critical accounting policy and the impact of the change, see Note 3 of the consolidated financial statements.

a) 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.

b) Leases

Effective January 1, 2019, the Company adopted ASC 842, Leases (ASC 842), using the required modified retrospective approach and utilizing the effective date as its date of initial application. As a result, prior periods are presented in accordance with the previous guidance in ASC 840, Leases (“ASC 840”).

At the inception of an arrangement, the Company determines whether the arrangement is or contains a lease based on the unique facts and circumstances present in the arrangement. Leases with a term greater than one year are recognized on the balance sheet as right-of-use assets and short-term and long-term lease liabilities, as applicable. The Company does not have financing leases.

Operating lease liabilities and their corresponding right-of-use assets are initially recorded based on the present value of lease payments over the expected remaining lease term. Certain adjustments to the right-of-use asset may be required for items such as incentives received. The interest rate implicit in lease contracts is typically not readily determinable. As a result, the Company utilizes its incremental borrowing rate to discount lease payments, which reflects the fixed rate at which the Company could borrow on a collateralized basis the amount of the lease payments in the same currency, for a similar term, in a similar economic environment. Prospectively, the Company will adjust the right-of-use assets for straight-line rent expense or any incentives received and remeasure the lease liability at the net present value using the same incremental borrowing rate that was in effect as of the lease commencement or transition date.

The Company has elected not to recognize leases with an original term of one year or less on the balance sheet. The Company typically only includes an initial lease term in its assessment of a lease arrangement. Options to renew a lease are not included in the Company’s assessment unless there is reasonable certainty that the Company will renew.

c) Share-Based Compensation

We recognize compensation costs related to share options granted to employees, consultants and directors based on the estimated fair value of the awards on the date of grant. We estimate the grant date fair value, and the resulting share-based compensation expense, using the Black-Scholes option-pricing model. This Black-Scholes option pricing model uses various inputs to measure fair value, including estimated fair value of our underlying common shares at the grant date, expected term, estimated volatility, risk-free interest rate and expected dividend yields of our common shares.

The 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.

As there had been no public market for our common shares prior to May 13, 2019, 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. Following the completion of our initial public offering on May 13, 2019, we have determined 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, 2018 and 2019:

	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
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
February 18, 2019	31,018	$ 9.415	$ 9.415	$ 6.655
March 9, 2019	33,086	$ 9.415	$ 9.415	$ 6.644
March 20, 2019	52,638	$ 9.415	$ 9.415	$ 6.714
May 8, 2019	46,998	$ 15.000	$ 15.000	$ 10.773
August 8, 2019	23,620	$ 15.870	$ 15.870	$ 11.125
September 9, 2019	167,000	$ 22.450	$ 22.450	$ 15.623
September 16, 2019	3,760	$ 21.280	$ 21.280	$ 14.851
October 31, 2019	3,760	$ 19.140	$ 19.140	$ 13.305
November 12, 2019	42,000	$ 17.780	$ 17.780	$ 12.160

The intrinsic value of all outstanding options as of December 31, 2019 was $32.7 million, based on the fair value of our common shares of $16.01 per share at December 31, 2019, of which approximately $17.4 million related to vested options and approximately $15.5 million related to unvested options.

Recent Accounting Prononcements

Refer to Note 2, "Summary of Significant Accounting Policies," in the accompanying notes to our audited consolidated financial statements 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 comply with new or revised accounting standards when they are required to be adopted by public companies that are not emerging growth companies.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK.

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 $119.8 million and $86.0 million as of December 31, 2019 and 2018, 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, 2019 and 2018, our net monetary exposure denominated in Canadian dollars was $1.5 million and $0.3 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.

ITEM 8. FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

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

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Milestone Pharmaceuticals Inc. and its subsidiary (together, the Company) as of December 31, 2019 and 2018, and the related consolidated statements of loss and comprehensive loss, of shareholders' equity (deficit) and convertible preferred shares and of 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 December 31, 2019 and 2018, 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.

Change in Accounting Principle

As discussed in Note 3 to the consolidated financial statements, the Company changed the manner in which it accounts for leases in 2019.

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 audits. 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. 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
March 5, 2020

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

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

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

	December 31, 2019	December 31, 2018
Assets		
Current assets		
Cash and cash equivalents	$ 119,818	$ 85,947
Short-term investments	—	29
Research and development tax credits receivable	578	290
Prepaid expenses	1,845	1,398
Other receivables	258	387
Total current assets	122,499	88,051
Operating lease right-of-use assets (note 3)	524	—
Property and equipment (note 4)	405	30
Total assets	$ 123,428	$ 88,081
Liabilities		
Current liabilities		
Accounts payable and accrued liabilities (note 5)	$ 7,997	$ 4,477
Current portion of operating lease liabilities (note 3)	330	—
Income taxes payable	—	56
Total current liabilities	8,327	4,533
Operating lease liabilities (note 3)	184	—
Total liabilities	8,511	4,533
Convertible Preferred Shares (notes 1 and 6)	—	138,758
Shareholders' Equity (Deficit) (notes 1 and 7)		
Share capital		
Common shares, no par value, unlimited shares authorized, 24,505,748 shares issued and outstanding as of December 31, 2019, 596,787 shares issued and outstanding as of December 31, 2018	226,245	2,039
Additional paid-in capital	3,805	2,655
Cumulative translation adjustment	(1,634)	(1,634)
Accumulated deficit	(113,499)	(58,270)
Total shareholders' equity (deficit)	114,917	(55,210)
Total liabilities, convertible preferred shares and shareholders' equity (deficit)	$ 123,428	$ 88,081

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,	
	2019	**2018**
Operating expenses		
Research and development, net of tax credits (note 8)	$ 41,985	$ 16,849
General and administrative	7,004	3,052
Commercial	8,892	3,921
Loss from operations	(57,881)	(23,822)
Interest income, net of bank charges	2,596	711
Loss and comprehensive loss before income taxes	(55,285)	(23,111)
Income tax (recovery) expense (note 9)	(56)	74
Net loss and comprehensive loss for the period	$ (55,229)	$ (23,185)
Weighted average number of shares outstanding, basic and diluted (note 1)	15,784,750	319,202
Net loss per share, basic and diluted (note 8)	$ 3.50	$ 72.63

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

Milestone Pharmaceuticals Inc.
Consolidated Statements of Shareholders' Equity (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	Total
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)	$ 25,98
Transactions in 2018																		
Net loss and comprehensive loss	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	(23,185)	(23,18
Issuance of Class D1 preferred shares, net of share issuance costs	—	—	—	—	—	—	—	—	—	—	6,893,236	64,719	—	—	—	—	—	64,71
Issuance of Class D2 preferred shares, net of share issuance costs	—	—	—	—	—	—	—	—	—	—	—	—	1,223,656	14,935		—	—	14,93
Exercise of stock options (note 7)	356,797	811	—	—	—	—	—	—	—	—	—	—	—	—	(350)	—	—	46
Share-based compensation (note 7)	—	—	—	—	—	—	—	—	—	—	—	—	—	—	633	—	—	63
Balance at December 31, 2018	596,787	$ 2,039	372,211	$ 2,027	2,443,914	$ 12,643	2,830,907	$ 17,198	3,786,878	$ 27,236	6,893,236	64,719	1,223,656	14,935	$ 2,655	$ (1,634)	— (58,270)	$ 83,54
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)	$ 83,54
Transactions in 2019																		
Net loss and comprehensive loss	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	(55,229)	(55,22
Exercise of stock options (note 7)	33,159	85	—	—	—	—	—	—	—	—	—	—	—	—	(41)	—	—	4
Share-based compensation (note 7)	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1,191	—	—	1,19
Inital public offering (note 7)	6,325,000	85,363	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	85,36
Preferred share conversion (note 7)	17,550,802	138,758	(372,211)	(2,027)	(2,443,914)	(12,643)	(2,830,907)	(17,198)	(3,786,878)	(27,236)	(6,893,236)	(64,719)	(1,223,656)	(14,935)	—	—	—	–
Balance as of December 31, 2019	24,505,748	$226,245	—	$ —	—	$ —	—	$ —	—	$ —	—	$ —	—	$ —	$ 3,805	$ (1,634)	$ (113,499)	$114,91

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)

	Year ended December 31,	
	2019	2018
Cash flows from		
Operating activities		
Net loss for the year	$ (55,229)	$ (23,185)
Adjustments to reconcile net loss to net cash used in operating activities:		
Amortization of property and equipment (note 4)	38	10
Share-based compensation expense (note 7)	1,191	633
Changes in operating assets and liabilities:		
Other receivables	119	(271)
Research and development tax credits receivable	(288)	137
Prepaid expenses	(447)	(1,298)
Accounts payable and accrued liabilities	3,520	2,876
Income taxes payable (receivable)	(56)	52
Net cash used in operating activities	(51,152)	(21,046)
Investing activities		
Acquisition of property and equipment	(413)	(5)
Acquisition of short-term investments	(35,000)	(3,029)
Redemption of short-term investments	35,029	19,032
Net cash (used in) provided by investing activities	(384)	15,998
Financing activities		
Issuance of Class D1 preferred shares	—	64,719
Issuance of Class D2 preferred shares	—	14,935
Net proceeds from issuance of common shares in Initial Public Offering (note 7)	85,363	—
Issuance of common shares on exercise of share options (note 7)	44	461
Net cash provided by financing activities	85,407	80,115
Net increase in cash and cash equivalents during the year	33,871	75,067
Cash and cash equivalents – Beginning of year	85,947	10,880
Cash and cash equivalents – End of year	$ 119,818	$ 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 biopharmaceutical company incorporated under the Business Corporations Act of Québec. Milestone is focused on the development and commercialization of innovative cardiovascular medicines. Milestone's lead product candidate, etripamil, is a novel, potent short-acting calcium channel blocker that the Company designed and is developing as a rapid-onset nasal spray to be self-administered by patients. The Company is developing etripamil to treat paroxysmal supraventricular tachycardia, atrial fibrillation, and other cardiovascular indications.

