

PROSPECTUS SUPPLEMENT
(To Prospectus Dated November 12, 2021)**Up to \$47,249,368**
Common Shares

This prospectus supplement amends and restates the information in our prospectus supplement dated July 29, 2020 and, accordingly, the information in this prospectus supplement supersedes the information contained in that prospectus supplement, or the prior prospectus supplement. Pursuant to that prior prospectus supplement and accompanying base prospectus contained in our Registration Statement on Form S-3 (File No. 333-239318), or the prior prospectus, we have issued and sold 361,236 common shares, no par value, under the Open Market Sale AgreementSM, or the sales agreement, with Jefferies LLC, or Jefferies, dated July 29, 2020, for gross proceeds of approximately \$2.75 million. In accordance with the terms of the sales agreement, we may offer and sell common shares, without par value, having an aggregate offering price of up to \$50,000,000 from time to time through Jefferies, acting as our sales agent. In accordance with the terms of the sales agreement, under this prospectus supplement we may offer and sell common shares having an aggregate offering price of up to \$47,249,368 from time to time through Jefferies, acting as our sales agent, resulting in an aggregate of \$50,000,000 of common shares that may be sold under the sales agreement, including the \$2,750,632 of sales previously made through the date of this prospectus supplement pursuant to the prior prospectus.

Our common shares are listed on The Nasdaq Stock Market LLC, or Nasdaq, under the trading symbol "MIST." On May 26, 2023, the last reported sale price of our common shares on Nasdaq was \$3.98 per share.

Sales of our common shares, if any, under this prospectus supplement and the accompanying prospectus may be made in sales deemed to be "at the market offerings" as defined in Rule 415 promulgated under the Securities Act of 1933, as amended, or the Securities Act. Jefferies is not required to sell any specific number or dollar amount of our common shares, but will act as our sales agent and use commercially reasonable efforts to sell on our behalf all of the common shares requested to be sold by us, consistent with its normal sales and trading practices, on mutually agreed terms between Jefferies and us. There is no arrangement for funds to be received in any escrow, trust or similar arrangement.

Jefferies will be entitled to compensation under the terms of the sales agreement at a fixed commission rate of up to 3.0% of the gross sales price per share sold under the sales agreement. See "Plan of Distribution" beginning on page S-11 for additional information regarding Jefferies' compensation. In connection with the sale of our common shares on our behalf, Jefferies will be deemed to be an "underwriter" within the meaning of the Securities Act and the compensation of Jefferies will be deemed to be underwriting commissions or discounts. We have also agreed to provide indemnification and contribution to Jefferies with respect to certain liabilities, including liabilities under the Securities Act.

We are an "emerging growth company" as defined under federal securities laws and, as such, have elected to comply with certain reduced public company reporting requirements. See "Summary Implications of Being an Emerging Growth Company and Smaller Reporting Company."

Investing in our securities involves a high degree of risk. You should review carefully the risks and uncertainties described under the heading "Risk Factors," beginning on page S-5 of this prospectus supplement and under similar headings in the accompanying prospectus and the other documents that are incorporated by reference into this prospectus supplement and the accompanying prospectus.

NEITHER THE SECURITIES AND EXCHANGE COMMISSION NOR ANY STATE SECURITIES COMMISSION HAS APPROVED OR DISAPPROVED OF THESE SECURITIES OR DETERMINED IF THIS PROSPECTUS SUPPLEMENT IS TRUTHFUL OR COMPLETE. ANY REPRESENTATION TO THE CONTRARY IS A CRIMINAL OFFENSE.

Jefferies

The date of this prospectus supplement is May 31, 2023.

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ABOUT THIS PROSPECTUS SUPPLEMENT

This document is part of a “shelf” registration statement on Form S-3 that we filed with the Securities and Exchange Commission, or the SEC, and is in two parts. The first part is this prospectus supplement, which describes the specific terms of this offering and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference herein. The second part, the accompanying prospectus dated November 12, 2021, provides more general information. Generally, when we refer to this prospectus, we are referring to both parts of this document combined. To the extent there is a conflict between the information contained in this prospectus supplement and the information contained in the accompanying prospectus or any document incorporated by reference therein filed prior to the date of this prospectus supplement, you should rely on the information in this prospectus supplement; provided that if any statement in one of these documents is inconsistent with a statement in another document having a later date—for example, a document incorporated by reference in the accompanying prospectus—the statement in the document having the later date modifies or supersedes the earlier statement.

We further note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference herein were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreements, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

Neither we nor Jefferies have authorized any person to provide any information or to make any representation other than those contained or incorporated by reference in this prospectus supplement or in the accompanying prospectus. We and Jefferies take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you.

The information contained in this prospectus supplement or the accompanying prospectus, or incorporated by reference herein or therein is accurate only as of the respective dates thereof, regardless of the time of delivery of this prospectus supplement and the accompanying prospectus or of any sale of our securities. It is important for you to read and consider all information contained in this prospectus supplement and the accompanying prospectus, including the documents incorporated by reference herein and therein, in making your investment decision. You should also read and consider the information in the documents to which we have referred you in the sections entitled “Where You Can Find More Information” and “Incorporation of Certain Information by Reference” in this prospectus supplement and in the accompanying prospectus.

We are not, and Jefferies is not, making an offer to sell our shares in any jurisdiction where the offer and sale is not permitted. The distribution of this prospectus supplement and the accompanying prospectus and this offering in certain jurisdictions may be restricted by law. Persons outside the United States who come into possession of this prospectus supplement and the accompanying prospectus must inform themselves about, and observe any restrictions relating to, this offering and the distribution of this prospectus supplement and the accompanying prospectus outside the United States. This prospectus supplement and the accompanying prospectus do not constitute, and may not be used in connection with, an offer to sell, or a solicitation of an offer to buy, any securities offered by this prospectus supplement and the accompanying prospectus by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation.

Unless otherwise mentioned or unless the context requires otherwise, all references in this prospectus to “Milestone,” “company,” “we,” “us” and “our” or similar references refer to Milestone Pharmaceuticals Inc. and its consolidated subsidiary.

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights certain information about us, this offering and selected information contained elsewhere in or incorporated by reference into this prospectus supplement or the accompanying prospectus. This summary is not complete and does not contain all of the information that you should consider before deciding whether to invest in our common shares. For a more complete understanding of our company and this offering, we encourage you to read and consider carefully the more detailed information in this prospectus supplement and the accompanying prospectus, including the information incorporated by reference in this prospectus supplement or the accompanying prospectus, and the information included in any free writing prospectus that we have authorized for use in connection with this offering, including the information under the heading "Risk Factors" in this prospectus supplement and under similar headings in our most recently filed [Annual Report on Form 10-K](#) and in our subsequently filed [Quarterly Reports on Form 10-Q](#), which are incorporated by reference into this prospectus supplement and the accompanying prospectus along with our consolidated financial statements and notes to those consolidated financial statements, before making an investment decision.

Unless the context indicates otherwise, references in this prospectus to "Milestone," "company," "we," "us" and "our" refer to Milestone Pharmaceuticals Inc. and its wholly-owned subsidiary Milestone Pharmaceuticals USA Inc.

COMPANY OVERVIEW

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

PSVT is a highly symptomatic and impactful heart arrhythmia characterized by unpredictable attacks of a racing heart, often exceeding 150 beats per minute. Symptoms of PSVT often arise suddenly and include palpitations, sweating, chest pressure or pain, shortness of breath, sudden onset of fatigue, lightheadedness or dizziness, fainting, and anxiety, causing many patients to interrupt their daily activities at the time of symptom-onset. The impact and morbidity from an episode of PSVT can be especially detrimental in patients with underlying cardiovascular or medical conditions, such as heart failure, obstructive coronary disease, or dehydration. The uncertainty of when such an attack of PSVT will strike or how long it will persist is anxiety-provoking, reduces patients' quality of life and prevents participation in many desired activities. Drugs approved for the treatment of PSVT attacks include adenosine, verapamil, and diltiazem, with all being administered intravenously under medical supervision, usually in the emergency department. Other oral drugs are sometimes used to treat attacks in a concept called "pill in the pocket." However, those drugs have never been proven effective or safe and are not approved for this use. Doctors are frustrated by the lack of effective treatment options besides a prolonged, unpleasant, and costly trip to the emergency department or, for some patients, an invasive ablation procedure. PSVT is traumatic for patients, frustrating for healthcare providers, and costly for payers. With no pharmaceutical innovation in the treatment of PSVT for over 30 years and a movement in the healthcare system to enable patient centered care, there is an opportunity to help patients living with PSVT to take greater control over their PSVT attacks.

Atrial Fibrillation, or AFib, is a common form of arrhythmia with an irregular and often rapid heart rate that is often markedly symptomatic and, without proper treatment, can increase the risk of stroke, heart failure, and other cardiovascular complications. A common complication of AFib is a rapid ventricular rate, or AFib-RVR, which is frequently defined as a heart rate ≥ 110 beats per minute. The occurrence of a rapid ventricular rate in patients with atrial fibrillation increases the likelihood of symptoms including heart palpitations, shortness of breath and weakness. There are two commonly used pharmacological approaches to chronically manage AFib, rhythm control and rate control. Regardless of the chronic approach, when faced with an episode of AFib-RVR, acute rate control is called for most commonly in the form of oral AV-nodal targeted drugs such as a beta blocker or calcium channel blockers. However, these oral rate control drugs, when used acutely, do not

adequately provide immediate ventricular rate control due to a 30- to 60-minute delayed onset of action, and, as a result, many patients seek faster and more certain rate reduction and symptom resolution by going to the emergency department for acute treatment utilizing intravenous rate control and/or electrical cardioversion of their atrial fibrillation. Similar to PSVT, patients feel a loss of control by needing to visit the emergency department for overcoming their atrial fibrillation attack, doctors are frustrated by the lack of options for patients to self-manage these acute rate attacks and payer organizations would prefer to treat the AFib-RVR attacks in a more cost effective and time-efficient manner.

Our objective is to develop and commercialize etripamil as a fast-acting nasal spray to be prescribed by the doctor so that the patient can carry etripamil with them for use wherever and whenever an attack occurs. We have completed patient conduct (last patient last visit) in the Phase 3 clinical trials for the lead indication and we plan to submit a New Drug Application, or NDA, for marketing approval in the United States for etripamil for the treatment of PSVT in the third quarter of 2023. If approved, we believe that etripamil will provide the patient with a portable treatment to stop an attack in at-home and to reduce the reliance on the emergency department. We believe that this may help patients to live their lives with less concern over when their next PSVT attack will occur. For health care providers, etripamil could represent a new tool they can offer to their patients to better self-manage their PSVT attacks resulting in fewer calls to their office, a more efficient use of healthcare resources, and more empowered, satisfied patients.

Etripamil is currently in Phase 2 clinical development for assessing its safety and effectiveness in AFib-RVR. Similar to our approach for PSVT, we believe that etripamil has the potential to help the patient experiencing a symptomatic episode of AFib-RVR to self-manage their condition by conveniently, reliably and quickly reducing their elevated heart rate wherever and whenever the episode occurs, thereby reducing the need for emergency department utilization that many patients currently seek.

We believe that PSVT is a large and under-recognized market that we estimate affects approximately two million Americans and results in over 150,000 emergency department visits and hospital admissions and up to 80,000 ablations per year. From this diagnosed population, we define the target addressable market for etripamil as the 40 to 60% of patients who experience frequent and longer, moderate to severe episodes each year. After being exposed to the data from the RAPID clinical study in market research, cardiologists reported a willingness to prescribe etripamil to approximately 50% of the patients with PSVT in their care, which suggests 500,000 to 800,000 patients can potentially be treated with etripamil in the peak year. Additionally, we believe that these target patients will use etripamil to treat a median of five episodes per year based on the projected number of longer or more intense episodes (self-reported) experienced by the patient. This implies demand in the US for etripamil of 2.5 million to 4 million episodes treated in the peak year.

The American Heart Association estimates a prevalence for AFib of seven million by 2030, while the Centers for Disease Control (CDC) reports this prevalence as increasing to 12 million over the same time period. According to the Healthcare and Utilization Project, AFib resulted in 660,000 patient visits to the emergency department and 465,000 admissions to the hospital in 2016. From market research we estimate the target addressable market for etripamil in patients with AFib and rapid ventricular rate (RVR) as approximately 30 to 40% of the diagnosed prevalent population, defined as patients experiencing at least one symptomatic episode of AFib-RVR requiring treatment per year.

Corporate Information

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

Implications of Being an Emerging Growth Company and a Smaller Reporting Company

We are an “emerging growth company” as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. For so long as we remain an emerging growth company, we are permitted and intend to take

advantage of specified reduced reporting and other burdens that are otherwise applicable generally to public 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 in our periodic reports, proxy statements and registration statements; and
- not being required to hold a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved.

We may take advantage of these reporting exemptions until we are no longer an emerging growth company. We will remain an emerging growth company 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 \$1.235 billion; (iii) the last day of the fiscal year in which we are deemed to be a large accelerated filer, which means the market value of our common shares held by non-affiliates exceeds \$700 million as of June 30 of such fiscal year; or (iv) the date on which we have issued more than \$1 billion in non-convertible debt during the prior three-year period. We may choose to take advantage of some or all of these available exemptions. We have taken advantage of some reduced reporting requirements in our public filings. Accordingly, the information that we provide stockholders may be different than the information you receive from other public companies in which you hold stock.

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

We are also a smaller reporting company as defined in the Securities Exchange Act of 1934, as amended, or the Exchange Act. We may continue to be a smaller reporting company even after we are no longer an emerging growth company. We may take advantage of certain of the scaled disclosures available to smaller reporting companies and will be able to take advantage of these scaled disclosures for so long as (i) our voting and non-voting common shares held by nonaffiliates is less than \$250.0 million measured on the last business day of our second fiscal quarter or (ii) our annual revenue is less than \$100.0 million during the most recently completed fiscal year and our voting and non-voting common shares held by non-affiliates is less than \$700.0 million measured on the last business day of our second fiscal quarter.

THE OFFERING

Common Shares Offered by Us	Common shares having an aggregate offering price of up to \$47,249,368.
Plan of Distribution	“At the market offering” that may be made from time to time through our sales agent, Jefferies. See “Plan of Distribution” on page S-12 of this prospectus supplement.
Use of Proceeds	We currently intend to use the net proceeds from this offering primarily for working capital and general corporate purposes. See “Use of Proceeds” on page S-11 of this prospectus supplement.
Risk Factors	Investing in our common shares involves significant risks. See “Risk Factors” on page S-5 of this prospectus supplement, and under similar headings in other documents that we have filed or that are filed after the date hereof and incorporated by reference into this prospectus supplement.
Nasdaq Stock Market LLC Symbol	“MIST”

RISK FACTORS

Investing in our common shares involves a high degree of risk. Before deciding whether to invest in our common shares, you should carefully review the risks and uncertainties described below and under the section titled "Risk Factors" in our [Annual Report on Form 10-K for the year ended December 31, 2022](#) and our [Quarterly Report on Form 10-Q for the quarter ended March 31, 2023](#), which are incorporated by reference into this prospectus supplement and the accompanying prospectus in their entirety, as updated or superseded by the risks and uncertainties described under similar headings in the other documents that are filed after the date hereof and incorporated by reference into this prospectus supplement, together with other information in this prospectus supplement, the accompanying prospectus, the information and documents incorporated by reference herein and therein, and in any free writing prospectus that we have authorized for use in connection with this offering. Each of the risk factors could adversely affect our business, operating results and financial condition, as well as adversely affect the value of an investment in our shares, and the occurrence of any of these risks might cause you to lose all or part of your investment. Additional risks not presently known to us or that we currently believe are immaterial may also significantly impair our business operations. Please also read carefully the section below titled "Special Note Regarding Forward-Looking Statements."

Additional Risks Related to This Offering

You may experience immediate and substantial dilution.

The offering price per share in this offering may exceed the net tangible book value per share of our common shares outstanding prior to this offering. Assuming that an aggregate of 11,871,700 of our common shares are sold at a price of \$3.98 per share, the last reported sale price of our common shares on Nasdaq on May 26, 2023, for aggregate gross proceeds of \$47.25 million, and after deducting commissions and estimated offering expenses payable by us, you would experience immediate dilution of \$1.77 per share, representing the difference between our as adjusted net tangible book value per share as of March 31, 2023 after giving effect to this offering at the assumed offering price. The exercise of outstanding shares options would result in further dilution of your investment. See the section entitled "Dilution" below for a more detailed illustration of the dilution you would incur if you participate in this offering. Because the sales of the shares offered hereby will be made directly into the market or in negotiated transactions, the prices at which we sell these shares will vary and these variations may be significant. Purchasers of the shares we sell, as well as our existing shareholders, will experience significant dilution if we sell shares at prices significantly below the price at which they invested.

You may experience future dilution as a result of future equity offerings.

To raise additional capital, we may in the future offer additional common shares or other securities convertible into or exchangeable for our common shares at prices that may not be the same as the price per share in this offering. We may sell shares or other securities in any other offering at a price per share that is less than the price per share paid by investors in this offering, and investors purchasing shares or other securities in the future could have rights superior to existing shareholders. The price per share at which we sell additional common shares, or securities convertible or exchangeable into common shares, in future transactions may be higher or lower than the price per share paid by investors in this offering.

The common shares offered hereby will be sold in "at the market offerings," and investors who buy shares at different times will likely pay different prices.

Investors who purchase shares in this offering at different times will likely pay different prices, and so may experience different outcomes in their investment results. We will have discretion, subject to market demand, to vary the timing, prices, and numbers of shares sold, and there is no minimum or maximum sales price. Investors may experience a decline in the value of their shares as a result of share sales made at prices lower than the prices they paid.

Our management will have broad discretion as to the use of the net proceeds from this offering and might apply the net proceeds from this offering in ways with which you do not agree and in ways that may impair the value of your investment.

We currently intend to use the net proceeds from this offering primarily for working capital and general corporate purposes. Pending these uses, we expect to invest the net proceeds in short-term, interest-bearing obligations, certificates of deposit or direct or guaranteed obligations of the United States. Our management has broad discretion as to the use of these proceeds and you will be relying on the judgment of our management regarding the application of these proceeds. We might apply these proceeds in ways with which you do not agree, or in ways that do not yield a favorable return. If our management applies these proceeds in a manner that does not yield a significant return, if any, on our investment of these net proceeds, it could compromise our ability to pursue our growth strategy and adversely affect the market price of our common shares.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus, the documents incorporated by reference herein and therein and any free writing prospectus that we have authorized for use in connection with this offering contain may contain forward-looking statements within the meaning of the federal securities laws about us and our industry that involve substantial risks and uncertainties. All statements other than statements of historical facts contained in this prospectus, including statements regarding our strategy, future financial condition, future operations, projected costs, prospects, plans, objectives of management and expected market growth, are forward-looking statements pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995 and other federal securities laws. In some cases, you can identify forward-looking statements by terminology such as “aim,” “anticipate,” “assume,” “believe,” “contemplate,” “continue,” “could,” “design,” “due,” “estimate,” “expect,” “goal,” “intend,” “may,” “objective,” “plan,” “predict,” “positioned,” “potential,” “seek,” “should,” “target,” “will,” “would” and other similar expressions that are predictions of or indicate future events and future trends, or the negative of these terms or other comparable terminology.

We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our financial condition, results of operations, business strategy and financial needs. These forward-looking statements are subject to a number of known and unknown risks, uncertainties and assumptions, including risks described in the section titled “Risk Factors” and elsewhere in this prospectus supplement, the accompanying prospectus, the documents incorporated by reference herein or therein, or in any free writing prospectus that we have authorized for use in connection with this offering. Within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act, these forward-looking statements include statements regarding:

- the initiation, timing, progress and results of our current and future clinical trials of etripamil, including our Phase 3 clinical trials of etripamil for the treatment of paroxysmal supraventricular tachycardia, our Phase 2 clinical trial of etripamil for the treatment of atrial fibrillation with rapid ventricular rate, and of our research and development programs;
- our plans to develop and commercialize etripamil and any future product candidates;
- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing;
- our ability to develop and, if approved by regulatory authorities, commercialize etripamil in China and Taiwan through our license agreement with Ji Xing Pharmaceuticals;
- our ability to establish collaborations or obtain additional funding;
- our ability to obtain regulatory approval of our current and future product candidates;
- our expectations regarding the potential market size and the rate and degree of market acceptance of etripamil and any future product candidates;
- our ability to fund our working capital requirements and expectations regarding the sufficiency of our capital resources;
- the implementation of our business model and strategic plans for our business, etripamil and any future product candidates;
- our intellectual property position and the duration of our patent rights;
- developments or disputes concerning our intellectual property or other proprietary rights;
- our expectations regarding government and third-party payer coverage and reimbursement;
- our ability to compete in the markets we serve;
- the impact of government laws and regulations;
- developments relating to our competitors and our industry; and
- other factors that may impact our financial results.

The foregoing list of risks is not exhaustive. Other sections of this prospectus supplement, the accompanying prospectus, the documents incorporated by reference herein or therein, or in any free writing prospectus that we

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

In light of the significant uncertainties in these forward-looking statements, you should not rely upon forward-looking statements as predictions of future events. Although we believe that we have a reasonable basis for each forward-looking statement contained in this prospectus supplement, the accompanying prospectus, the documents incorporated by reference herein or therein, or in any free writing prospectus that we have authorized for us in connection with this offering, 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. Factors that may cause actual results to differ materially from current expectations include, among other things, those listed under the section entitled "Risk Factors" in this prospectus, as may be updated from time to time by our future filings under the Securities Exchange Act of 1934, as amended, or the Exchange Act, and discussed elsewhere in this prospectus supplement, the accompanying prospectus, the documents incorporated by reference herein or therein, or in any free writing prospectus that we have authorized for us in connection with this offering. You should carefully review all of these factors. 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, or the Securities Act, do not protect any forward-looking statements that we make in connection with this prospectus supplement, the accompanying prospectus, the documents incorporated by reference herein or therein, or in any free writing prospectus that we have authorized for us in connection with this offering.

This prospectus supplement, the accompanying prospectus, the documents incorporated by reference herein or therein, or in any free writing prospectus that we have authorized for us in connection with this offering may also contain estimates, projections and other information concerning our industry, our business, and the markets for certain diseases, including data regarding the estimated size of those markets. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances reflected in this information.

DILUTION

Investors purchasing our common shares in this offering may experience substantial dilution in the net tangible book value of their common shares. Our historical net tangible book value as of March 31, 2023 was approximately \$53.9 million, or \$1.62 per common share. Net tangible book value per share is determined by dividing our total tangible assets, less total liabilities, by the number of common shares outstanding as of March 31, 2023. Dilution with respect to net tangible book value per share represents the difference between the amount per share paid by purchasers of common shares in this offering and the net tangible book value per share of our common shares immediately after this offering.

After giving effect to the sale of 11,871,700 shares of our common stock in this offering at an assumed public offering price of \$3.98 per share, the last reported sale price of our common stock on Nasdaq on May 26, 2023, and after deducting estimated commissions and offering expenses payable by us, our as adjusted net tangible book value as of March 31, 2023 would have been \$99.8 million, or \$2.21 per share. This represents an immediate increase in net tangible book value of \$0.59 per share to existing stockholders and immediate dilution of \$1.77 per share to investors purchasing our common stock in this offering at the public offering price. The following table illustrates this dilution on a per share basis:

Assumed public offering price per share	\$3.98
Net tangible book value per share as of March 31, 2023	\$1.62
Increase in adjusted net tangible book value per share attributable to this offering	\$0.59
As adjusted net tangible book value per share as of March 31, 2023, after giving effect to this offering	\$2.21
Dilution per share to investors purchasing our common stock in this offering	\$1.77

The table above assumes for illustrative purposes that an aggregate of 11,871,700 common shares are sold during the term of the sales agreement with Jefferies at a price of \$3.98 per share, the last reported sale price of our common shares on Nasdaq on May 26, 2023, for aggregate gross proceeds of \$47.25 million. The shares subject to the sales agreement with Jefferies are being sold from time to time at various prices. An increase of \$1.00 per share in the price at which the shares are sold from the assumed offering price of \$3.98 per share shown in the table above, assuming all of our common shares in the aggregate amount of \$47.25 million during the term of the sales agreement with Jefferies is sold at that price, would increase our as adjusted net tangible book value per share after the offering to \$2.33 per share and would increase the dilution in net tangible book value per share to new investors in this offering to \$2.65 per share, after deducting commissions and estimated aggregate offering expenses payable by us. A decrease of \$1.00 per share in the price at which the shares are sold from the assumed offering price of \$3.98 per share shown in the table above, assuming all of our common shares in the aggregate amount of \$47.25 million during the term of the sales agreement with Jefferies is sold at that price, would decrease our as adjusted net tangible book value per share after the offering to \$2.03 per share and would decrease the dilution in net tangible book value per share to new investors in this offering to \$0.95 per share, after deducting commissions and estimated aggregate offering expenses payable by us. This information is supplied for illustrative purposes only.

The above discussion and table are based on 33,337,214 common shares outstanding as of March 31, 2023, and exclude:

4,728,819 common shares issuable upon the exercise of outstanding options as of March 31, 2023, at a weighted-average exercise price of \$6.62 per share;

1,347,085 common shares reserved for future issuance under our 2019 Equity Incentive Plan, or the 2019 Plan, as well as any future increases in the number of common shares reserved for issuance under the 2019 Plan;

497,000 common shares reserved for future issuance under our 2021 Inducement Plan, or the 2021 Plan, as well as any future increases in the number of common shares reserved for issuance under the 2021 Plan;

1,420,948 common shares reserved for future issuance under our 2019 Employee Share Purchase Plan, or the ESPP, as of March 31, 2023, as well as any future increases in the number of common shares reserved for issuance under the ESPP;

9,577,257 common shares issuable upon the exercise of outstanding pre-funded warrants as of March 31, 2023, at an exercise price of \$0.01 per share; and

up to 13,888,850 common shares, of which (a) 9,552,740 common shares are issuable upon the conversion of Milestone's senior secured convertible promissory notes, or the Notes, and (b) 4,336,110 additional common shares, which represents the maximum number of additional common shares issuable in connection with an adjustment to the conversion rate of the Notes if a holder of Notes exercises its conversion right upon the occurrence of certain transactions, in each case as of March 31, 2023.

To the extent that outstanding options or warrants outstanding as of March 31, 2023 have been or may be exercised or other shares issued, investors purchasing our common shares in this offering may experience further dilution. We will require more capital to pursue our preclinical and clinical activities, regulatory approval and the commercialization of our current or future drug candidates. In addition, we may choose to raise additional capital due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. To the extent that additional capital is raised through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our shareholders.