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

a) Basis of consolidation

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

b) Basis of presentation and use of accounting estimates

These consolidated financial statements of the Company have been presented in United States dollars (USD) and have been prepared in accordance with accounting principles generally accepted in the United States of America (U.S. GAAP), including the applicable rules and regulations of the Securities and Exchange Commission (SEC) regarding financial reporting.

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.

c) Segment information

The Company manages its operations as a single operating segment for the purposes of assessing performance and making operating decisions while focusing on the development and commercialization of innovative cardiovascular medicines.

d) 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.

e) 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.

f) 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.

g) 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.

h) 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

i) Leases

Effective January 1, 2019, the Company adopted ASC 842, Leases (ASC 842), using the required modified retrospective approach and utilizing the effective date as its date of initial application. As a result, prior periods are presented in accordance with the previous guidance in ASC 840, Leases (“ASC 840”).

At the inception of an arrangement, the Company determines whether the arrangement is or contains a lease based on the unique facts and circumstances present in the arrangement. Leases with a term greater than one year are recognized on the balance sheet as right-of-use assets and short-term and long-term lease liabilities, as applicable. The Company does not have financing leases.

Operating lease liabilities and their corresponding right-of-use assets are initially recorded based on the present value of lease payments over the expected remaining lease term. Certain adjustments to the right-of-use asset may be required for items such as incentives received. The interest rate implicit in lease contracts is typically not readily determinable. As a result, the Company utilizes its incremental borrowing rate to discount lease payments, which reflects the fixed rate at which the Company could borrow on a collateralized basis the amount of the lease payments in the same currency, for a similar term, in a similar economic environment. Prospectively, the Company will adjust the right-of-use assets for

straight-line rent expense or any incentives received and remeasure the lease liability at the net present value using the same incremental borrowing rate that was in effect as of the lease commencement or transition date.

The Company has elected not to recognize leases with an original term of one year or less on the balance sheet. The Company typically only includes an initial lease term in its assessment of a lease arrangement. Options to renew a lease are not included in the Company's assessment unless there is reasonable certainty that the Company will renew.

j) Share issuance costs

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

k) 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.

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.

l) 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.

m) Foreign currency translation and transactions

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.

n) Share based compensation

The Company has a share based compensation plan which is described in detail in note 7 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.

The Company approved an employee share purchase plan in April 2019, which became effective on May 8, 2019 and is described in detail in note 7. The plan provides a means by which eligible employees of the company and certain designated companies may be given an opportunity to purchase common shares. the plan permits the company to grant a series of purchase rights to eligible employees under an employee stock purchase plan.

o) 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.

p) Recent accounting pronouncement not yet adopted

In August 2018, the FASB issued Accounting Standard Update No. 2018-13, Changes to Disclosure Requirements for Fair Value Measurements (Topic 820) (ASU 2018-13), which improved the effectiveness of disclosure requirements for recurring and nonrecurring fair value measurements. The standard removes, modifies, and adds certain disclosure requirements. The adoption of this standard is not expected to have a material impact on the Company's consolidated financial statements and related disclosures.

In June 2016, the FASB issued ASU 2016-13, Financial Instruments - Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments ("ASU 2016-13"). ASU 2016-13 significantly changes the impairment model for most financial assets and certain other instruments. ASU 2016-13 will require immediate recognition of estimated credit losses expected to occur over the remaining life of many financial assets, which will generally result in earlier recognition of allowances for credit losses on loans and other financial instruments. ASU 2016-13 is effective for the Company's fiscal year beginning December 1, 2020 and subsequent interim periods. The adoption of this standard is not expected to have a material impact on the Company's consolidated financial statements and related disclosures.

q) Recently adopted accounting pronouncements

On January 1, 2019, we adopted Accounting Standards Update No. 2016-02, Leases (Topic 842) (ASU 2016-02) using the modified retrospective transition approach by applying the new standard to all leases existing at the date of initial application. Results and disclosure requirements for reporting periods beginning after January 1, 2019 are presented under Topic 842, while prior period amounts have not been adjusted and continue to be reported in accordance with our historical accounting under Topic 840. Adoption of this standard resulted in the recording of an operating lease right-of-use asset and corresponding operating lease liabilities of $0.3 million, for its headquarters located in Montréal (Québec), Canada. The Company's consolidated balance sheet beginning on January 1, 2019 are presented under the new guidance, while prior year amount was not adjusted and continue to be reported in accordance with previous guidance. This lease consisted of a 36-month period lease commencing December 1, 2017 and ending on November 30, 2020 for its office located in Montréal (Québec), Canada. It includes the possibility for the lessee to renew the term of the lease for a

further 36-month period beginning December 1, 2020 and ending November 30, 2023. Operating lease right-of-use asset and operating lease liabilities are recognized upon the adoption date based on the present value of lease payments over the remaining lease term. The company was not reasonably certain of renewing the lease following the initial term and recognized the right-of-use asset and operating lease liabilities over the remaining lease term.

The Company did not record an operating lease right-of-use asset and corresponding lease liability for leases with an initial term of twelve months or less and recognizes lease expense for these leases as incurred over the lease term. Upon adoption date, the Company had only one operating lease with a remaining term of less than 12 months for its offices located in Charlotte, NC, which had a termination date of July 31, 2019, and for which the Company was not reasonably certain of renewing the lease. The lease was extended for two months and terminated in September 2019.

The Company does not have a public credit rating and carries no debt. As such, several factors were considered in the determination of its incremental borrowing rate used in determining the present value of lease payments. The Company examined the Bloomberg credit ratings for similar companies; assumed equivalency between the Canadian and US markets for collateralized debt; factored in the cumulative dividend rate on convertible preferred shares; and used short-term rates based on the remaining lease term of 23 months upon the standard adoption on January 1, 2019 and on 36 months for the new lease agreement entered into in September 2019. This resulted in an incremental borrowing rate of 8%. Lease expenses are recognized on a straight-line basis over the lease term, which is accomplished by increasing the amortization of the right-of-use asset as interest expense on the lease liability declines over the lease term. The Company’s lease arrangements do not have lease and non-lease components which are accounted for separately. The adoption of the accounting standard did not materially impact the Company’s consolidated statement of operations or its consolidated statement of cash flow for the twelve months ended December 31, 2019.

3 Leases

On June 3, 2019, the Company entered into a new lease arrangement for a three-year term for its office located in Charlotte, NC. The Company recognized the operating lease right-of-use asset and operating lease liabilities at the lease commencement date on September 10, 2019. This resulted in an incremental borrowing rate of 8%. Lease expenses are recognized on a straight-line basis over the lease term, which is accomplished by increasing the amortization of the right-of-use asset as interest expense on the lease liability declines over the lease term. The company was not reasonably certain of renewing the lease following the initial term and recognized the right-of-use asset and operating lease liabilities over the 36-month period ending September 30, 2022.

The Company's two operating leases right-of-use assets are as follows as at December 31, 2019:

Right-of-use adoption date of January 1, 2019	$ 321
New operating lease right-of-use asset	401
Amortization of right-of-use asset during the year ending December 31, 2019	(198)
	$ 524

Operating lease expenses of $277 are included in general and administrative operating expenses in the consolidated statement loss and comprehensive loss, and within operating activities in the statement of cash flows for the twelve-month period ended December 31, 2019, and are comprised of two operating lease right-of-use assets and one operating lease of less than 12 months.