USE OF PROCEEDS

We may issue and sell common shares having aggregate sales proceeds of up to \$47,249,368 from time to time. Because there is no minimum offering amount required as a condition to close this offering, the actual total public offering amount, commissions and proceeds to us, if any, are not determinable at this time. There can be no assurance that we will sell any shares under or fully utilize the sales agreement with Jefferies as a source of financing.

We currently intend to use the net proceeds from this offering primarily for working capital and general corporate purposes. We may also use a portion of the net proceeds to invest in or acquire businesses or technologies that we believe are complementary to our own, although we have no current plans, commitments or agreements with respect to any acquisitions as of the date of this prospectus supplement. Pending these uses, we expect to invest the net proceeds in short-term, interest bearing obligations, certificates of deposit or direct or guaranteed obligations of the United States.

PLAN OF DISTRIBUTION

We have entered into a sales agreement with Jefferies, under which we may offer and sell up to \$50.0 million of our common shares from time to time through Jefferies acting as agent. Sales of our common shares, if any, under this prospectus supplement and the accompanying prospectus will be made by any method that is deemed to be an "at the market offering" as defined in Rule 415(a)(4) under the Securities Act.

Each time we wish to issue and sell our common shares under the sales agreement, we will notify Jefferies of the number of shares to be issued, the dates on which such sales are anticipated to be made, any limitation on the number of shares to be sold in any one day and any minimum price below which sales may not be made. Once we have so instructed Jefferies, unless Jefferies declines to accept the terms of such notice, Jefferies has agreed to use its commercially reasonable efforts consistent with its normal trading and sales practices to sell such shares up to the amount specified on such terms. The obligations of Jefferies under the sales agreement to sell our common shares are subject to a number of conditions that we must meet.

The settlement of sales of shares between us and Jefferies is generally anticipated to occur on the second trading day following the date on which the sale was made. Sales of our common shares as contemplated in this prospectus supplement will be settled through the facilities of The Depository Trust Company or by such other means as we and Jefferies may agree upon. There is no arrangement for funds to be received in an escrow, trust or similar arrangement.

We will pay Jefferies a commission of up to 3.0% of the aggregate gross proceeds we receive from each sale of our common shares under the sales agreement. Because there is no minimum offering amount required as a condition to close this offering, the actual total public offering amount, commissions and proceeds to us, if any, are not determinable at this time. In addition, we have agreed to reimburse Jefferies for the fees and disbursements of its counsel, payable upon execution of the sales agreement, in an amount not to exceed \$65,000. We estimate that the total expenses for the offering, excluding any commissions or expense reimbursement payable to Jefferies under the terms of the sales agreement, will be approximately \$250,000. The remaining sale proceeds, after deducting any other transaction fees, will equal our net proceeds from the sale of such shares.

Jefferies will provide written confirmation to us before the open on Nasdaq on the day following each day on which our common shares are sold under the sales agreement. Each confirmation will include the number of shares sold on that day, the aggregate gross proceeds of such sales and the proceeds to us.

In connection with the sale of our common shares on our behalf, Jefferies will be deemed to be an "underwriter" within the meaning of the Securities Act, and the compensation of Jefferies will be deemed to be underwriting commissions or discounts. We have agreed to indemnify Jefferies against certain civil liabilities, including liabilities under the Securities Act. We have also agreed to contribute to payments Jefferies may be required to make in respect of such liabilities.

The offering of our common shares pursuant to the sales agreement will terminate upon the earlier of (i) the sale of all common shares subject to the sales agreement and (ii) the termination of the sales agreement as permitted therein. We and Jefferies may each terminate the sales agreement at any time upon five (5) trading days' prior notice.

This summary of the material provisions of the sales agreement does not purport to be a complete statement of its terms and conditions. A copy of the sales agreement is filed as Exhibit 10.1 to a Current Report on Form 8-K filed under the Exchange Act with the SEC on July 29, 2020 and incorporated by reference in this prospectus supplement.

Jefferies and its affiliates may in the future provide various investment banking, commercial banking, financial advisory and other financial services for us and our affiliates, for which services they may in the future receive customary fees. In the course of its business, Jefferies may actively trade our securities for its own account or for the accounts of customers, and, accordingly, Jefferies may at any time hold long or short positions in such securities.

A prospectus supplement and the accompanying prospectus in electronic format may be made available on a website maintained by Jefferies, and Jefferies may distribute the prospectus supplement and the accompanying prospectus electronically.

LEGAL MATTERS

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

EXPERTS

The consolidated financial statements incorporated in this prospectus by reference to the [Annual Report on Form 10-K for the year ended December 31, 2022](#) have been so incorporated in reliance on the report of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

SERVICE OF PROCESS AND ENFORCEMENT OF LIABILITIES

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

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

WHERE YOU CAN FIND MORE INFORMATION

This prospectus is part of a registration statement we filed with the SEC. This prospectus does not contain all of the information set forth in the registration statement and the exhibits to the registration statement. For further information with respect to us and the securities we are offering under this prospectus, we refer you to the registration statement and the exhibits and schedules filed as a part of the registration statement. You should rely only on the information contained in this prospectus or incorporated by reference. We have not authorized anyone else to provide you with different information. We are not making an offer of these securities in any state where the offer is not permitted. You should not assume that the information in this prospectus is accurate as of any date other than the date on the front page of this prospectus, regardless of the time of delivery of this prospectus or any sale of the securities offered by this prospectus.

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

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows the Company to "incorporate by reference" the information that is filed by the Company with the SEC, which means that the Company can disclose important information to you by referring you to those documents. The documents incorporated by reference are:

1. [The Company's Annual Report on Form 10-K for the year ended December 31, 2022, which was filed with the SEC on March 29, 2023](#), as amended by the Form 10-K/A, which was filed with the SEC on May 30, 2023;
2. [The Company's Quarterly Report on Form 10-Q for the fiscal quarter ended March 31, 2023, which was filed with the SEC on May 11, 2023](#);
3. The information specifically incorporated by reference in the Company's [Annual Report on Form 10-K for the year ended December 31, 2022, which was filed with the SEC on March 29, 2023](#), from the Company's [Definitive Proxy Statement on Schedule 14A relating to the Company's 2023 Annual Meeting of Stockholders, which was filed with the SEC on April 28, 2023](#);
4. The Company's Current Reports on Form 8-K filed with the SEC on [March 27, 2023](#), [March 28, 2023](#) and [March 31, 2023](#); and
5. [The description of the Company's common shares, which is contained in a registration statement on Form 8-A filed on May 6, 2019 \(File No. 001-38899\) under Section 12\(b\) of the Exchange Act, including any amendment or report filed for the purpose of updating such description](#).

Notwithstanding the statements in the preceding paragraphs, no document, report or exhibit (or portion of any of the foregoing) or any other information that we have "furnished" to the SEC pursuant to the Exchange Act shall be incorporated by reference into this prospectus supplement.

All documents we file with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act, other than any information furnished pursuant to Item 2.02, Item 7.01 or Item 9.01 of any Current Report on Form 8-K (unless we specifically state in such Current Report that such information is to be considered "filed" under the Exchange Act, or otherwise specifically incorporate the information by reference into this prospectus supplement or any other filing under the Securities Act or the Exchange Act), on or after the date of this prospectus until the earlier of the date on which all of the securities registered hereunder have been sold or the registration statement of which this prospectus is a part has been withdrawn, shall be deemed incorporated by reference in this prospectus and to be a part of this prospectus from the date of filing of those documents.

Any statement contained in a document incorporated or deemed to be incorporated by reference herein shall be deemed to be modified or superseded, for purposes of this prospectus supplement, to the extent that a statement contained in or omitted from this prospectus supplement, or in any other subsequently filed document that also is or is deemed to be incorporated by reference herein, modifies or supersedes such statement. Any such statement so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this prospectus. Except as set forth in the parenthetical in the immediately precedent paragraph, nothing in this prospectus supplement shall be deemed to incorporate information furnished, but not filed, with the SEC pursuant to Item 2.02 or Item 7.01 of Form 8-K.

Upon written or oral request, we will provide, without charge, to each person, including any beneficial owner, to whom a copy of a prospectus is delivered, upon such person's written or oral request, a copy of any and all of the information incorporated by reference in this prospectus supplement, other than exhibits to such documents, unless such exhibits are specifically incorporated by reference into the information that this prospectus supplement incorporates. Requests should be directed to Milestone Investor Relations at Milestone Pharmaceuticals Inc., 1111 Dr. Frederik-Philips Boulevard, Suite 420, Montréal, Québec, Canada H4M 2X6, or send an email to Milestone Investor Relations at ir@milestonepharma.com. You may also find these documents in the "Investors & Media" section of our website, www.milestonepharma.com. The information on our website is not incorporated into this prospectus supplement.

PROSPECTUS



\$250,000,000

**Common Shares
Preferred Shares
Debt Securities
Warrants**

From time to time, we may offer and sell up to \$250,000,000 of any combination of the securities described in this prospectus in one or more offerings. We may also offer securities as may be issuable upon conversion, redemption, repurchase, exchange or exercise of any securities registered hereunder, including any applicable anti-dilution provisions.

This prospectus provides a general description of the securities we may offer. Each time we offer securities, we will provide specific terms of the securities offered in a supplement to this prospectus. We may also authorize one or more free writing prospectuses to be provided to you in connection with these offerings. The prospectus supplement and any related free writing prospectus may also add, update or change information contained in this prospectus. You should carefully read this prospectus, the applicable prospectus supplement and any related free writing prospectus, as well as any documents incorporated by reference, before you invest in any of the securities being offered.

This prospectus may not be used to consummate a sale of any securities unless accompanied by a prospectus supplement.

We will sell these securities directly to investors, through agents designated from time to time or to or through underwriters or dealers, on a continuous or delayed basis. For additional information on the methods of sale, you should refer to the section entitled "Plan of Distribution" in this prospectus and in the applicable prospectus supplement. If any agents or underwriters are involved in the sale of any securities with respect to which this prospectus is being delivered, the names of such agents or underwriters and any applicable fees, commissions, discounts or over-allotment options will be set forth in a prospectus supplement. The price to the public of such securities and the net proceeds we expect to receive from such sale will also be set forth in a prospectus supplement.

Our common shares trade on the Nasdaq Global Select Market under the symbol "MIST." On November 11, 2021, the last reported sale price of our common shares was \$5.60 per share. The applicable prospectus supplement will contain information, where applicable, as to any other listing on the Nasdaq Global Select Market or any securities market or other exchange of the securities, if any, covered by the prospectus supplement.

We are an "emerging growth company" as defined under federal securities laws and, as such, have elected to comply with certain reduced public company reporting requirements. See "Summary — Implications of Being an Emerging Growth Company and Smaller Reporting Company."

Investing in our securities involves a high degree of risk. You should review carefully the risks and uncertainties described under the heading "Risk Factors" contained in the applicable prospectus supplement and any related free writing prospectus we have authorized for use in connection with a specific offering, and under similar headings in the other documents that are incorporated by reference into this prospectus as described on page 44 of this prospectus.

NEITHER THE SECURITIES AND EXCHANGE COMMISSION NOR ANY STATE SECURITIES COMMISSION HAS APPROVED OR DISAPPROVED OF THESE SECURITIES OR DETERMINED IF THIS PROSPECTUS IS TRUTHFUL OR COMPLETE. ANY REPRESENTATION TO THE CONTRARY IS A CRIMINAL OFFENSE.

The date of this prospectus is November 12, 2021.

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ABOUT THIS PROSPECTUS

This prospectus is a part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission, or SEC, utilizing a “shelf” registration process. Under this shelf registration statement, we may sell any combination of the securities described in this prospectus in one or more offerings up to a total aggregate offering price of \$250,000,000. This prospectus provides you with a general description of the securities we may offer.

Each time we sell securities under this prospectus, we will provide a prospectus supplement that will contain specific information about the terms of that offering. We may also authorize one or more free writing prospectuses to be provided to you that may contain material information relating to these offerings. The prospectus supplement and any related free writing prospectus that we may authorize to be provided to you may also add, update or change information contained in this prospectus or in any documents that we have incorporated by reference into this prospectus. You should read this prospectus, any applicable prospectus supplement and any related free writing prospectus, together with the information incorporated herein by reference as described under the heading “Incorporation of Certain Information by Reference,” before investing in any of the securities offered.

THIS PROSPECTUS MAY NOT BE USED TO CONSUMMATE A SALE OF SECURITIES UNLESS IT IS ACCOMPANIED BY A PROSPECTUS SUPPLEMENT.

Neither we, nor any agent, underwriter or dealer has authorized any person to give any information or to make any representation other than those contained or incorporated by reference in this prospectus, any applicable prospectus supplement or any related free writing prospectus prepared by or on behalf of us or to which we have referred you. This prospectus, any applicable supplement to this prospectus or any related free writing prospectus do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the registered securities to which they relate, nor do this prospectus, any applicable supplement to this prospectus or any related free writing prospectus constitute an offer to sell or the solicitation of an offer to buy securities in any jurisdiction to any person to whom it is unlawful to make such offer or solicitation in such jurisdiction.

You should not assume that the information contained in this prospectus, any applicable prospectus supplement or any related free writing prospectus is accurate on any date subsequent to the date set forth on the front of the document or that any information we have incorporated by reference is correct on any date subsequent to the date of the document incorporated by reference, even though this prospectus, any applicable prospectus supplement or any related free writing prospectus is delivered, or securities are sold, on a later date.

This prospectus and the information incorporated herein by reference contain summaries of certain provisions contained in some of the documents described herein, but reference is made to the actual documents for complete information. All of the summaries are qualified in their entirety by the actual documents. Copies of some of the documents referred to herein have been filed, will be filed or will be incorporated by reference as exhibits to the registration statement of which this prospectus is a part, and you may obtain copies of those documents as described below under the heading “Where You Can Find More Information.”

SUMMARY

This summary highlights selected information from this prospectus and does not contain all of the information that you need to consider in making your investment decision. You should carefully read the entire prospectus, the applicable prospectus supplement and any related free writing prospectus, including the risks of investing in our securities discussed under the heading “Risk Factors” contained in the applicable prospectus supplement and any related free writing prospectus, and under similar headings in the other documents that are incorporated by reference into this prospectus. You should also carefully read the information incorporated by reference into this prospectus, including our financial statements and related notes, and the exhibits to the registration statement of which this prospectus is a part, before making an investment decision.

Unless the context indicates otherwise, references in this prospectus to “Milestone,” “company,” “we,” “us” and “our” refer to Milestone Pharmaceuticals Inc.

Company 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.

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

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

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

When employing the updated SAP retrospectively to the NODE-301 data, the analysis results in 54% of etripamil patients vs. 35% of placebo patients converted within 30 minutes (HR 1.87, p=0.02). We also discussed the clinical benefit of 54% conversion rate with the FDA. We believe, based on interactions with

PSVT treating physicians and cardiovascular thought leaders, that a 50% conversion rate within 60 minutes is a clinically-meaningful outcome given the symptomatic nature of SVT episodes and the lack of approved at-home treatments.

Based on discussions with the FDA regarding maximizing the treatment effect of etripamil, the RAPID trial will allow for repeat administration of study drug (either 70 mg of etripamil or placebo) for patients who have not experienced symptom relief within ten minutes of the first study drug administration. This repeat dose regimen, which is similar to current PSVT treatment practices in the emergency department setting, is tailored to the pharmacokinetic profile of etripamil to deliver increased exposure over approximately the first 30 minutes following initial administration. We expect that the repeat administration could benefit a broader group of patients, including those with more persistent episodes.

The RAPID study, which was originally designed to collect double-blind data from randomized patients who had not yet experienced an SVT event after the NODE-301 study reached its target number of adjudicated SVT events, will be amended and expanded to serve as a pivotal efficacy and safety study should the RAPID study meet its primary objective. The study will include the 170 patients who are already enrolled, although many of those patients have been enrolled in the study for more than one year without reporting an SVT event. The study will be completed after a total of 180 confirmed SVT events are reached, including those that have already occurred in the study. Additional patients to be enrolled in the RAPID study will be randomized 1:1.

The FDA agreed that the single and repeat administrations of etripamil could be pooled and compared to placebo for the primary analysis, resulting in no increase in the study's sample size.

We initiated the RAPID study in the second half of 2020 and enrolled the first new patient in November of 2020. In the fourth quarter of 2020, we took initiatives to increase the number of clinical trial sites in North America but also planned for more clinical sites in European countries to diversify and better protect the study recruitment against COVID's geographical resurgences. The majority of planned clinical trial sites in Europe have been initiated and we plan to activate new clinical trial sites as new sites are identified and as local regulatory and institutional review board approvals are obtained. We continue to monitor enrollment as well as new clinical site activations and expect to report topline data in the second half of 2022.

Corporate Information

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

Implications of Being an Emerging Growth Company and a Smaller Reporting Company

We qualify as an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. An emerging growth company may take advantage of relief from some of the reporting requirements and other burdens that are otherwise applicable generally to public companies. These provisions include:

- being permitted to provide only two years of audited financial statements, in addition to any required unaudited interim financial statements, with correspondingly reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure;
- not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting;
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;

- reduced disclosure obligations regarding executive compensation in our periodic reports, proxy statements and registration statements; 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 may take advantage of some or all of these reporting exemptions until we are no longer an emerging growth company. We will remain an emerging growth company until December 31, 2024 or, if earlier, (1) the last day of a fiscal year in which we have total annual gross revenue of at least \$1.07 billion or in which we are deemed to be a large accelerated filer, which means the market value of our common shares that are held by non-affiliates exceeds \$700 million as of the prior June 30th and (2) the date on which we have issued more than \$1.0 billion in non-convertible debt during the prior three-year period. We may choose to take advantage of some but not all of these reduced burdens. For example, we have taken advantage of the reduced reporting requirements with respect to disclosure regarding our executive compensation arrangements, have presented only two years of audited financial statements and only two years of related “Management’s Discussion and Analysis of Financial Condition and Results of Operations” disclosure in our public filings, and have taken advantage of the exemption from auditor attestation on the effectiveness of our internal control over financial reporting. To the extent that we take advantage of these reduced burdens, the information that we provide shareholders may be different than you might obtain from other public companies in which you hold equity interests.

In addition, under the JOBS Act, emerging growth companies 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 emerging growth companies.

We are also a “smaller reporting company” as defined in Rule 12b-2 promulgated under the Securities Exchange Act of 1934, as amended, or the Exchange Act. We may remain a smaller reporting company until we have a non-affiliate public float in excess of \$250 million and annual revenues in excess of \$100 million, or a non-affiliate public float in excess of \$700 million, each as determined on an annual basis. Even after we no longer qualify as an emerging growth company, we may still qualify as a smaller reporting company, which would allow us to take advantage of many of the same exemptions from disclosure requirements.

The Securities We May Offer

We may offer common shares, preferred shares, various series of debt securities and/or warrants to purchase any of such securities, either individually or in combination, up to a total aggregate offering price of \$250,000,000 from time to time in one or more offerings under this prospectus, together with any applicable prospectus supplement and any related free writing prospectus, at prices and on terms to be determined by market conditions at the time of the relevant offering. This prospectus provides you with a general description of the securities we may offer. Each time we offer a type or series of securities under this prospectus, we will provide a prospectus supplement that will describe the specific amounts, prices and other important terms of the securities, including, to the extent applicable:

- designation or classification;
- aggregate principal amount or aggregate offering price;
- maturity;
- original issue discount, if any;
- rates and times of payment of interest or dividends, if any;
- redemption, conversion, exchange or sinking fund terms, if any;
- conversion or exchange prices or rates, if any, and, if applicable, any provisions for changes to or adjustments in the conversion or exchange prices or rates and in the securities or other property receivable upon conversion or exchange;
- ranking;

- restrictive covenants, if any;
- voting or other rights, if any; and
- important U.S. federal income tax and Canadian federal income tax considerations.

The applicable prospectus supplement and any related free writing prospectus that we may authorize to be provided to you may also add, update or change information contained in this prospectus or in documents we have incorporated by reference. However, no prospectus supplement or free writing prospectus will offer a security that is not registered and described in this prospectus at the time of the effectiveness of the registration statement of which this prospectus is a part.

We may sell the securities directly to investors or indirectly through underwriters, dealers or agents. We, and our underwriters, dealers or agents reserve the right to accept or reject all or part of any proposed purchase of securities. If we do offer securities through underwriters, dealers or agents, we will include in the applicable prospectus supplement:

- the names of those underwriters, dealers or agents;
- applicable fees, discounts and commissions to be paid to them;
- details regarding over-allotment options, if any; and
- the estimated net proceeds to us.

This prospectus may not be used to consummate a sale of securities unless it is accompanied by a prospectus supplement.

Common Shares. We may issue common shares from time to time. Under our articles, each holder of common shares is entitled to receive notice of, to attend and to vote at, all annual and special meetings of our shareholders. Each common share entitles the holder thereof to one vote at all meetings, other than meetings at which only holders of another particular class or series have the right to vote. Subject and subordinate to the prior rights and privileges of the holders of our preferred shares ranking before common shares, the holders of common shares are entitled to receive dividends as and when declared by our board of directors. Subject and subordinate to the prior payment to the holders of our preferred shares ranking before common shares, in the event of our liquidation, dissolution or winding-up, whether voluntary or involuntary, or other distribution of our assets among our shareholders for the purposes of winding up our affairs, the holders of common shares are entitled to share pro rata in the distribution of our remaining property and assets. 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 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 and privileges of the holders of common shares will be subject to and may be adversely affected by, the rights and privileges of the holders of any series of preferred shares that we may designate in the future or any other class or series of shares that may be created and that would rank senior to the common shares.

Preferred Shares. Pursuant to our articles, we may issue preferred shares at any time and from time to time, in one or more series. Under our articles, 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 *Business Corporations Act* (Québec), or the QBCA, having such designations, rights, privileges, restrictions and conditions, including dividend and voting rights and calculation methods, as our board of directors may determine, and such rights and privileges, including voting, dividend, asset distribution and return of capital rights, may be superior to those of the common shares. Any convertible preferred shares we may issue will be convertible into our common shares or exchangeable for our other securities. Conversion may be automatic, mandatory or at the holder's option and would be at prescribed conversion rates.

If we sell any series of preferred shares under this prospectus, we will fix the designations, voting powers, preferences and rights of such series of preferred shares, as well as the qualifications, limitations or restrictions thereof, in the articles of amendment containing a description of such series. Before issuing a series of preferred shares, we will file as an exhibit to the registration statement of which this prospectus is

a part, or will incorporate by reference from reports that we file with the SEC, any articles and certificates of amendment that describe the terms of the series of preferred shares that we are offering. We urge you to read the applicable prospectus supplement (and any free writing prospectus that we may authorize to be provided to you) related to the series of preferred shares being offered, as well as the complete articles and certificates of amendment that contain the terms of the applicable series of preferred shares.

Debt Securities. We may issue debt securities from time to time, in one or more series, as either senior or subordinated debt or as senior or subordinated convertible debt. The senior debt securities will rank equally with any other unsecured and unsubordinated debt. The subordinated debt securities will be subordinate and junior in right of payment, to the extent and in the manner described in the instrument governing the debt, to all of our senior indebtedness. Convertible debt securities will be convertible into or exchangeable for our common shares or other securities. Conversion may be automatic, mandatory or at the holder's option and would be at prescribed conversion rates.

The debt securities issued under this prospectus will be issued under one or more documents called indentures, which are contracts between us and a national banking association or other eligible party, as trustee. In this prospectus, we have summarized certain general features of the debt securities. We urge you, however, to read the applicable prospectus supplement (and any free writing prospectus that we may authorize to be provided to you) related to the series of debt securities being offered, as well as the complete indentures that contain the terms of the debt securities. A form of indenture has been filed as an exhibit to the registration statement of which this prospectus is a part, and supplemental indentures and forms of debt securities containing the terms of the debt securities being offered will be filed as exhibits to the registration statement of which this prospectus is a part or will be incorporated by reference from reports that we file with the SEC.

Warrants. We may issue warrants for the purchase of common shares, preferred shares and/or debt securities in one or more series. We may issue warrants independently or together with common shares, preferred shares and/or debt securities, and the warrants may be attached to or separate from these securities. In this prospectus, we have summarized certain general features of the warrants. We urge you, however, to read the applicable prospectus supplement (and any free writing prospectus that we may authorize to be provided to you) related to the particular series of warrants being offered, as well as the complete warrant agreements and warrant certificates that contain the terms of the warrants. Forms of the warrant agreements and forms of warrant certificates containing the terms of the warrants being offered have been filed as exhibits to the registration statement of which this prospectus is a part, and supplemental warrant agreements and forms of warrant certificates will be filed as exhibits to the registration statement of which this prospectus is a part or will be incorporated by reference from reports that we file with the SEC.

We will evidence each series of warrants by warrant certificates that we will issue. Warrants may be issued under an applicable warrant agreement that we enter into with a warrant agent. We will indicate the name and address of the warrant agent, if applicable, in the prospectus supplement relating to the particular series of warrants being offered.

RISK FACTORS

Investing in our securities involves a high degree of risk. You should carefully review the risks and uncertainties described under the heading “Risk Factors” contained in the applicable prospectus supplement and any related free writing prospectus, and under similar headings in our [Annual Report on Form 10-K for the year ended December 31, 2020](#), as updated by our annual, quarterly and other reports and documents that are incorporated by reference into this prospectus, before deciding whether to purchase any of the securities being registered pursuant to the registration statement of which this prospectus is a part. Each of the risk factors described in the documents referenced above could adversely affect our business, operating results and financial condition, as well as adversely affect the value of an investment in our securities, and the occurrence of any of these risks might cause you to lose all or part of your investment. Additional risks not presently known to us or that we currently believe are immaterial may also significantly impair our business operations.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and the documents incorporated by reference contain forward-looking statements. These are based on our management's current beliefs, expectations and assumptions about future events, conditions and results and on information currently available to us. Discussions containing these forward-looking statements may be found, among other places, in the Sections entitled "Business," "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" contained in the documents incorporated herein.

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" or the negative or plural of those terms, and similar expressions intended to identify statements about the future, although not all forward-looking statements contain these words. These forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from the information expressed or implied by these statements.