The following table summarizes the future minimum lease payments of right-of-use assets operating lease as at December 31, 2019:

January 1, 2020 to December 31, 2020	$ 354
January 1, 2021 to December 31, 2021	117
January 1, 2022 to December 31, 2022	80
	551
Less interest	(37)
	$ 514

As at December 31, 2018 in accordance with ASC 840, the Company had a lease commitment for its headquarters located in Montréal (Québec), Canada, 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, which had a termination date of July 31, 2019. The minimum lease payments as at December 31, 2018 were as follows:

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

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

4 Property and equipment

Property and equipment consist of the following at December 31:

	2019	2018
Computer hardware and software	$ 22	$ 9
Office equipment	406	28
Leasehold improvements	26	4
Total	$ 454	$ 41
Less accumulated depreciation and amortization	(49)	(11)
Property and equipment, net	$ 405	$ 30

During the year ended December 31, 2019 and December 31, 2018, the Company did not record any write off. For the year ended December 31, 2019, amortization expense was $38 (in 2018, amortization expense was $10) and was included in research and development expense.

5 Accounts payable and accrued liabilities

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

	2019	2018
Trade accounts payable	$ 4,376	$ 2,603
Accrued research and development liabilities	1,513	1,012
Other accrued liabilities	331	164
Accrued compensation and benefits payable	1,777	698
	$ 7,997	$ 4,477

6 Convertible preferred shares

In May 2019, the Company completed its initial public offering ("IPO"). Upon the closing of the IPO, all outstanding redeemable convertible preferred shares of Class A1, A2, B, C, D1 and D2 (collectively known as “Convertible Preferred Shares”) converted into 17,550,802 common shares.

Prior to converting to common shares in May 2019, the Company’s convertible preferred shares allowed the holders to redeem their shares upon a change in control in the Company. As a result, the Company classified its Convertible Preferred Shares as mezzanine equity. The Company charged specific incremental issuance costs incurred in the offering of Convertible Preferred Shares against the gross proceeds of the Convertible Preferred Shares.

Prior to May 2019, an authorized unlimited number of:

- Class A1 preferred shares, voting based on the number of common shares into which they could have been 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 were 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

- Class A2 preferred shares, voting based on the number of common shares into which they could have been 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 were eligible to their pro rata shares, on an as-converted basis, to any dividend paid on common shares. The Class A2 preferred shares were 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

- Class B preferred shares, voting based on the number of common shares into which they could have been 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 were eligible to their pro rata shares, on an as-converted basis, to any dividend paid on common shares. The Class B preferred shares were subject to a weighted average antidilution adjustment in the event of a common share issuance at a price per share lower than $6.1172

- Class C preferred shares, voting based on the number of common shares into which they could have been 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 were eligible to their pro rata shares, on an as-converted basis, to any dividend paid on common shares. The Class C preferred shares were subject to a weighted average antidilution adjustment in the event of a common share issuance at a price per share lower than $7.2619

- Class D1 preferred shares, voting based on the number of common shares into which they could have been 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 were 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 were subject to a weighted average antidilution adjustment in the event of a common share issuance at a price per share lower than $9.4295.

- Class D2 preferred shares, voting based on the number of common shares into which they could have been 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 were 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 were 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 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 would have 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 conversion rate of Class A1, A2, B, C, D1 and D2 preferred shares into common shares at the time of conversion was 1:1.

The holders of the Company’s Convertible Preferred Shares were 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 holders of the Convertible Preferred Shares also were entitled to participate pro rata in any dividends paid to the holders of the common shares on an as-converted basis. The Board of Directors had not declared any dividends as of May 2019 when the Preferred Shares were converted and therefore no dividends were paid.

Upon the liquidation of the Company, the holders of Convertible Preferred Stock were entitled to receive, in preference to the holders of the common stock and in order of priority, an 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 would have been 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, could have required 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 would have been the higher of the liquidation preference or the fair market value of such preferred shares. Class A1 preferred shares could have been only redeemed once Class A2, B, C, D1 and D2 preferred shares were fully redeemed.

For the year ended December 31, 2018, the Company issued the following Convertible Preferred Shares:

a) 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.

b) 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.

No convertible preferred shares were issued for the year ended December 31, 2019. All preferred shares were converted to common share upon closing of the IPO in May 2019.

7 Shareholders’ equity (deficit)

Authorized share capital

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

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

The Company's board of directors adopted and its shareholders approved the 2019 Employee Share Purchase Plan ("ESPP") in April 2019, which became effective on May 8, 2019. The number of common shares initially reserved for issuance under the ESPP was 278,734 common shares. The number of shares reserved for issuance will automatically increase on January 1 of each calendar year, beginning on January 1, 2020 through January 1, 2029, by the lesser of (1) 1% of the total number of shares of the Company's share capital outstanding on the last day of the calendar month before the date of the automatic increase and (2) 487,837 shares; provided that before the date of any such increase, the Company's board of directors may determine that such increase will be less than the amount set forth in clauses (1) and

(2). As of December 31, 2019, no common shares have been issued under the ESPP. The first offering period has not yet been decided by the Company's board of directors.

During the year ended December 31, 2019, the Company issued a total of 33,162 common shares (in 2018, 356,797) for a total cash consideration of $44 (in 2018, $461) pursuant to the exercise of 33,162 stock options (in 2018, 356,797) at an average exercise price of $1.326 per option (in 2018, $1.287 per option). As a result, an amount of $41 (in 2018, $350) 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

	2019	2018
Opening balance	$ 2,655	$ 2,372
Share-based compensation expense	1,191	633
Exercise of stock options	(41)	(350)
Closing balance	$ 3,805	$ 2,655

Share-based compensation

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

On October 15, 2018, the Company amended for a third time and restated the 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 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.

The 2011 Plan was terminated as of May 8, 2019 and a total of 2,364,526 options are outstanding at December 31, 2019.

As of December 31, 2019, there were 2,316,933 options available for awards under the 2019 Plan, of which 287,138 options were granted and 66,998 forfeited, leaving 2,096,793 available for future grant. The outstanding and exercisable options at December 31 were as follows:

	2019				2018	
	Number of shares			Weighted average exercise price	Number of shares	Weighted average exercise price
	2019 Plan	2011 Plan	Total		2011 Plan	
Outstanding at beginning of period	—	2,295,045	2,295,045	$ 1.771	968,782	$ 1.133
Granted - 2011 Plan	—	116,742	116,742	9.417	1,695,258	2.037
Granted - 2019 Plan	287,138	—	287,138	19.948	—	—
Exercised - 2011	—	(33,162)	(33,162)	1.326	(356,797)	1.287
Forfeited - 2011	—	(14,099)	(14,099)	2.660	(12,198)	1.096
Forfeited - 2019	(66,998)	—	(66,998)	17.224	—	—
Outstanding - 12/31/2019	220,140	2,364,526	2,584,666	$ 3.755	2,295,045	$ 1.771
Outstanding - 12/31/2019 - Weighted average exercise price	$ 20.777	$ 2.151				
Exercisable at end of period	1,165	1,212,226	1,213,391	$ 1.652	588,817	$ 1.314
Exercisable at end of period - Weighted average exercise price	$ 17.780	$ 1.637				

As of December 31, 2019, the weighted average remaining contractual life was 7.8 years (for 2018, 8.6 years). The weighted average remaining contractual life was 7.0 years for vested options (for 2018, 6.6 years). For the year ended December 31, 2019, 14,099 options and 66,998 options were forfeited under the 2011 Plan and the 2019 Plan, respectively, amounting to a total of 81,097 options forfeited in 2019 (for 2018, 12,198).

Options granted are valued using the Black-Scholes option pricing model. Amortization of the fair value of the options over vesting years has been expensed and credited to additional paid-in capital in shareholders' deficit. The weighted average fair values of options granted in 2019 was $6.649 for the 2011 Plan and $13.912 for the 2019 plan (in 2018 for the 2011 Plan, $1.463). Share-based compensation expense recognized for the year ended December 31, 2019 was $1,191 (in 2018, $633).

As of December 31, 2019, there was $6,464 (for 2018, $2,402) of total unrecognized compensation cost, related to non-vested share options, which is expected to be recognized over a remaining weighted average vesting period of 2.6 years (for 2018, 3.1 years).