Any statements in this prospectus, or incorporated by reference herein, about our expectations, beliefs, plans, objectives, assumptions or future events or performance are not historical facts and are forward-looking statements. Within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act, these forward-looking statements include statements regarding:

- the initiation, timing, progress and results of our current and future clinical trials of etripamil, including our Phase 3 clinical trials of etripamil for the treatment of paroxysmal supraventricular tachycardia, our Phase 2 clinical trial of etripamil for the treatment of atrial fibrillation with rapid ventricular rate, and of our research and development programs;
- uncertain impacts that the COVID-19 pandemic may have on our business, strategy, clinical trial progress and research and development efforts;
- our plans to develop and commercialize etripamil and any future product candidates;
- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing;
- the results of our collaborations or obtain additional funding, including our license agreement with Ji Xing Pharmaceuticals Limited to develop and, if approved by regulatory authorities, commercialize etripamil in China and Taiwan;
- our ability to establish additional collaborations or obtain additional funding;
- our ability to obtain regulatory approval of our current and future product candidates;
- our expectations regarding the potential market size and the rate and degree of market acceptance of etripamil and any future product candidates;
- our ability to fund our working capital requirements and expectations regarding the sufficiency of our capital resources;
- the implementation of our business model and strategic plans for our business, etripamil and any future product candidates;
- our intellectual property position and the duration of our patent rights;
- developments or disputes concerning our intellectual property or other proprietary rights;
- our expectations regarding government and third-party payer coverage and reimbursement;
- our ability to compete in the markets we serve;
- the impact of government laws and regulations;
- our expected use of proceeds from the sale of the securities offered hereby;
- developments relating to our competitors and our industry;

- other factors that may impact our financial results; and
- other risks and uncertainties, including those listed under the caption “Risk Factors” in our most recent Annual Report on Form 10-K, our most recent Quarterly Report on Form 10-Q and other filings we make with the SEC.

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

In light of the significant uncertainties in these forward-looking statements, you should not rely upon forward-looking statements as predictions of future events. Although we believe that we have a reasonable basis for each forward-looking statement contained in this prospectus, we cannot guarantee that the future results, levels of activity, performance or events and circumstances reflected in the forward-looking statements will be achieved or occur at all. You should refer to the “Risk Factors” section contained in the applicable prospectus supplement and any related free writing prospectus, and under similar headings in the other documents that are incorporated by reference into this prospectus, 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.

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

USE OF PROCEEDS

We will retain broad discretion over the use of the net proceeds from the sale of the securities offered hereby. Except as described in any applicable prospectus supplement or in any free writing prospectuses that we may authorize to be provided to you in connection with a specific offering, we currently intend to use the net proceeds from the sale of the securities offered hereby, if any, for working capital, capital expenditures and general corporate purposes. We may also use a portion of the net proceeds to invest in or acquire businesses or technologies that we believe are complementary to our own, although we have no current plans, commitments or agreements with respect to any acquisitions as of the date of this prospectus. We will set forth in the applicable prospectus supplement or free writing prospectus our intended use for the net proceeds received from the sale of any securities sold pursuant to the prospectus supplement or free writing prospectus. Pending these uses, we plan to invest these net proceeds in short-term, interest-bearing investments, investment-grade instruments, certificates of deposit or direct or guaranteed obligations of the United States.

DESCRIPTION OF SHARE CAPITAL

The following is a description of the material terms of our common shares and preferred shares as set forth in our articles. The following description of our share capital is intended as a summary only and is qualified in its entirety by reference to our articles and all amendments thereto, which are filed as exhibits to the registration statement of which this prospectus is a part, and to the applicable provisions of the QBCA.

General

Our share capital consists of an unlimited number of common shares, no par value per share, and an unlimited number of preferred shares, no par value per share.

Common Shares

Outstanding Shares

As of September 30, 2021 we had 29,869,785 common shares issued and outstanding, which were held by approximately 80 shareholders of record.

Voting Rights

Under our articles, each holder of common shares is entitled to receive notice of, to attend and to vote at all meetings of our shareholders, except meetings at which only holders of another particular class or series shall have the right to vote. At each such meeting at which a holder of common shares is entitled to vote, each common share shall entitle the holder thereof to one vote.

Dividends

Subject and subordinate to the prior rights of the holders of our preferred shares ranking before the common shares, the holders of common shares are entitled to receive dividends as and when declared by our board of directors. See “Dividend Policy.”

Liquidation

Subject and subordinate to the prior payment to the holders of our preferred shares ranking before the common shares, in the event of our liquidation, dissolution or winding-up or other distribution of our assets among our shareholders for the purposes of winding-up our affairs, the holders of common shares are entitled to share *pro rata* in the distribution of our remaining property and 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 requiring the holders of common shares to contribute additional capital or permitting or restricting the issuance of additional securities or any other material restrictions. The rights, preferences and privileges of the holders of common shares will be subject to and may be adversely affected by, the rights of the holders of any series of preferred shares that we may designate in the future or any other class or series of shares that may be created and that would rank senior to the common shares.

Preferred Shares

We do not have any preferred shares issued and outstanding. Under our articles, 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 QBCA, having such designations, rights, privileges, restrictions and conditions, including voting, dividend, asset distribution and return of capital rights, as our board of directors may determine, and such rights and privileges, including voting, dividend, asset distribution and return of capital rights, may be superior to those of the common shares.

Subject to the filing with the applicable enterprise registrar of the articles of amendment containing a description of such series of preferred shares and the issuance of the certificate of amendment by the enterprise registrar, preferred shares could be issued relatively quickly with terms designed to delay or prevent a change in control of our company or make removal of management more difficult. Additionally, the issuance of preferred shares may have the effect of decreasing the market price of the common shares and may adversely affect the voting power of holders of common shares and reduce the likelihood that common shareholders will receive dividend payments and payments upon liquidation, dissolution, winding-up or other distribution of assets.

Our board of directors will fix the designations, voting powers, preferences and rights of the each series, as well as the qualifications, limitations or restrictions thereof, of the preferred shares of each series that we offer under this prospectus and applicable prospectus supplements in the articles of amendment relating to that series. Before issuing a series of preferred shares, we will file as an exhibit to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, any articles and certificate of amendment that describes the terms of such series of preferred shares. The description of such series of preferred shares in any applicable registration statement, prospectus supplement or report filed with the SEC will include, to the extent applicable:

- the title and stated value;
- the number of shares we are offering;
- the liquidation preference per share;
- the purchase price per share;
- the dividend rate per share, dividend period and payment dates and method of calculation for dividends;
- whether dividends will be cumulative or non-cumulative and, if cumulative, the date from which dividends will accumulate;
- our right, if any, to defer payment of dividends and the maximum length of any such deferral period;
- the procedures for any auction and remarketing, if any;
- the provisions for a sinking fund, if any;
- the provisions for redemption or repurchase, if applicable, and any restrictions on our ability to exercise those redemption and repurchase rights;
- any listing of the preferred shares on any securities exchange or market;
- whether the preferred shares will be convertible into our common shares or other securities of ours, including depositary shares and warrants, and, if applicable, the conversion period, the conversion price, or how it will be calculated, and under what circumstances it may be adjusted;
- whether the preferred shares will be exchangeable into debt securities, and, if applicable, the exchange period, the exchange price, or how it will be calculated, and under what circumstances it may be adjusted;
- voting rights, if any, of the preferred shares;
- preemption rights, if any;
- restrictions on transfer, sale or other assignment, if any;
- whether interests in the preferred shares will be represented by depositary shares;
- a discussion of any material or special U.S. and Canadian federal income tax considerations applicable to the preferred shares;
- the relative ranking and preferences of the preferred shares as to dividend rights and rights if we liquidate, dissolve or wind up our affairs;

- any limitations on issuances of any class or series of preferred shares ranking senior to or on a parity with the series of preferred shares being issued as to dividend rights and rights if we liquidate, dissolve or wind up our affairs; and
- any other specific terms, rights, preferences, privileges, qualifications or restrictions of the preferred shares.

Section 191 of the QBCA provides for a general rule that a special resolution that favours certain shareholders of a class or series of shares or changes prejudicially the rights attaching to all the shares of a class or series of shares must be approved by the shareholders of that class or series. The same applies to a special resolution authorizing the articles to be amended in order to allow the board of directors to change prejudicially the rights attaching to all the shares of a class or series of shares without shareholder authorization. Such approval is given by a special resolution adopted separately by the holders of each class or series of shares concerned, whether or not the shares otherwise carry voting rights. Such approval is not required if (i) the special resolution changes prejudicially in the same manner the rights attaching to all the shares issued by the corporation or (ii) under the amendment to the articles authorized by the special resolution, it is only possible to change prejudicially the rights attaching to all the shares issued by the corporation. This general rule in Section 191 of the QBCA may give rise to separate class or series votes in addition to any other vote or approval requirement set out in the QBCA or the articles. Therefore, to the extent provided for in the QBCA, the holders of preferred shares or series of preferred shares, as holders of distinct class or series of shares, would in certain circumstances have the right to vote separately as a class or as a series, as the case may be.

Options

As of September 30, 2021, 2,702,579 common shares were issuable upon the exercise of outstanding share options, at a weighted-average exercise price of \$5.39 per common share.

Registration Rights

Certain holders of our common shares are entitled to certain rights with respect to registration under the Securities Act and qualification under Canadian securities laws of any securities held by them. These shares are referred to as registrable securities. The holders of these registrable securities possess registration and qualification rights pursuant to the terms of our third amended and restated registration rights agreement dated as of October 15, 2018 and are described in additional detail below. The registration, or qualification, 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, or Canadian securities laws, when the applicable registration statement or prospectus 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 (i) demand registrations, (ii) piggyback registrations and (iii) short form demand registrations or qualifications pursuant to Form S-3 or F-3, a form under the Canada-United States Multijurisdictional Disclosure System, or the MJDS, and/or a short form prospectus under the Canadian short form qualification procedure under Regulation 44-101 respecting Short Form Prospectus Distributions, in each case as 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 short form demand 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 or Regulation S of the Securities Act and (y) pursuant to Section 2.5 of Regulation 45-102 respecting Resale of Securities, as adopted by the Canadian securities commissions, and (iii) five years after the completion of our initial public offering.

Demand Registration Rights

Certain holders of the common shares issued upon conversion of preferred shares in our initial public offering will be entitled to certain demand registration rights. These demand rights permit holders of at least 25% of the registrable securities then outstanding, to request, on not more than two occasions, that we register or qualify 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 commissions, or both.

Short Form Demand Registration Rights

As further described in this paragraph, certain holders of the common shares issued upon conversion of all preferred shares in connection with our initial public offering are entitled to certain rights to request that we register or qualify such common shares pursuant to Form S-3 or F-3 registration, a form under the MJDS, and/or a short form prospectus under the Canadian short form qualification procedure under Regulation 44-101 respecting Short Form Prospectus Distributions. These demand rights permit holders of at least 25% of the registrable securities then outstanding to request, on not more than two occasions within any 12-month period, that we register all or a portion of their shares on Form S-3 or F-3, a form under the MJDS, and/or a short form prospectus under the Canadian short form qualification procedure under Regulation 44-101 respecting Short Form Prospectus Distributions, in each case if we are qualified to file and subject to specified exceptions. Such request for registration or qualification must cover securities with an aggregate offering price which equals or exceeds \$10.0 million. The right to have such shares so registered or qualified is further subject to other specified conditions and limitations.

Piggyback Registration Rights

Holders of any common shares issued upon conversion of preferred shares in our initial public offering are entitled to include their shares of registrable securities in any registration statement or prospectus we file in the event that we propose to register or qualify any of our securities under the Securities Act or Canadian securities laws in an offering, either for our own account, for the account of other security holders or for both, subject to specified conditions and limitations. All piggyback registration rights have been waived as they may apply to the filing of the registration statement of which this prospectus is a part.

Indemnification

The third amended and restated registration rights agreement dated as of October 15, 2018 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, Québec H3A 3S8.

Nasdaq Global Select Market Listing

Our common shares are listed on The Nasdaq Global Select Market under the trading symbol "MIST".

Advance Notice Procedures and Shareholder Proposals

Under the QBCA, shareholders may make shareholder proposals for matters, including the nomination of a director, to be considered at the annual 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 QBCA. The notice must include information on the business the shareholder intends to bring before the meeting.

In addition, the QBCA and our bylaws require that shareholders provide us with advance notice of their intention to nominate any persons for election to our board of directors at a meeting of shareholders.

These provisions in the QBCA and our bylaws 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.

DESCRIPTION OF DEBT SECURITIES

We may issue debt securities from time to time, in one or more series, as either senior or subordinated debt or as senior or subordinated convertible debt. While the terms we have summarized below will apply generally to any debt securities that we may offer under this prospectus, we will describe the particular terms of any debt securities that we may offer in more detail in the applicable prospectus supplement. The terms of any debt securities offered under a prospectus supplement may differ from the terms described below. Unless the context requires otherwise, whenever we refer to the indenture, we also are referring to any supplemental indentures that specify the terms of a particular series of debt securities.

We will issue the debt securities under the indenture that we will enter into with the trustee named in the indenture. The indenture will be qualified under the Trust Indenture Act of 1939, as amended, or the Trust Indenture Act. We have filed the form of indenture as an exhibit to the registration statement of which this prospectus is a part, and supplemental indentures and forms of debt securities containing the terms of the debt securities being offered will be filed as exhibits to the registration statement of which this prospectus is a part or will be incorporated by reference from reports that we file with the SEC.