	2019				2018	
	Number of options			Weighted average fair value	Number of options	Weighted average fair value
	2019 Plan	2011 Plan	Total		2011 Plan	
Non-vested share options at beginning of period	—	1,706,303	1,706,303	$ 1.346	451,113	$ 1.027
Granted - 2011 Plan	—	116,742	116,742	6.649	1,695,258	1.463
Granted - 2019 Plan	287,138	—	287,138	13.912	—	—
Vested, outstanding	—	(656,646)	(656,646)	1.333	(427,870)	1.479
Vested, outstanding	(1,165)	—	(1,165)	12.160	—	—
Forfeited - 2011	—	(14,099)	(14,099)	1.906	(12,198)	1.064
Forfeited - 2019	(66,998)	—	(66,998)	12.221	—	—
Non-vested share options at end of period	218,975	1,152,300	1,371,275	$ 3.889	1,706,303	$ 1.346
Non-vested share options at end of period - Weighted average fair value	$ 14.439	$ 1.884				

The following table summarizes information with respect to share options outstanding as of December 31, 2019:

	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	235,497	3.3	$ 0.914	235,497	3.3	$ 0.914
$1.12	261,913	6.3	$ 1.117	207,319	6.2	$ 1.117
$1.54	956,688	7.9	$ 1.543	429,175	7.9	$ 1.543
$1.91	82,772	8.6	$ 1.915	40,122	9	$ 2
$2.66	710,914	8.9	$ 2.660	300,113	8.9	$ 2.660
$9.42	116,742	9.2	$ 9.415	—	—	$ —
$15.87	23,620	9.6	$ 15.870	—	—	$ —
$17.78	42,000	9.9	$ 17.780	1,165	9.9	$ 17.780
$19.14	3,760	9.8	$ 19.140	—	—	$ —
$21.28	3,760	9.7	$ 21.280	—	—	$ —
$22.45	147,000	9.7	$ 22.450	—	—	$ —
Total	**2,584,666**	**7.8**	**$ 3.755**	**1,213,391**	**7.0**	**$ 1.652**

The intrinsic value of all outstanding options as of December 31, 2019 was $32.7 million, based on the fair value of our common shares of $16.01 per share at December 31, 2019, of which approximately $17.4 million related to vested options and approximately $15.5 million related to unvested options.

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

The fair value of options granted was estimated using the Black-Scholes option pricing model, resulting in the following weighted average assumptions for the options granted for the years ended December 31, 2019 and 2018:

	2019	2018
Exercise price	$ 16.900	$ 2.037
Share price	$ 16.900	$ 2.037
Volatility	80 %	82 %
Risk-free interest rate	1.92 %	2.84 %
Expected life	6.21 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, 2019 and 2018:

	2019	2018
Administration	$ 574	$ 209
Research and development	495	371
Commercial activities	122	53
	$ 1,191	$ 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 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, 2019 and 2018, as they would be anti-dilutive:

	2019	2018
Redeemable convertible preferred shares	—	17,550,802
Share options and unvested restricted share awards	2,584,666	2,295,045
	2,584,666	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, 2019 and 2018 is as follows:

	2019	2018
Loss before income taxes	$ (55,285)	$ (23,111)
Basic income tax rate	26.30 %	26.67 %
Computed income tax recovery	(14,542)	(6,164)
Effect on income tax rate resulting from		
Accounting charges not deductible for tax purposes	23	12
Non-deductible share-based compensation	317	169
Share issue costs	(2,739)	
Unrecorded potential tax benefits of current period losses and other tax assets	16,829	6,183
Non-refundable investment tax credit used (earned) in the year	—	(145)
Valuation allowance for prior year adjustment	77	—
Other	(21)	19
Income tax expense (recovery)/expense reported in the consolidated statements of loss and comprehensive loss	$ (56)	$ 74

The Company has incurred Canadian federal and provincial net operating losses (NOLs) from inception. As of December 31, 2019, the Company has NOL carry-forwards of approximately $86,591 and $86,085, respectively, for Canadian federal and Québec purposes, available to reduce future taxable income, which expire beginning in 2027 through 2039. The Company also has scientific research and experimental development expenditures of approximately $9,377 and $11,127, 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-forward period. Research

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

The Company has incurred NOLs for U.S. tax purposes. As of December 31, 2019, the Company has carry-forwards of approximately $12,439 related to U.S. NOLs that may be carried forward indefinitely and are available to reduce future taxable income.

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, 2019 and 2018:

	2019	2018
Net operating loss carry-forwards	25,965	12,209
Tax basis of property and equipment in excess of carrying values	103	93
Federal SR&ED investment tax credits	535	273
Taxation of federal SR&ED investment tax credits	(142)	(72)
Research and development expenditures	2,686	1,791
Financing costs	2,103	138
Others	16	21
Total gross deferred tax assets	31,266	14,453
Valuation allowance	(31,266)	(14,453)
Net deferred tax assets	—	—

The Company files income tax returns in Canada and in the United States. The Company is subject to Canada Revenue Agency and Revenu Québec examination for fiscal years 2014 to 2019 due to unexpired statute of limitation periods and is subject to US Federal and state income tax examination for fiscal years 2017 to 2019.

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 $392 for the year ended December 31, 2019 (for 2018, $257).

11 Commitments

In the normal course of business, the Company enter into contracts with clinical research organizations, drug manufacturers and other vendors for preclinical and clinical research studies, research and development supplies and other services and products for operating purposes. These contracts generally provide for termination on notice, and therefore are cancellable contracts. Therefore, as at December 31, 2019 there are no contractual commitments.

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:

	2019	2018
Cash	$ 149	$ 246
Short-term investments	—	29
Accounts payable and accrued liabilities	1,680	538
Net financial position exposure	$ 1,531	$ 263

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 inputs are inputs that reflect the assumptions market participants would use in pricing the asset or liability based on the best information available in the circumstances.

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

Level 1 — Valuations are based on quoted prices in active markets for identical assets or liabilities and readily accessible by the Company at the reporting date.
Level 2 — Valuations based on inputs other than the quoted prices in active markets that are observable either directly or indirectly in active markets.
Level 3 — Valuations based on unobservable inputs in which there is little or no market data, which requires the Company to develop its own assumptions.

The Company's fair value hierarchy for all its financial assets (by major security type measured at fair value on a recurring basis) for the year ending December 31, 2019 is nil, as there was no financial instruments measured at fair value on a recurring basis as of that date. For the year ended December 31, 2018, the Company held a Guaranteed investment certificates at Level 1 with a fair value of $29.

ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE.

None.

ITEM 9A. CONTROLS AND PROCEDURES.

Evaluation of Disclosure Controls and Procedures

We maintain disclosure controls and procedures, as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934 (the Exchange Act) that are designed to ensure that information required to be disclosed in our periodic and current reports that we file with the SEC is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms, and that such information is accumulated and communicated to our management, including our principle executive officer and principle financial officer, as appropriate, to allow timely decisions regarding required disclosure. In designing and evaluating the disclosure controls and procedures, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable and not absolute assurance of achieving the desired control objectives. In reaching a reasonable level of assurance, management necessarily is required to apply its judgment in evaluating the cost-benefit relationship of possible controls and procedures. In addition, the design of any system of controls also is based in part upon certain assumptions about the likelihood of future events, and there can be no assurance that any design will succeed in achieving its stated goals under all potential future conditions; over time, control may become inadequate because of changes in conditions, or the degree of compliance with policies or procedures may deteriorate. Because of the inherent limitations in a cost-effective control system, misstatements due to error or fraud may occur and not be detected.

We carried out an evaluation, under the supervision and with the participation of our management, including our principle executive officer and principle financial officer, of the effectiveness of the design and operation of our disclosure controls and procedures, as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act. Based on this evaluation, our principle executive officer and principle financial officer concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of December 31, 2019.

Management's Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting as such term is defined in Rules 13a-15(f) and 15-d-15(f) of the Exchange Act. Internal control over financial reporting is a process designed under the supervision and with the participation of our management, including our principle executive officer and principle financial officer, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with accounting principles generally accepted in the United States of America.

As of December 31, 2019, management assessed and management concluded the effectiveness of internal control over financial reporting using the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission in Internal Control – 2013 Integrated Framework (2013 Framework). Based on this assessment, management concluded that our internal control over financial reporting was effective as of December 31, 2019.

This Annual Report on Form 10-K does not include an attestation report of our independent registered public accounting firm due to a transition period established by the JOBS Act for emerging growth companies.

Inherent Limitations of Internal Controls

Our management, including our principle executive officer and principle financial officer, does not expect that our disclosure controls and procedures or our internal controls will prevent all errors and all fraud. A control system, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that all control issues and instances of fraud, if any, within the company have been detected. These

inherent limitations include the realities that judgments in decision-making can be faulty, and that breakdowns can occur because of a simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people, or by management override of the control. The design of any system of controls also is based in part upon certain assumptions about the likelihood of future events, and there can be no assurance that any design will succeed in achieving its stated goals under all potential future conditions. Over time, controls may become inadequate because of changes in conditions, or the degree of compliance with the policies or procedures may deteriorate. Because of the inherent limitations in a cost-effective control system, misstatements due to error or fraud may occur and not be detected.

Changes in Internal Control Over Financial Reporting

During the year ended December 31, 2019, there have been no changes in our internal control over financial reporting, as such term is defined in Rules 13a-15(f) and 15d-15(f) promulgated under the Exchange Act, that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

ITEM 9B. OTHER INFORMATION.