The following summary of material provisions of the debt securities and the indenture is subject to, and qualified in its entirety by reference to, all of the provisions of the indenture applicable to a particular series of debt securities that we may issue. We urge you to read the applicable prospectus supplements and any related free writing prospectuses related to the debt securities that we may offer under this prospectus, as well as the complete indenture that contains the terms of the debt securities.

General

The indenture does not limit the amount of debt securities that we may issue. It provides that we may issue debt securities up to the principal amount that we may authorize and may be in any currency or currency unit that we may designate. Except for the limitations on consolidation, arrangement, amalgamation, merger and sale of all or substantially all of our assets contained in the indenture, the terms of the indenture do not contain any covenants or other provisions designed to give holders of any debt securities protection against changes in our operations, financial condition or transactions involving us.

We may issue the debt securities issued under the indenture as “discount securities,” which means they may be sold at a discount below their stated principal amount. These debt securities, as well as other debt securities that are not issued at a discount, may be issued with “original issue discount,” or OID, for U.S. federal income tax purposes because of interest payment and other characteristics or terms of the debt securities. Material U.S. federal income tax considerations applicable to debt securities issued with OID will be described in more detail in any applicable prospectus supplement. The applicable prospectus supplement may also describe material Canadian federal income tax considerations generally applicable to investors described therein of purchasing, holding and disposing of debt securities that we may issue, including, in the case of an investor who is not a resident of Canada, Canadian withholding tax considerations.

We will describe in the applicable prospectus supplement the terms of the series of debt securities being offered, including:

- the title of the series of debt securities;
- any limit upon the aggregate principal amount that may be issued;
- the maturity date or dates;
- the form of the debt securities of the series;
- the applicability of any guarantees;
- whether or not the debt securities will be secured or unsecured, and the terms of any secured debt;
- whether the debt securities rank as senior debt, senior subordinated debt, subordinated debt or any combination thereof, and the terms of any subordination;
- if the price (expressed as a percentage of the aggregate principal amount thereof) at which such debt securities will be issued is a price other than the principal amount thereof, the portion of the

principal amount thereof payable upon declaration of acceleration of the maturity thereof, or if applicable, the portion of the principal amount of such debt securities that is convertible into another security or the method by which any such portion shall be determined;

- the interest rate or rates, which may be fixed or variable, or the method for determining the rate and the date interest will begin to accrue, the dates interest will be payable and the regular record dates for interest payment dates or the method for determining such dates;
- our right, if any, to defer payment of interest and the maximum length of any such deferral period;
- if applicable, the date or dates after which, or the period or periods during which, and the price or prices at which, we may, at our option, redeem the series of debt securities pursuant to any optional or provisional redemption provisions and the terms of those redemption provisions;
- the date or dates, if any, on which, and the price or prices at which we are obligated, pursuant to any mandatory sinking fund or analogous fund provisions or otherwise, to redeem, or at the holder's option to purchase, the series of debt securities and the currency or currency unit in which the debt securities are payable;
- the denominations in which we will issue the series of debt securities, if other than denominations of \$1,000 and any integral multiple thereof;
- any and all terms, if applicable, relating to any auction or remarketing of the debt securities of that series and any security for our obligations with respect to such debt securities and any other terms which may be advisable in connection with the marketing of debt securities of that series;
- whether the debt securities of the series shall be issued in whole or in part in the form of a global security or securities; the terms and conditions, if any, upon which such global security or securities may be exchanged in whole or in part for other individual securities; and the depositary for such global security or securities;
- if applicable, the provisions relating to conversion or exchange of any debt securities of the series and the terms and conditions upon which such debt securities will be so convertible or exchangeable, including the conversion or exchange price, as applicable, or how it will be calculated and may be adjusted, any mandatory or optional (at our option or the holders' option) conversion or exchange features, the applicable conversion or exchange period and the manner of settlement for any conversion or exchange;
- if other than the full principal amount thereof, the portion of the principal amount of debt securities of the series which shall be payable upon declaration of acceleration of the maturity thereof;
- additions to or changes in the covenants applicable to the particular debt securities being issued, including, among others, the consolidation, arrangement, amalgamation, merger or sale covenant;
- additions to or changes in the events of default with respect to the securities and any change in the right of the trustee or the holders to declare the principal, premium, if any, and interest, if any, with respect to such securities to be due and payable;
- additions to or changes in or deletions of the provisions relating to covenant defeasance and legal defeasance;
- additions to or changes in the provisions relating to satisfaction and discharge of the indenture;
- additions to or changes in the provisions relating to the modification of the indenture both with and without the consent of holders of debt securities issued under the indenture;
- the currency of payment of debt securities if other than U.S. dollars and the manner of determining the equivalent amount in U.S. dollars;
- whether interest will be payable in cash or additional debt securities at our or the holders' option and the terms and conditions upon which the election may be made;
- the terms and conditions, if any, upon which we will pay amounts in addition to the stated interest, premium, if any and principal amounts of the debt securities of the series to any holder that is not a

“United States person” for U.S. federal tax purposes or any holder that is not a “resident of Canada” for Canadian federal income tax purposes;

- any restrictions on transfer, sale or assignment of the debt securities of the series; and
- any other specific terms, preferences, rights or limitations of, or restrictions on, the debt securities, any other additions or changes in the provisions of the indenture, and any terms that may be required by us or advisable under applicable laws or regulations.

Conversion or Exchange Rights

We will set forth in the applicable prospectus supplement the terms on which a series of debt securities may be convertible into or exchangeable for our common shares or our other securities. We will include provisions as to settlement upon conversion or exchange and whether conversion or exchange is mandatory, at the option of the holder or at our option. We may include provisions pursuant to which the number of our common shares or our other securities that the holders of the series of debt securities receive would be subject to adjustment.

Consolidation, Arrangement, Amalgamation, Merger or Sale

Unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, the indenture will not contain any covenant that restricts our ability to carry out an arrangement or to merge, amalgamate or consolidate, or sell, convey, transfer or otherwise dispose of our assets as an entirety or substantially as an entirety. However, any successor to or acquirer of such assets (other than a subsidiary of ours) must assume all of our obligations under the indenture or the debt securities, as appropriate.

Events of Default under the Indenture

Unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, the following are events of default under the indenture with respect to any series of debt securities that we may issue:

- if we fail to pay any installment of interest on any series of debt securities, as and when the same shall become due and payable, and such default continues for a period of 90 days; provided, however, that a valid extension of an interest payment period by us in accordance with the terms of any indenture supplemental thereto shall not constitute a default in the payment of interest for this purpose;
- if we fail to pay the principal of, or premium, if any, on any series of debt securities as and when the same shall become due and payable whether at maturity, upon redemption, by declaration or otherwise, or in any payment required by any sinking or analogous fund established with respect to such series; provided, however, that a valid extension of the maturity of such debt securities in accordance with the terms of any indenture supplemental thereto shall not constitute a default in the payment of principal or premium, if any;
- if we fail to observe or perform any other covenant or agreement contained in the debt securities or the indenture, other than a covenant specifically relating to another series of debt securities, and our failure continues for 90 days after we receive written notice of such failure, requiring the same to be remedied and stating that such is a notice of default thereunder, from the trustee or holders of at least 25% in aggregate principal amount of the outstanding debt securities of the applicable series; and
- if specified events of bankruptcy, insolvency or reorganization occur.

If an event of default with respect to debt securities of any series occurs and is continuing, other than an event of default specified in the last bullet point above, the trustee or the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series, by notice to us in writing, and to the trustee if notice is given by such holders, may declare the unpaid principal of, premium, if any, and accrued interest, if any, due and payable immediately. If an event of default specified in the last bullet

point above occurs with respect to us, the principal amount of and accrued interest, if any, of each issue of debt securities then outstanding shall be due and payable without any notice or other action on the part of the trustee or any holder.

The holders of a majority in principal amount of the outstanding debt securities of an affected series may waive any default or event of default with respect to the series and its consequences, except defaults or events of default regarding payment of principal, premium, if any, or interest, unless we have cured the default or event of default in accordance with the indenture. Any waiver shall cure the default or event of default.

Subject to the terms of the indenture, if an event of default under an indenture shall occur and be continuing, the trustee will be under no obligation to exercise any of its rights or powers under such indenture at the request or direction of any of the holders of the applicable series of debt securities, unless such holders have offered the trustee reasonable indemnity. The holders of a majority in principal amount of the outstanding debt securities of any series will have the right to direct the time, method and place of conducting any proceeding for any remedy available to the trustee, or exercising any trust or power conferred on the trustee, with respect to the debt securities of that series, provided that:

- the direction so given by the holder is not in conflict with any law or the applicable indenture; and
- subject to its duties under the Trust Indenture Act, the trustee need not take any action that might involve it in personal liability or might be unduly prejudicial to the holders not involved in the proceeding.

A holder of the debt securities of any series will have the right to institute a proceeding under the indenture or to appoint a receiver or trustee, or to seek other remedies only if:

- the holder has given written notice to the trustee of a continuing event of default with respect to that series;
- the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series have made written request,
- such holders have offered to the trustee indemnity satisfactory to it against the costs, expenses and liabilities to be incurred by the trustee in compliance with the request; and
- the trustee does not institute the proceeding, and does not receive from the holders of a majority in aggregate principal amount of the outstanding debt securities of that series other conflicting directions within 90 days after the notice, request and offer.

These limitations do not apply to a suit instituted by a holder of debt securities if we default in the payment of the principal, premium, if any, or interest on, the debt securities.

We will periodically file statements with the trustee regarding our compliance with specified covenants in the indenture.

Modification of Indenture; Waiver

We and the trustee may change an indenture without the consent of any holders with respect to specific matters:

- to cure any ambiguity, defect or inconsistency in the indenture or in the debt securities of any series;
- to comply with the provisions described above under “Description of Debt — General — Amalgamation, Merger or Sale;”
- to provide for uncertificated debt securities in addition to or in place of certificated debt securities;
- to add to our covenants, restrictions, conditions or provisions such new covenants, restrictions, conditions or provisions for the benefit of the holders of all or any series of debt securities, to make the occurrence, or the occurrence and the continuance, of a default in any such additional covenants, restrictions, conditions or provisions an event of default or to surrender any right or power conferred upon us in the indenture;

- to add to, delete from or revise the conditions, limitations, and restrictions on the authorized amount, terms, or purposes of issue, authentication and delivery of debt securities, as set forth in the indenture;
- to make any change that does not adversely affect the interests of any holder of debt securities of any series in any material respect;
- to provide for the issuance of and establish the form and terms and conditions of the debt securities of any series as provided above under “Description of Debt Securities — General” to establish the form of any certifications required to be furnished pursuant to the terms of the indenture or any series of debt securities, or to add to the rights of the holders of any series of debt securities;
- to evidence and provide for the acceptance of appointment under any indenture by a successor trustee; or
- to comply with any requirements of the SEC in connection with the qualification of any indenture under the Trust Indenture Act.

In addition, under the indenture, the rights of holders of a series of debt securities may be changed by us and the trustee with the written consent of the holders of at least a majority in aggregate principal amount of the outstanding debt securities of each series that is affected. However, unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, we and the trustee may make the following changes only with the consent of each holder of any outstanding debt securities affected:

- extending the fixed maturity of any debt securities of any series;
- reducing the principal amount, reducing the rate of or extending the time of payment of interest, or reducing any premium payable upon the redemption of any series of any debt securities; or
- reducing the percentage of debt securities, the holders of which are required to consent to any amendment, supplement, modification or waiver.

Discharge

Each indenture provides that we can elect to be discharged from our obligations with respect to one or more series of debt securities, except for specified obligations, including obligations to:

- provide for payment;
- register the transfer or exchange of debt securities of the series;
- replace stolen, lost or mutilated debt securities of the series;
- pay principal of and premium and interest on any debt securities of the series;
- maintain paying agencies;
- hold monies for payment in trust;
- recover excess money held by the trustee;
- compensate and indemnify the trustee; and
- appoint any successor trustee.

In order to exercise our rights to be discharged, we must deposit with the trustee money or government obligations sufficient to pay all the principal of, any premium, if any, and interest on, the debt securities of the series on the dates payments are due.

Form, Exchange and Transfer

We will issue the debt securities of each series only in fully registered form without coupons and, unless we provide otherwise in the applicable prospectus supplement, in denominations of \$1,000 and any integral multiple thereof. The indenture provides that we may issue debt securities of a series in temporary or permanent global form and as book-entry securities that will be deposited with, or on behalf of, The

Depository Trust Company, or DTC, or another depository named by us and identified in the applicable prospectus supplement with respect to that series. To the extent the debt securities of a series are issued in global form and as book-entry, a description of terms relating to any book-entry securities will be set forth in the applicable prospectus supplement.

At the option of the holder, subject to the terms of the indenture and the limitations applicable to global securities described in the applicable prospectus supplement, the holder of the debt securities of any series can exchange the debt securities for other debt securities of the same series, in any authorized denomination and of like tenor and aggregate principal amount.

Subject to the terms of the indenture and the limitations applicable to global securities set forth in the applicable prospectus supplement, holders of the debt securities may present the debt securities for exchange or for registration of transfer, duly endorsed or with the form of transfer endorsed thereon duly executed if so required by us or the security registrar, at the office of the security registrar or at the office of any transfer agent designated by us for this purpose. Unless otherwise provided in the debt securities that the holder presents for transfer or exchange, we will impose no service charge for any registration of transfer or exchange, but we may require payment of any taxes or other governmental charges.