None.

PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE.

The following table sets forth information regarding our executive officers and directors, including their ages as of March 1, 2020:

NAME	AGE	POSITION(S)
Executive Officers		
Joseph Oliveto	52	President, Chief Executive Officer and Director
Lorenz Muller	56	Chief Commercial Officer
Francis Plat, M.D.	62	Chief Medical Officer
Amit Hasija	47	Chief Financial Officer and Executive Vice President of Corporate Development
Non-Employee Directors		
Paul Edick[2][3]	64	Director and Chairperson of the Board
Richard Pasternak[2]	71	Director
Debra K. Liebert [1][2]	63	Director
Michael Tomsicek[1]	54	Director
Paul Truex[1][3]	51	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

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.

Amit Hasija has served as our Chief Financial Officer and Executive Vice President of Corporate Development, since September 2019. Prior to Milestone Pharmaceuticals, Mr. Hasija served as Chief Financial Officer and Chief Business Officer at Fulcrum Therapeutics. Prior to Fulcrum, he spent five years at Sanofi, most recently serving as Vice President of Integrated Care. At Sanofi, he also served as Vice President of North America Pharmaceutical Business Development. Prior to joining Sanofi over approximately 10 years, Mr. Hasija held positions in investment banking at Credit Suisse, Goldman Sachs and Deutsche Bank. He began his career at Merck. Mr. Hasija received a BS in Chemical Engineering from Drexel University and an MBA from New York University’s Stern School of Business.

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

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.

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, from 2007 to December 2019, and as a Managing Director from January 2014 to December 2019. Ms. Liebert previously served in various positions at CancerVax Corporation, Ataigin 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.

Richard Pasternak, MD has served as a member of our board of directors since November 2019. He is currently a Clinical Professor at the Weill Cornell Medical College. In 2019, Dr. Pasternak retired from Cerenis Therapeutics (now ABIONYX Pharma), a French publicly-traded company focused on developing treatments for cardiovascular diseases, where he served since 2011, most recently as Chief Executive Officer and Chair of the Board of Directors. He previously served as Vice President, Head of Cardiovascular Clinical Research, and Head of Global Scientific Affairs and Scientific Leadership, at Merck & Co. from 2004 to 2010. Prior to joining Merck & Co., he was the Director of Preventive Cardiology and Cardiac Rehabilitation at Massachusetts General Hospital, and an Associate Professor of Medicine at Harvard Medical School. Dr. Pasternak also serves on the Boards of Anthos Therapeutics and Magenta Medical Ltd. He previously served on the Boards of Essentialis Therapeutics and Haptocure Ltd., as well as several nonprofit organizations. He was also previously a senior advisor to Bay City Capital and Bridge Medicines. Dr. Pasternak received his BA and MD from Yale University, and completed his medical and cardiology training at Massachusetts General Hospital. We believe Dr. Pasternak’s clinical, industry and management experience, including his experience serving on public company boards of directors, qualifies him 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. Debra K. Liebert was designated as a director to our board of directors by Domain Partners VIII, L.P., in connection with a shareholders agreement, which terminated in connection with our initial public offering.

Board Composition

Our board of directors currently consists of six members. Our articles of incorporation and 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.

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 is posted on our website at www.milestonepharma.com.

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 registered accounting firm reports 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 Debra K. Liebert, 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 Paul Edick, Debra Liebert and Richard Pasternak. 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 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 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

We have adopted 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 is available on our website at www.milestonepharma.com. The nominating and corporate governance committee of our board of directors is 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.

ITEM 11. EXECUTIVE COMPENSATION

Our named executive officers for the year ended December 31, 2019, which consist of our principal executive officer and our next two most highly compensated executive officers who were serving as executive officers at the end of 2019, and one individual who would have been among the most highly compensated if he had been still serving as an executive officer at the end of 2019, are:

- Joseph Oliveto;
- Amit Hasija;
- Francis Plat; and
- Timothy Maness.

Summary Compensation Table

The following table provides information regarding the compensation provided to our named executive officers for the years ended December 31, 2019 and 2018.

NAME AND PRINCIPAL POSITION	YEAR	SALARY ($)[1]	NON-EQUITY INCENTIVE PLAN COMPENSATION ($)[2]	OPTION AWARDS ($)[3]	ALL OTHER COMPENSATION ($)[4]	TOTAL ($)
Joseph Oliveto	2019	458,488	325,000		1,500	784,988
Chief Executive Officer	2018	360,000	190,000	866,653	20,184	1,436,837
Amit Hasija	2019	121,250	45,500	2,296,562	—	2,463,312
Chief Financial Officer and Executive Vice President of Corporate Development						
Francis Plat	2019	380,692	198,400	—	—	579,092
Chief Medical Officer	2018	330,000	83,000	223,609	—	636,609
Timothy Maness	2019	292,885[5]	—	818,568	—	1,111,453
Former Chief Accounting Officer						

Salary amounts represent actual amounts paid during 2019 and 2018. See "—Narrative to the Summary Compensation Table—Annual Base Salary" below.

(1) 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.

(2) In accordance with SEC rules, this column reflects the aggregate grant date fair value of the option awards granted during fiscal years 2019 and 2018 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 Annual Report on Form 10-K. 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.

(3) Reflects (i) reimbursements paid with respect to expenses incurred by Mr. Oliveto for Canadian tax return preparations in 2019 ($1,500), and (ii) reimbursements paid with respect to medical ($18,676), dental ($1,355), and life ($153) insurance policies obtained by Mr. Oliveto in 2018.

(4) Reflects (i) $142,885 of base salary paid to Mr. Maness in 2019 and (ii) $150,000 paid in consulting fees to Mr. Maness in 2019 prior to the effective date of his employment agreement with us. See "—Narrative to the Summary Compensation Table—Annual Base Salary" below.

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. Following the completion of our initial public offering in May 2019, the compensation committee determined our executive officers' compensation and followed this process, and the compensation committee itself, rather than our board of directors, approves the compensation of each executive officer other than our Chief 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 2018, the base salaries of Mr. Oliveto and Dr. Plat were $360,000 and $330,000, respectively, and for 2019, the base salaries of Mr. Oliveto, Mr. Hasija, Dr. Plat and Mr. Maness were $500,000, $390,000, $400,000, and $300,000, respectively. 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 percentages for each of Mr. Oliveto and Dr. Plat in 2018 and 2019 were: Mr. Oliveto, 50% (2018 and 2019); and Dr. Plat, 25% in 2018 and 35% in 2019. The target bonus percentages for each of Mr. Hasija and Mr. Maness in 2019 were 35% and 30%, respectively.

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 and the compensation committee are responsible for approving equity grants. As of the date of this Annual Report on Form 10-K, 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. In addition, in connection with our initial public offering in May 2019, our board of directors delegated certain authority to our compensation committee to grant equity awards. 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 our initial public offering in May 2019, we granted all share options pursuant to our Stock Option Plan, or the 2011 Plan. Following our initial public offering, we have granted 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, 2019. Unless otherwise indicated below, all awards were granted pursuant to the 2011 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	74,001	47,573	1.12	9/19/2026
Chief Executive Officer	01/03/2017	9/19/2016	5,514	3,446	1.12	1/3/2027
	12/12/2017	9/19/2016	66,446	47,410	1.54	12/12/2027
	10/26/2018	9/19/2016	155,576	35,903	2.66	10/25/2028
	11/21/2018	11/21/2018	71,281	191,911	2.66	11/20/2028
Amit Hasija	9/9/2019[2]	9/9/2019	—	147,000	22.45	9/92029
Chief Financial Officer and Executive Vice President of Corporate Development						
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	19,729	—	1.12	8/26/2025
	2/21/2018	10/15/2018	50,448	33,053	1.54	10/15/2028
	2/21/2018	7/21/2017	15,517	37,685	1.54	7/21/2027
	11/21/2018	11/21/2018	10,182	27,416	2.66	11/20/2028
Timothy Maness[3]	8/15/2018	8/15/2018	18,799	—	1.92	8/15/2028
Former Chief Accounting Officer	11/21/2018	11/21/2018	4,700	—	2.66	11/21/2028

(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 named executive officer's continued service through each vesting date.

(2) Granted pursuant to the terms of our 2019 Plan. See "— Equity Incentive Plans — 2019 Plan" below for additional information.

(3) The vesting of the unvested shares underlying the option grants was accelerated by our board of directors, effective upon the date of Mr. Maness' resignation, in accordance with the terms of our 2011 Plan. See "— Equity Incentive Plans — 2011 Plan" below for additional information.

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 up to an aggregate of 252,853 common shares.

In April 2019 in connection with our initial public 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 50% of his gross base salary.

Agreement with Amit Hasija

We entered into an employment agreement with Mr. Hasija, our Chief Financial Officer and Executive Vice President of Corporate Development, in September 2019 that governs the terms of his employment with us. Pursuant to his agreement, Mr. Hasija is entitled to an annual base salary of $390,000, is eligible to receive an annual target performance bonus of 35% of his gross base salary, and was granted an option to purchase up to 147,000 common shares.

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 of C$300,000, was eligible to receive an annual target performance bonus of, as a percentage of his gross base salary, 25% for 2018, and was granted an option to purchase up to 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 our initial public 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 35% of his gross base salary.

Agreement with Timothy Maness

In April 2019, in connection with our initial public offering, we entered into an employment agreement with Mr. Maness that governed the terms of his employment with us prior to his resignation in October 2019. Pursuant to his agreement, Mr. Maness was entitled to an annual base salary of $280,000 and was eligible to receive an annual target performance bonus of 30% of his gross base salary. Prior to his employment with us, Mr. Maness served as a financial and accounting consultant to us.

On September 9, 2019, Mr. Maness, who was serving as our Vice President, Finance and our principal financial officer, was promoted by our board of directors to the position of Chief Accounting Officer and principal financial officer and principal accounting officer. In connection with his appointment, Mr. Maness also received an option to purchase up to 20,000 of our common shares, under the terms of our 2019 Plan.

On October 31, 2019, Mr. Maness resigned from his positions with us, including as Chief Accounting Officer, principal financial officer and principal accounting officer. In connection with his resignation, our board of directors authorized the acceleration of vesting for certain of Mr. Maness' outstanding and unvested option grants issued under our 2011 Plan.

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.

Amit Hasija

Under his employment agreement, if Mr. Hasija is terminated by us without cause or if Mr. Hasija 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. Hasija 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.

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.

Timothy Maness

Under the employment agreement, in effect prior to his resignation, if Mr. Maness was terminated by us without cause or if Mr. Maness resigned for good reason, he was entitled to salary continuation and reimbursement of premiums to continue health care benefits for a period of six months, subject to his execution of a general release in favor of our company. If Mr. Maness was terminated without cause or resigned for good reason within 30 days prior to, or 12 months following, a change in control, he was entitled to receive (i) salary continuation and reimbursement of premiums to continue health care benefits for a period of nine months, and (ii) a one-time bonus equal to his target bonus for the year in which he was terminated, subject in the case of the foregoing clauses (i) and (ii), to his execution of a general release in favor of our company.

As mentioned above, Mr. Maness resigned from his positions with us, including as Chief Accounting Officer, principal financial officer and principal accounting officer, on October 31, 2019. Mr. Maness did not receive severance benefits

under his employment agreement. However, our board of directors authorized the acceleration of vesting for certain of Mr. Maness' outstanding and unvested option grants issued under our 2011 Plan in connection with his resignation.

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, 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. 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. In November 2019, our compensation committee authorized the creation of a 401(k) plan and a registered retirement savings plan for our employees in the United States or Canada, which we have subsequently implemented for participation by our employees. 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 the completion of our initial public offering in May 2019. Since the effectiveness of the 2019 Plan, no further grants have been or 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. The maximum number of our common shares that may be issued under our 2019 Plan was initially 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. As of December 31, 2019, options to purchase 220,140 common shares, at exercise prices ranging from $15.00 to $22.45 per share, or a weighted-average exercise price of $20.777 per share, were outstanding under our 2019 Plan.

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, has the authority to 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, the plan administrator 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 plan administrator 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 an 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 both not serving on our board of directors on the date of the underwriting agreement related to our initial public offering, or the incumbent board, and 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 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. No future stock awards will be made under our 2011 Plan. As of December 31, 2019, options to purchase 2,364,526 common shares, at exercise prices ranging from $0.96 to $9.42 per share, or a weighted-average

exercise price of $2.151 per share, were outstanding under our 2011 Plan. Any shares of common stock subject to awards 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 will become available for issuance under our 2019 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 provided 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 have only been granted only to employees.

Options. The exercise price of options granted under our 2011 Plan was equal to or exceeded 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 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 in connection with our initial public offering in May 2019. 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. The ESPP initially authorized 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 automatically increases 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

Prior to our initial public offering in May 2019, we did not historically have a formal compensation policy with respect to service on our board of directors, but we had 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 became effective in connection with our initial public offering in May 2019. Under this policy, we 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 receives 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 were paid in respect of any period prior to the completion of our initial public offering in May 2019. The retainers 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 receives an option to purchase 19,000 of our common shares. The shares subject to each such option 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 shareholders, each non-employee director that continues to serve as a non-employee member on our board of directors will receive an option to purchase 11,000 of our common shares. The shares subject to each such 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 shares 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 shareholders.

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 during the year ended December 31, 2019. 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."

NAME	FEES EARNED OR PAID IN CASH ($)	OPTION AWARDS ($)[1][2]	TOTAL ($)
Paul Edick	59,250	353,437	412,687
Debra K. Liebert	30,214	231,040	261,254
Richard Pasternak	10,250	231,040	241,296
Michael Tomsicek	41,667	182,257	224,024
Paul Truex	37,036	48,460	85,676
Marco Boorsma[3]	—	—	—
Nilesh Kumar[4]	—	—	—

(1) In accordance with SEC rules, this column reflects the aggregate grant date fair value of the option awards granted during fiscal year 2019 computed in accordance with ASC 718. Assumptions used in the calculation of these amounts are included in Note 7 to our audited consolidated financial statements included elsewhere in this Annual Report on Form 10-K. 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, 2019:

NAME	OPTION AWARDS OUTSTANDING AT YEAR-END
Paul Edick	52,638
Debra K. Liebert	19,000
Richard Pasternak	19,000
Michael Tomsicek	27,447
Paul Truex	83,556

(3) Mr. Boorsma resigned from our board of directors, effective November 29, 2019.

(4) Mr. Kumar resigned from our board of directors, effective September 18, 2019.

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS.

The following table sets forth information regarding beneficial ownership of our share capital as of December 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 is based on 24,505,748 common shares outstanding as of December 31, 2019.

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 December 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.

NAME	NUMBER OF SHARES BENEFICIALLY OWNED	PERCENTAGE OF SHARES BENEFICIALLY OWNED
Greater than 5% Shareholders:		
RTW Investments L.P.[1]	3,958,264	16.15%
Fonds de solidarité des travailleurs du Québec (F.T.Q.)[2]	2,720,310	11.10%
Novo Holdings A/S[3]	2,434,470	9.93%
BDC Capital, Inc. and affiliates[4]	2,388,008	9.74%
Entities affiliated with Venrock[5]	2,215,089	9.04%
Domain Associates, L.L.C. and affiliates[6]	1,873,105	7.64%
Entities affiliated with Forbion[7]	1,303,902	5.32%
T. Rowe Price Associates, Inc.[8]	1,286,507	5.25%
Directors and Named Executive Officers:		
Joseph Oliveto[9]	693,990	2.83%
Amit Hasija	-	*
Francis Plat[10]	145,711	*
Timothy Maness[11]	23,499	*
Paul Edick	-	*
Debra K. Liebert[12]	1,583	
Richard Pasternak[13]	1,583	*
Michael Tomsicek	-	*
Paul Truex[14]	46,260	*
All current executive officers and directors as a group (9 persons)	993,708	4.05%

* Represents beneficial ownership of less than 1%.

(1) Based solely on a Schedule 13G as filed by RTW Investments, LP on February 14, 2020. Consists of (i) 2,871,793 shares held directly by RTW Master Fund, Ltd. and (ii) 1,086,471 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 address for this entity is 545 Cremazie Blvd. East, Suite 200, Montréal, Québec, H2M 2W4, Canada.

(3) Based solely on a Schedule 13D/A as filed by Novo Holdings A/S on November 27, 2019. The board of directors of Novo Holdings A/S, or Novo, has sole 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.

(4) Based solely on a Form 4 filed by BDC Capital, Inc., or BDC Capital, on May 8, 2019. Consists of 1,294,004 shares held by 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) Based solely on a Schedule 13G filed by Venrock Healthcare Capital Partners II, L.P. on February 14, 2020. Consists of (i) 105,720 shares owned by Venrock Healthcare Capital Partners II, L.P., (ii) 42,840 shares owned by VHCP Co-Investment Holdings II, LLC, (iii) 1,878,682 shares owned by Venrock Healthcare Capital Partners III, L.P. and (iv) 187,847 shares owned by VHCP Co-Investment Holdings III, LLC. VHCP Management II, LLC is the general partner of Venrock Healthcare Capital Partners II, L.P. and the manager of VHCP Co-Investment Holdings II, LLC and may be deemed to beneficially own such common shares. 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) Based solely on a Schedule 13G filed by Domain Partners VIII, L.P. on January 9, 2020. Represents shares held directly by Doman 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) Based solely on a Schedule 13G filed by Forbion Capital Fund III Cooperatief U.A. on February 11, 2020. 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.