We will name in the applicable prospectus supplement the security registrar, and any transfer agent in addition to the security registrar, that we initially designate for any debt securities. We may at any time designate additional transfer agents or rescind the designation of any transfer agent or approve a change in the office through which any transfer agent acts, except that we will be required to maintain a transfer agent in each place of payment for the debt securities of each series.

If we elect to redeem the debt securities of any series, we will not be required to:

- issue, register the transfer of, or exchange any debt securities of that series during a period beginning at the opening of business 15 days before the day of mailing of a notice of redemption of any debt securities that may be selected for redemption and ending at the close of business on the day of the mailing; or
- register the transfer of or exchange any debt securities so selected for redemption, in whole or in part, except the unredeemed portion of any debt securities we are redeeming in part.

Information Concerning the Trustee

The trustee, other than during the occurrence and continuance of an event of default under an indenture, undertakes to perform only those duties as are specifically set forth in the applicable indenture. Upon an event of default under an indenture, the trustee must use the same degree of care as a prudent person would exercise or use in the conduct of his or her own affairs. Subject to this provision, the trustee is under no obligation to exercise any of the powers given it by the indenture at the request of any holder of debt securities unless it is offered reasonable security and indemnity against the costs, expenses and liabilities that it might incur.

Payment and Paying Agents

Unless we otherwise indicate in the applicable prospectus supplement, we will make payment of the interest on any debt securities on any interest payment date to the person in whose name the debt securities, or one or more predecessor securities, are registered at the close of business on the regular record date for the interest.

We will pay principal of and any premium and interest on the debt securities of a particular series at the office of the paying agents designated by us, except that unless we otherwise indicate in the applicable prospectus supplement, we will make interest payments by check that we will mail to the holder or by wire transfer to certain holders. Unless we otherwise indicate in the applicable prospectus supplement, we will designate the corporate trust office of the trustee as our sole paying agent for payments with respect to debt securities of each series. We will name in the applicable prospectus supplement any other paying agents that we initially designate for the debt securities of a particular series. We will maintain a paying agent in each place of payment for the debt securities of a particular series.

All money we pay to a paying agent or the trustee for the payment of the principal of or any premium or interest on any debt securities that remains unclaimed at the end of two years after such principal, premium or interest has become due and payable will be repaid to us, and the holder of the debt security thereafter may look only to us for payment thereof.

Governing Law

The indenture and the debt securities will be governed by and construed in accordance with the internal laws of the State of New York, except to the extent that the Trust Indenture Act of 1939 is applicable, or, generally, with respect to, among other things, corporate law operations, in which case the QBCA may be applicable.

DESCRIPTION OF WARRANTS

The following description, together with the additional information we may include in any applicable prospectus supplements and in any related free writing prospectuses, summarizes the material terms and provisions of the warrants that we may offer under this prospectus, which may consist of warrants to purchase common shares, preferred shares or debt securities and may be issued in one or more series.

Warrants may be offered and issued independently or together with common shares, preferred shares or debt securities offered by any prospectus supplement, and may be attached to or separate from those securities. While the terms we have summarized below will apply generally to any warrants that we may offer under this prospectus, we will describe the particular terms of any series of warrants that we may offer in more detail in the applicable prospectus supplement and any applicable free writing prospectus. The terms of any warrants offered under a prospectus supplement may differ from the terms described below. However, no prospectus supplement will fundamentally change the terms that are set forth in this prospectus or offer a security that is not registered and described in this prospectus at the time of its effectiveness.

We have filed forms of the warrant agreements and forms of warrant certificates containing the terms of the warrants that may be offered as exhibits to the registration statement of which this prospectus is a part. We will file as exhibits to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of warrant agreement, if any, including a form of warrant certificate, that describes the terms of the particular series of warrants we are offering. The following summaries of material provisions of the warrants and the warrant agreements are subject to, and qualified in their entirety by reference to, all the provisions of the warrant agreement and warrant certificate applicable to the particular series of warrants that we may offer under this prospectus. We urge you to read the applicable prospectus supplements related to the particular series of warrants that we may offer under this prospectus, as well as any related free writing prospectuses, and the complete warrant agreements and warrant certificates that contain the terms of the warrants.

General

We will describe in the applicable prospectus supplement the terms relating to a series of warrants being offered, including, to the extent applicable:

- the title of such securities;
- the offering price or prices and aggregate number of warrants offered;
- the currency or currencies for which the warrants may be purchased;
- if applicable, the designation and terms of the securities with which the warrants are issued and the number of warrants issued with each such security or each principal amount of such security;
- if applicable, the date on and after which the warrants and the related securities will be separately transferable;
- if applicable, the minimum or maximum amount of such warrants which may be exercised at any one time;
- in the case of warrants to purchase debt securities, the principal amount of debt securities purchasable upon exercise of one warrant and the price at which, and currency in which, this principal amount of debt securities may be purchased upon such exercise;
- in the case of warrants to purchase common shares or preferred shares, the number of shares of common shares or preferred shares, as the case may be, purchasable upon the exercise of one warrant and the price at which, and the currency in which, these shares may be purchased upon such exercise;
- the effect of any arrangement, amalgamation, merger, consolidation, sale or other disposition of our business on the warrant agreements and the warrants;
- the terms of any rights to redeem or call the warrants;
- the terms of any rights to force the exercise of the warrants;

- any provisions for changes to or adjustments in the exercise price or number of securities issuable upon exercise of the warrants;
- the dates on which the right to exercise the warrants will commence and expire;
- the manner in which the warrant agreements and warrants may be modified;
- a discussion of any material or special U.S. and Canadian federal income tax consequences of holding or exercising the warrants;
- the terms of the securities issuable upon exercise of the warrants; and
- any other specific terms, preferences, rights or limitations of or restrictions on the warrants.

Before exercising their warrants, holders of warrants will not have any of the rights of holders of the securities purchasable upon such exercise, including:

- in the case of warrants to purchase debt securities, the right to receive payments of principal of, or premium, if any, or interest on, the debt securities purchasable upon exercise or to enforce covenants in the applicable indenture; or
- in the case of warrants to purchase common shares or preferred shares, the right to receive dividends, if any, or, payments upon our liquidation, dissolution or winding up or to exercise voting rights, if any.

Exercise of Warrants

Each warrant will entitle the holder to purchase the securities that we specify in the applicable prospectus supplement at the exercise price that we describe in the applicable prospectus supplement. Unless we otherwise specify in the applicable prospectus supplement, holders of the warrants may exercise the warrants at any time up to the specified time on the expiration date that we set forth in the applicable prospectus supplement. After the close of business on the expiration date, unexercised warrants will become void.

Unless we otherwise specify in the applicable prospectus supplement, holders of the warrants may exercise the warrants by delivering the warrant certificate representing the warrants to be exercised together with specified information, and paying the required amount to the warrant agent in immediately available funds, as provided in the applicable prospectus supplement. We will set forth on the reverse side of the warrant certificate and in the applicable prospectus supplement the information that the holder of the warrant will be required to deliver to the warrant agent in connection with the exercise of the warrant.

Upon receipt of the required payment and the warrant certificate properly completed and duly executed at the corporate trust office of the warrant agent or any other office indicated in the applicable prospectus supplement, we will issue and deliver the securities purchasable upon such exercise. If fewer than all of the warrants represented by the warrant certificate are exercised, then we will issue a new warrant certificate for the remaining amount of warrants. If we so indicate in the applicable prospectus supplement, holders of the warrants may surrender securities as all or part of the exercise price for warrants.

Governing Law

Unless we provide otherwise in the applicable prospectus supplement, the warrants and warrant agreements, and any claim, controversy or dispute arising under or related to the warrants or warrant agreements, will be governed by and construed in accordance with the laws of the State of New York, or, generally, with respect to, among other things, corporate law operations, in which case the QBCA may be applicable.

Enforceability of Rights by Holders of Warrants

Each warrant agent will act solely as our agent under the applicable warrant agreement and will not assume any obligation or relationship of agency or trust with any holder of any warrant. A single bank or trust company may act as warrant agent for more than one issue of warrants. A warrant agent will have no duty or responsibility in case of any default by us under the applicable warrant agreement or warrant,

including any duty or responsibility to initiate any proceedings at law or otherwise, or to make any demand upon us. Any holder of a warrant may, without the consent of the related warrant agent or the holder of any other warrant, enforce by appropriate legal action its right to exercise, and receive the securities purchasable upon exercise of, its warrants.

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

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

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

	Delaware	QBCA
	<p>directors, at an election of the class of directors of which he is a part.</p>	
<i>Vacancies on the Board of Directors</i>	<p>Under the DGCL, vacancies and newly created directorships may be filled by a majority of the directors then in office (even though less than a quorum) or by a sole remaining director unless (i) otherwise provided in the certificate of incorporation or bylaws of the corporation or (ii) the certificate of incorporation directs that a particular class of stock is to elect such director, in which case a majority of the other directors elected by such class, or a sole remaining director elected by such class, will fill such vacancy.</p>	<p>Under the QBCA, vacancies that exist on the board of directors may generally be filled by the board if the remaining directors constitute a quorum. In the absence of a quorum, the remaining directors shall call a meeting of shareholders to fill the vacancy. If the directors refuse or fail to call a meeting or if there are no directors then in office, the meeting may be called by any shareholder.</p>
<i>Board of Director Quorum and Vote Requirements</i>	<p>Under the DGCL, a majority of the total number of directors shall constitute a quorum for the transaction of business unless the certificate of incorporation or bylaws require a greater number. The bylaws may lower the number required for a quorum to one-third the number of directors, but no less.</p> <p>Under the DGCL, the board of directors may take action by the majority vote of the directors present at a meeting at which a quorum is present unless the certificate of incorporation or bylaws require a greater vote.</p>	<p>Under the QBCA, subject to the corporation's bylaws, a majority of the directors in office constitutes a quorum at any meeting of the board. Our bylaws also provide that a majority of the directors in office constitutes a quorum at any meeting of the board.</p> <p>Under the QBCA, a quorum of directors may exercise all the powers of the directors despite any vacancy on the board.</p>
<i>Transactions with Directors and Officers</i>	<p>The DGCL generally provides that no transaction between a corporation and one or more of its directors or officers, or between a corporation and any other corporation or other organization in which one or more of its directors or officers, are directors or officers, or have a financial interest, shall be void or voidable solely for this reason, or solely because the director or officer is present at or participates</p>	<p>Under the QBCA, every director or officer of a corporation must disclose the nature and value of any interest he or she has in a contract or transaction to which the corporation is a party. For the purposes of this rule, "interest" means any financial stake in a contract or transaction that may reasonably be considered likely to influence decision-making. Furthermore, a proposed contract or a proposed</p>

Delaware	QBCA
<p>in the meeting of the board or committee which authorizes the transaction, or solely because any such director's or officer's votes are counted for such purpose, if (i) the material facts as to the director's or officer's interest and as to the transaction are known to the board of directors or the committee, and the board or committee in good faith authorizes the transaction by the affirmative votes of a majority of the disinterested directors, even though the disinterested directors be less than a quorum (ii) the material facts as to the director's or officer's interest and as to the transaction are disclosed or are known to the stockholders entitled to vote thereon, and the transaction is specifically approved in good faith by vote of the stockholders; or (iii) the transaction is fair as to the corporation as of the time it is authorized, approved or ratified, by the board of directors, a committee or the stockholders.</p>	<p>transaction, including related negotiations, is considered a contract or transaction. In addition, a director or an officer must disclose any contract or transaction to which the corporation and any of the following are a party: (i) an associate of the director or officer; (ii) a group of which the director or officer is a director or officer; or (iii) a group in which the director or officer or an associate of the director or officer has an interest. Such disclosure is required even for a contract or transaction that does not require approval by the board of directors. If a director is required to disclose his or her interest in a contract or transaction, such director is not allowed to vote on any resolution to approve, amend or terminate the contract or transaction or be present during deliberations concerning the approval, amendment or termination of such contract or transaction, unless the contract or transaction (i) relates primarily to the remuneration of the director or an associate of the director as a director, officer, employee or mandatory of the corporation or an affiliate of the corporation, (ii) is for indemnity or liability insurance under the QBCA, or (iii) is with an affiliate of the corporation, and the sole interest of the director is as a director or officer of the affiliate.</p> <p>If a director or officer does not disclose his or her interest in accordance with the QBCA, or (in the case of a director) votes in respect of a resolution on a contract or transaction in which he or she is interested contrary to the QBCA, the corporation or a shareholder may ask the court to declare the contract or transaction null and to require</p>

	Delaware	QBCA
<i>Limitation on Liability of Directors</i>	Under the DGCL, a corporation's certificate of incorporation may include a provision eliminating or limiting the personal liability of a director to the corporation and its stockholders for damages arising from a breach of fiduciary duty as a director. However, no provision can limit the liability of a director for:	<p>the director or officer to account to the corporation for any profit or gain realized on it by the director or officer or the associates of the director or officer, and to remit the profit or gain to the corporation, according to the conditions the court considers appropriate. However, the contract or transaction may not be declared null if it was approved by the board of directors and the contract or transaction was in the interest of the corporation when it was approved, nor may the director or officer concerned, in such a case, be required to account for any profit or gain realized or to remit the profit or gain to the corporation. In addition, the contract or transaction may not be declared null if it was approved by ordinary resolution by the shareholders entitled to vote who do not have an interest in the contract or transaction, the required disclosure was made to the shareholders in a sufficiently clear manner and the contract or transaction was in the best interests of the corporation when it was approved, and if the director or officer acted honestly and in good faith, he or she may not be required to account for the profit or gain realized and to remit the profit or gain to the corporation.</p> <p>The QBCA does not permit the limitation of a director's liability as the DGCL does.</p>