(8) Based solely on a Schedule 13G filed by T. Rowe Price Associates, Inc. on February 14, 2020. The address for this entity is 100 E. Pratt Street, Baltimore, MD 21202.

(9) Includes 413,635 common shares issuable upon the exercise of options.

(10) Includes 134,255 common shares issuable upon the exercise of options.

(11) Consists of 23,499 common shares issuable upon the exercise of options. Mr. Maness resigned from his positions with us on October 31, 2019.

(12) Consists of 1,583 common shares issuable upon the exercise of options.

(13) Consists of 1,583 common shares issuable upon the exercise of options.

(14) Consists of 46,260 common shares issuable upon the exercise of options.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE.

The following includes a summary of transactions since January 1, 2018 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 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 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 was converted into one common share upon the completion of the Initial Public 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, who was then 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, and he resigned from our board of directors effective September 18, 2019.

(2) Marco Boorsma, who was then a member of our board of directors, is a general partner at Forbion and was designated to our board by Forbion. Mr. Boorsma resigned from our board of directors effective November 29, 2019.

(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, was a managing director at Domain Associates, LLC, the manager of Domain,until December 31, 2019, and was designated to our board by Domain.

Initial Public Offering

On May 13, 2019, we closed our initial public offering, pursuant to which we issued and sold 6,325,000 common shares, including full exercise of the underwriters' over-allotment option to purchase an additional 825,000 shares, at a public offering price of $15.00 per share. The following table sets forth the aggregate cash purchase price of the common shares purchased by our directors, executive officers and 5% shareholders and their affiliates and the number of common shares issued in consideration of such amounts. Such purchases were made through the underwriters at the initial public offering price of $15.00 per share.

NAME	CASH PURCHASE PRICE	NUMBER OF COMMON SHARES
BDC Capital, Inc. and affiliates	$ 6,499,995	433,333
Fonds de solidarité des travailleurs du Québec (F.T.Q.)	3,000,000	200,000
Novo Holdings A/S	4,999,995	333,333
RTW Investments, LP	10,015,005	667,667
	$ 24,514,995	1,634,333

Registration Rights Agreement

We are party to a third amended and restated registration rights agreement, dated October 15, 2018, with certain holders of common shares issued upon conversion of 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.

Option Awards

In November 2019, our board of directors approved the issuance of option grants under our 2019 Plan to certain directors that had been serving on our board prior to our initial public offering and the implementation of our non-employee director compensation policy. Our board of directors approved the one-time option grants to these directors in order to compensate such directors for their service to us in connection with our initial public offering completed in May 2019. The following table provides information regarding the number of common shares underlying the share options issued pursuant to this one-time grant. Each of the option grants vests in equal monthly installments beginning on the one month anniversary of the date of the grant, over a period of three years, subject to the recipient's continued service to us through each such vesting date.

NAME	OPTION AWARDS
Paul Truex	4,000
Debra K. Liebert	19,000

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 Compensation."

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 Compensation."

Indemnity Agreements

We have entered, and intend to continue to enter, into separate indemnity agreements with each 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 the completion of our initial public offering in May 2019, our board of directors 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. 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 that occurred prior to the completion of our initial public offering in May 2019 were entered into prior to the adoption of this policy. Although prior to May 2019 we did not have a written policy for the review and approval of transactions with related persons, our board of directors had 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. Since the completion of our initial public offering in May 2019 and the implementation

of our related persons transactions policy, our board of directors has complied with the provisions of this policy in analyzing such transactions.

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.

ITEM 14. PRINCIPAL ACCOUNTING FEES AND SERVICES.

Information on the fees paid by the Company to PricewaterhouseCoopers LLP, the Company's independent registered public accounting firm and independent registered public accounting firm for the years ended December 31, 2019 and December 31, 2018 is set forth below.

	YEAR ENDED DECEMBER 31,	
Fee Category	**2019**	**2018**
Audit Fees[1]	209,417	114,000
All Other Fees[2]	84,407	455,148
	$ 293,824	$ 569,148

(1) "Audit Fees" consist of fees for the audit of our annual consolidated financial statements and the review of the interim condensed financial statements included in our quarterly reports on Form 10-Q.

(2) "All Other Fees" consist of fees for Canadian and US Tax Compliance and other tax services. Additonally, fees related to IPO services were incurred in 2018.

All auditor fees must be approved by our Audit Committee and all fees described above were pre-approved by the Audit Committee**.**

Pre-Approval Policies and Procedures

Pre-Approval Policies and Procedures Our Audit Committee has adopted procedures requiring the pre-approval of all non-audit services performed by our independent registered public accounting firm in order to assure that these services do not impair the auditor's independence. These procedures generally approve the performance of specific services subject to a cost limit for all such services. This general approval is reviewed, and if necessary modified, at least annually. Management must obtain the specific prior approval of the Audit Committee for each engagement of the independent registered public accounting firm to perform other audit-related or other non-audit services. The Audit Committee does not delegate its responsibility to approve services performed by the independent registered public accounting firm to any member of management. The standard applied by the Audit Committee in determining whether to grant approval of any type of non-audit service, or of any specific engagement to perform a non-audit service, is whether the services to be performed, the compensation to be paid therefore and other related factors are consistent with the independent registered public accounting firm's independence under guidelines of the SEC and applicable professional standards. Relevant considerations include whether the work product is likely to be subject to, or implicated in, audit procedures during the audit of our financial statements, whether the independent registered public accounting firm would be functioning in the role of management or in an advocacy role, whether the independent registered public accounting firm's performance of the service would enhance our ability to manage or control risk or improve audit quality, whether such performance would increase efficiency because of the independent registered public accounting firm's familiarity with our business, personnel, culture, systems, risk profile and other factors, and whether the amount of fees involved, or the non-audit services portion of the total fees payable to the independent registered public accounting firm in the period would tend to reduce the independent registered public accounting firm's ability to exercise independent judgment in performing the audit.

PART IV

ITEM 15. EXHIBITS, FINANCIAL STATEMENT SCHEDULES.

(a)(1) Financial Statements

See Index to Consolidated Financial Statements on page 88 of this Annual Report on Form 10-K, which is incorporated into this item by reference.

(a)(2) Financial Statement Schedules

All financial statement schedules are omitted because they are not applicable or the required information is shown in the financial statements or notes thereto.

(b) Exhibits

The following list of exhibits includes exhibits submitted with this Annual Report on Form 10-K as filed with the SEC and others incorporated by reference to other filings.

(a) Exhibits.

The exhibits listed below are filed as part of this registration statement.

EXHIBIT NUMBER	DESCRIPTION
3.1	Amended Articles of Incorporation (incorporated herein by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K (File No. 001-38899), filed with the SEC on May 15, 2019).
3.2	Amended and Restated Bylaws (incorporated herein by reference to Exhibit 3.2 to the Registrant's Current Report on Form 8-K (File No. 001-38899), filed with the SEC on May 15, 2019).
4.1	Form of Common Share Certificate (incorporated herein by reference to Exhibit 4.1 to Amendment No. 1 to the Registrant's Registration Statement on Form S-1 (File No. 333-230846), filed with the SEC on April 29, 2019).
4.2	Third Amended and Restated Registration Rights Agreement, by and among the Company and certain of its shareholders, dated October 15, 2018 (incorporated herein by reference to Exhibit 4.2 to the Registrant's Registration Statement on Form S-1 (File No. 333-230846), filed with the SEC on April 12, 2019).
4.3	Description of Securities Registered pursuant to Section 12 of the Securities Exchange Act of 1934, as amended
10.1+	Third Amended and Restated Stock Option Plan (incorporated herein by reference to Exhibit 10.1 to the Registrant's Registration Statement on Form S-1 (File No. 333-230846), filed with the SEC on April 12, 2019).
10.2+	Form of Award and Grant Notices under the Third Amended and Restated Stock Option Plan (incorporated herein by reference to Exhibit 10.2 to the Registrant's Registration Statement on Form S-1 (File No. 333-230846), filed with the SEC on April 12, 2019).
10.3+	2019 Equity Incentive Plan (incorporated herein by reference to Exhibit 4.8 to the Registrant's Registration Statement on Form S-8 (File No. 333-231347), filed with the SEC on May 9, 2019).
10.4+	Form of U.S. Stock Option Grant Notice and Stock Option Agreement under the 2019 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.4 to Amendment No. 1 to the Registrant's Registration Statement on Form S-1 (File No. 333-230846), filed with the SEC on April 29, 2019).
10.5+	Form of U.S. Restricted Stock Unit Grant Notice and Restricted Stock Unit Award Agreement under the 2019 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.5 to Amendment No. 1 to the Registrant's Registration Statement on Form S-1 (File No. 333-230846), filed with the SEC on April 29, 2019).
10.6+	Form of Canadian Stock Option Grant Notice and Option Agreement under the 2019 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.6 to Amendment No. 1 to the Registrant's Registration Statement on Form S-1 (File No. 333-230846), filed with the SEC on April 29, 2019).

10.7+	Form of Canadian Restricted Stock Unit Grant Notice and Restricted Stock Unit Award Agreement under the 2019 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.7 to Amendment No. 1 to the Registrant's Registration Statement on Form S-1 (File No. 333-230846), filed with the SEC on April 29, 2019).
10.8+	2019 Employee Share Purchase Plan (incorporated herein by reference to Exhibit 4.13 to the Registrant's Registration Statement on Form S-8 (File No. 333-231347), filed with the SEC on May 9, 2019).
10.9+	Amended and Restated Employment Agreement between Joseph Oliveto and Milestone Pharmaceuticals USA, Inc. (incorporated herein by reference to Exhibit 10.9 to Amendment No. 1 to the Registrant's Registration Statement on Form S-1 (File No. 333-230846), filed with the SEC on April 29, 2019).
10.10+	Employment Agreement between Amit Hasija and Milestone Pharmaceuticals USA, Inc. (incorporated herein by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K (File No. 001-38899), filed with the SEC on September 9, 2019).
10.11+	Amended and Restated Employment Agreement between Francis Plat and Milestone Pharmaceuticals Inc. (incorporated herein by reference to Exhibit 10.11 to Amendment No. 1 to the Registrant's Registration Statement on Form S-1 (File No. 333-230846), filed with the SEC on April 29, 2019).
10.12+	Amended and Restated Employment Agreement between Lorenz Muller and Milestone Pharmaceuticals USA, Inc. (incorporated herein by reference to Exhibit 10.12 to Amendment No. 1 to the Registrant's Registration Statement on Form S-1 (File No. 333-230846), filed with the SEC on April 29, 2019).
10.13+	Employment Agreement between Timothy L. Maness and Milestone Pharmaceuticals USA, Inc. (incorporated herein by reference to Exhibit 10.13 to Amendment No. 1 to the Registrant's Registration Statement on Form S-1 (File No. 333-230846), filed with the SEC on April 29, 2019).
10.14+	Form of Indemnity Agreement (incorporated herein by reference to Exhibit 10.14 to the Registrant's Registration Statement on Form S-1 (File No. 333-230846), filed with the SEC on April 12, 2019).
23.1	Consent of PricewaterhouseCoopers LLP, an Independent Registered Public Accounting Firm.
24.1	Power of Attorney (included on the signature page to this registration statement).
31.1	Certification of Principal Executive Officer pursuant to Rules 13a-14(a) and 15d-14(a) promulgated under the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
31.2	Certification of Principal Financial Officer pursuant to Rules 13a-14(a) and 15d-14(a) promulgated under the Securities Exchange Act of 1934, as adopted pursuant to section 302 of the Sarbanes-Oxley Act of 2002
32.1^	Certification of Principal Executive Officer and Principal Financial Officer pursuant to Rules 13a-14(b) and 15d-14(b) promulgated under the Securities Exchange Act of 1934 and 18 U.S.C. Section 1350, as adopted pursuant to section 906 of The Sarbanes-Oxley Act of 2002
101.INS	XBRL Instance Document
101.SCH	XBRL Taxonomy Extension Schema Document
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	XBRL Taxonomy Extension Label Linkbase Document
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document

+ Indicates a management contract or compensatory plan

^ These certifications are being furnished solely to accompany this Annual Report pursuant to 18 U.S.C. Section 1350, and are not being filed for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, and are not to be incorporated by reference into any filing of the Registrant, whether made before or after the date hereof, regardless of any general incorporation language in such filing.

ITEM 16. FORM 10-K SUMMARY

Not applicable

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the Company has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

Milestone Pharmaceuticals Inc.

Dated: March 5, 2020

/s/ Joseph Oliveto
Joseph Oliveto
Chief Executive Officer

POWER OF ATTORNEY

KNOW ALL BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Joseph Oliveto and Amit Hasija, and each of them, as his or her true and lawful attorneys-in-fact and agents, each with the full power of substitution, for him or her and in his or her name, place or stead, in any and all capacities, to sign any and all amendments to this report, with exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in and about the premises, as fully to all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, or their, his substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the Company and in the capacities indicated on the 5th of March 2020.

/s/ Joseph Oliveto Joseph Oliveto	Chief Executive Officer (principal executive officer)
/s/ Amit Hasija Amit Hasija	Chief Financial Officer (principal financial officer and principle accounting officer)
/s/ Paul Edick Paul Edick	Chairman of the Board
/s/ Michael Tomsicek Michael Tomsicek	Director
/s/ Paul Truex Paul Truex	Director
/s/ Debra K. Liebert Debra K. Liebert	Director
/s/ Richard Pasternak Richard Pasternak	Director

DESCRIPTION OF THE REGISTRANT'S SECURITIES REGISTERED PURSUANT TO SECTION 12 OF THE SECURITIES EXCHANGE ACT OF 1934

The following description sets forth certain material terms and provisions of the securities of Milestone Pharmaceuticals Inc. (the "Company") that are registered under Section 12 of the Securities Exchange Act of 1934, as amended. The following description of our securities is intended as a summary only and is qualified in its entirety by reference to our articles of incorporation and amendments thereto and our bylaws, each of which are filed as exhibits to the Annual Report on Form 10-K of which this description is a part, and to the applicable provisions of the Business Corporations Act (Québec) (BCA).

General

Based upon shares outstanding as of December 31, 2019, our share capital consists of an unlimited number of common shares, no par value per share, of which 24,505,748 shares are issued and outstanding, and an unlimited number of preferred shares, no par value per share, none of which are issued and outstanding.

Common Shares

Outstanding Shares

As of December 31, 2019, we had 24,505,748 common shares outstanding, which were held by approximately 30 shareholders of record.

Voting Rights

Under our articles of incorporation, the holders of common shares are entitled to one vote for each share held at any meeting of the shareholders.

Dividends

Subject to the prior rights of holders of our preferred shares, if applicable, the holders of common shares are entitled to receive dividends as and when declared by our board of directors. 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.

Liquidation

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

Rights and Preferences

The holders of common shares have no preemptive, conversion rights or other subscription rights. There are no redemption or sinking fund provisions applicable to our common shares. There is no provision in

our articles of incorporation 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 may be subject to, and adversely affected by, the rights of the holders of any series of preferred shares that we may designate in the future.

Preferred Shares

We do not have any preferred shares outstanding. Under our articles of incorporation, we are 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.

Options

As of December 31, 2019, 2,584,666 common shares were issuable upon the exercise of outstanding share options, at a weighted-average exercise price of $3.755 per share. For additional information regarding terms of our equity incentive plans, see the section titled “— Equity Incentive Plans” elsewhere in this Annual Report on Form 10-K.

Registration Rights

Holders of certain of the common shares issued upon the conversion of our preferred shares in connection with our initial public offering on May 13, 2019 are 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 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 our initial public offering.

Demand Registration Rights

Beginning on May 13, 2020, the one year anniversary of the closing of our initial public offering, certain holders of the common shares issued upon conversion of our preferred shares will be entitled to certain demand registration rights. These demand rights permit holders of at least 25% of the registrable

securities then outstanding, on not more than two occasions, to 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

Holders of certain of the common shares issued upon conversion of our preferred shares are 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

Holders of certain of the common shares issued upon conversion of our preferred shares are entitled to certain Form S-3 registration rights. The holders of at least 25% of the 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 are listed on The Nasdaq Global 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 bylaws 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.

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in the Registration Statement on Form S-8 (No. 333-231347) of Milestone Pharmaceuticals Inc. of our report dated March 5, 2020 relating to the consolidated financial statements, which appears in this Form 10-K.

/s/ PricewaterhouseCoopers LLP[1]
Montréal, Québec, Canada

March 5, 2020

[1] CPA auditor, CA, public accountancy permit No. A113048

Exhibit 31.1

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

I, Joseph Oliveto, certify that:

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

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

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

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

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

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

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

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

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

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

Date: March 5, 2020

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

Exhibit 31.2

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

I, Amit Hasija, certify that:

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

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

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

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

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

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

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

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

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

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

Date: March 5, 2020

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

Exhibit 32.1

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

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

1. The Company's Annual Report on Form 10-K for the period ended December 31, 2019, to which this Certification is attached as Exhibit 32.1 (the "Periodic Report"), fully complies with the requirements of Section 13(a) or Section 15(d) of the Exchange Act; and

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

Dated: March 5, 2020

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