	<u>Delaware</u>	<u>QBCA</u>
<i>Indemnification of Directors and Officers</i>	<ul style="list-style-type: none"> • breach of the director’s duty of loyalty to the corporation or its stockholders; • acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of the law; • intentional or negligent payment of unlawful dividends or stock purchases or redemptions; or • for any transaction from which the director derived an improper personal benefit. <p>The DGCL permits indemnification for derivative suits only for expenses (including legal fees) and only if the person is not found liable, unless a court determines the person is fairly and reasonably entitled to the indemnification.</p>	<p>Under the QBCA, a corporation must indemnify a director or officer, a former director or officer or a person who acts or acted at the corporation’s request as a director or officer, or an individual acting in a similar capacity of another group (who is referred to in this document as an indemnifiable person) against all costs, charges and expenses, including an amount paid to settle an action or satisfy a judgment, reasonably incurred by the indemnifiable person on the exercise of the person’s functions or arising from any investigative or other proceeding in which the person is involved if:</p> <ul style="list-style-type: none"> • the person acted honestly and loyally in the interest of the corporation or other group, and • in the case of a proceeding enforceable by a monetary penalty, the person had reasonable grounds for believing the person’s conduct was lawful. <p>In the case of a derivative action, indemnity may be made only with court approval.</p>
<i>Call and Notice of Shareholder Meetings</i>	<p>Under the DGCL, an annual or special stockholder meeting is</p>	<p>Under the QBCA, an annual meeting of shareholders must be</p>

	<u>Delaware</u>	<u>QBCA</u>
	held on such date, at such time and at such place as may be designated by the board of directors or any other person authorized to call such meeting under the corporation's certificate of incorporation or bylaws. If an annual meeting for election of directors is not held on the date designated or an action by written consent to elect directors in lieu of an annual meeting has not been taken within 30 days after the date designated for the annual meeting, or if no date has been designated, for a period of 13 months after the later of the last annual meeting or the last action by written consent to elect directors in lieu of an annual meeting, the Delaware Court of Chancery may summarily order a meeting to be held upon the application of any stockholder or director.	held no later than 15 months after holding the last preceding annual meeting. Under the QBCA, the directors of a corporation may call a special meeting at any time. In addition, holders of not less than 10% of the issued shares of a corporation that carry the right to vote at a meeting sought to be held may requisition the directors to call a meeting of shareholders for the purposes stated in the requisition.
<i>Shareholder Action by Written Consent</i>	Under the DGCL, a majority of the stockholders of a corporation may act by written consent without a meeting unless such action is prohibited by the corporation's certificate of incorporation.	Under the QBCA, a written resolution signed by all the shareholders of a corporation who would have been entitled to vote on the resolution at a meeting is effective to approve the resolution.
<i>Shareholder Nominations and Proposals</i>	Not applicable.	Under the QBCA, a shareholder entitled to vote at a shareholders' meeting may submit a shareholder proposal relating to matters which the shareholder wishes to propose and discuss at an annual shareholders' meeting and, subject to such shareholder's compliance with the prescribed time periods and other requirements of the QBCA pertaining to shareholder proposals, the corporation is required to include such proposal in the information circular pertaining to any annual meeting at which it solicits proxies, subject to certain exceptions. Notice of such a proposal must be provided to the corporation at least 90 days

	Delaware	QBCA
<i>Shareholder Quorum and Vote Requirements</i>	Under the DGCL, quorum for a stock corporation is a majority of the shares entitled to vote at the meeting unless the certificate of incorporation or bylaws specify a different quorum, but in no event may a quorum be less than one-third of the shares entitled to vote. Unless the DGCL, certificate of incorporation or bylaws provide for a greater vote, generally the required vote under the DGCL is a majority of the shares present in person or represented by proxy, except for the election of directors which requires a plurality of the votes cast.	<p>before the anniversary date of the notice of meeting for the last annual shareholders' meeting.</p> <p>In addition, the QBCA requires that any shareholder proposal that includes nominations for the election of directors must be signed by one or more holders of shares representing in the aggregate not less than five per cent of the shares or five per cent of the shares of a class of shares of the corporation entitled to vote at the meeting to which the proposal is to be presented.</p> <p>Our bylaws require shareholders wishing to nominate directors or propose business for a meeting of shareholders to give timely advance notice in writing, as described in our bylaws.</p> <p>Under the QBCA, unless the bylaws otherwise provide, the holders of a majority of the shares of a corporation entitled to vote at a meeting of shareholders, whether present in person or represented by proxy, constitute a quorum.</p>
<i>Amendment of Certificate of Incorporation</i>	Generally, under the DGCL, the affirmative vote of the holders of a majority of the outstanding stock entitled to vote is required to approve a proposed amendment to the certificate of incorporation, following the adoption of the amendment by the board of directors of the corporation, provided that the certificate of incorporation may provide for a greater vote. Under	Under the QBCA, amendments to the articles generally require the approval of not less than two-thirds of the votes cast by shareholders entitled to vote on the resolution. Specified amendments may also require the separate approval of other classes of shares. If the amendment is of a nature affecting a particular class or series in a manner requiring a separate class or series

	<u>Delaware</u>	<u>QBCA</u>
	<p>the DGCL, holders of outstanding shares of a class or series are entitled to vote separately on an amendment to the certificate of incorporation if the amendment would have certain consequences, including changes that adversely affect the rights and preferences of such class or series.</p>	<p>vote, that class or series is entitled to vote on the amendment whether or not it otherwise carries the right to vote.</p>
<i>Amendment of Bylaws</i>	<p>Under the DGCL, after a corporation has received any payment for any of its stock, the power to adopt, amend or repeal bylaws shall be vested in the stockholders entitled to vote; provided, however, that any corporation may, in its certificate of incorporation, provide that bylaws may be adopted, amended or repealed by the board of directors. The fact that such power has been conferred upon the board of directors shall not divest the stockholders of the power nor limit their power to adopt, amend or repeal the bylaws.</p>	<p>Under the QBCA, the directors may, by resolution, make, amend or repeal any bylaws that regulates the business or affairs of the corporation. Where the directors make, amend or repeal a bylaw, they are required under the QBCA to submit that action to the shareholders at the next meeting of shareholders and the shareholders may ratify, reject or amend that action by simple majority, or ordinary resolution. If the action is rejected by shareholders, or the directors of a corporation do not submit the action to the shareholders at the next meeting of shareholders, the action in respect of the bylaws will cease to be effective, and no subsequent resolution of the directors to make, amend or repeal a bylaw having substantially the same purpose or effect will be effective until it is confirmed.</p>
<i>Votes on Amalgamations, Mergers, Consolidations and Sales of Assets</i>	<p>The DGCL provides that, unless otherwise provided in the certificate of incorporation or bylaws, the adoption of a merger agreement requires the approval of a majority of the outstanding stock of the corporation entitled to vote thereon.</p>	<p>Under the QBCA, certain extraordinary corporate actions, such as amalgamations (other than with certain affiliated corporations), continuances and sales, leases or exchanges of the property of a corporation if as a result of such alienation the corporation would be unable to retain a significant part of its business activities, and other extraordinary corporate actions such as liquidations, dissolutions and (if ordered by a court) arrangements, are required to be approved by “special resolution.”</p>

	Delaware	QBCA
<i>Dissenter’s Rights of Appraisal</i>	<p>Under the DGCL, a stockholder of a Delaware corporation generally has the right to dissent from a merger or consolidation in which the Delaware corporation is participating, subject to specified procedural requirements, including that such dissenting stockholder does not vote in favor of the merger or consolidation. However, the DGCL does not confer appraisal rights, in certain circumstances, including if the dissenting stockholder owns shares traded on a national securities exchange and will receive publicly traded shares in the merger or consolidation. Under the DGCL, a stockholder asserting appraisal rights does not receive any payment for his or her shares until the court determines the fair value or the parties otherwise agree to a value. The costs of the proceeding may be determined by the court and assessed against the parties as the court deems equitable under the circumstances.</p>	<p>A “special resolution” is a resolution passed by not less than two-thirds of the votes cast by the shareholders who voted in respect of the resolution or signed by all shareholders entitled to vote on the resolution. In specified cases, a special resolution to approve the extraordinary corporate action is also required to be approved separately by the holders of a class or series of shares, including in certain cases a class or series of shares not otherwise carrying voting rights.</p> <p>The QBCA provides that shareholders of a corporation are entitled to exercise dissent rights (called “the right to demand the repurchase of shares”) and to be paid the fair value of their shares in connection with specified matters, including:</p> <ul style="list-style-type: none"> • amalgamation with another corporation (other than with certain affiliated corporations); • amendment to the corporation’s articles to add, change or remove any provisions restricting or constraining the transfer of shares; • amendment to the corporation’s articles to add, change or remove any restriction upon the businesses or businesses that the corporation may carry on; • continuance under the laws of another jurisdiction; • alienation of the property of the corporation or of its subsidiaries if, as a result of such alienation, the corporation is unable to retain a significant part of its business activity; • a court order permitting a shareholder to exercise his right

	Delaware	QBCA
<i>Oppression Remedy</i>	The DGCL does not provide for a similar remedy.	<p>to demand the repurchase of his shares in connection with an application to the court for an order approving an arrangement proposed by the corporation;</p> <ul style="list-style-type: none"> • certain amendments to the articles of a corporation which require a separate class or series vote by a holder of shares of any class or series. <p>The QBCA provides an oppression remedy (called “rectification of abuse of power or iniquity”) that enables a court to make any order, whether interim or final, to rectify matters that are oppressive or unfairly prejudicial to the interests of any securityholder, director or officer of the corporation if an application is made to a court by an “applicant”. An “applicant” with respect to a corporation means any of the following:</p> <ul style="list-style-type: none"> • a present or former registered holder or beneficiary of securities of the corporation or any of its affiliates; • a present or former officer or director of the corporation or any of its affiliates; and • any other person who in the discretion of the court has the interest required to make the application. <p>The oppression remedy provides the court with very broad and flexible powers to intervene in corporate affairs to protect shareholders and other complainants. While conduct that is in breach of fiduciary duties of directors or that is contrary to the legal right of a complainant will normally trigger the court’s jurisdiction under the oppression remedy, the exercise of that jurisdiction does not depend on a finding of a breach of those legal</p>

	Delaware	QBCA
<i>Shareholder Derivative Actions</i>	<p>Under the DGCL, stockholders may bring derivative actions on behalf of, and for the benefit of the corporation. The plaintiff in a derivative action on behalf of the corporation either must be or have been a stockholder of the corporation at the time of the transaction or must be a stockholder who became a stockholder by operation of law in the transaction regarding which the stockholder complains. A stockholder may not sue derivatively on behalf of the corporation unless the stockholder first makes demand on the corporation that it bring suit and the demand is refused, unless it is shown that making the demand would have been a futile act.</p>	<p>and equitable rights. Furthermore, the court may order a corporation to pay the interim expenses of an applicant seeking an oppression remedy, but the applicant may be held accountable for interim costs on final disposition of the complaint (as in the case of a derivative action as described in “Shareholder Derivative Actions” below).</p> <p>Under the QBCA, a shareholder of a corporation may apply to a Québec court for leave to bring an action in the name of, and on behalf of, the corporation or any subsidiary, or to intervene in an existing action to which the corporation or any of its subsidiaries is a party, for the purpose of prosecuting, defending or discontinuing an action on behalf of the corporation or its subsidiary. Under the QBCA, no action may be brought and no intervention in an action may be made unless a court is satisfied that:</p> <ul style="list-style-type: none"> • the shareholder has given the required 14-day notice to the directors of the corporation or the subsidiary of the shareholder’s intention to apply to the court if the directors do not bring, diligently prosecute or defend or discontinue the action; • the shareholder is acting in good faith; and • it appears to be in the interests of the corporation or the relevant subsidiary that the action be brought, prosecuted, defended or discontinued. <p>Under the QBCA, the court in a derivative action may make any order it thinks fit. In addition, under the QBCA, a court may order the corporation or its</p>

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

Delaware

QBCA

related party transaction including related to the valuation.

Multilateral Instrument 61-101 also requires, subject to certain exceptions, that an issuer not engage in a related party transaction unless the shareholders of the issuer, other than the related parties, approve the transaction by a simple majority of the votes cast.

LEGAL OWNERSHIP OF SECURITIES

We can issue securities in registered form or in the form of one or more global securities. We describe global securities in greater detail below. We refer to those persons who have securities registered in their own names on the books that we or any applicable trustee, depository or warrant agent maintain for this purpose as the “holders” of those securities. These persons are the legal holders of the securities. We refer to those persons who, indirectly through others, own beneficial interests in securities that are not registered in their own names, as “indirect holders” of those securities. As we discuss below, indirect holders are not legal holders, and investors in securities issued in book-entry form or in street name will be indirect holders.

Book-Entry Holders

We may issue securities in book-entry form only, as we will specify in the applicable prospectus supplement. This means securities may be represented by one or more global securities registered in the name of a financial institution that holds them as depository on behalf of other financial institutions that participate in the depository’s book-entry system. These participating institutions, which are referred to as participants, in turn, hold beneficial interests in the securities on behalf of themselves or their customers.

Only the person in whose name a security is registered is recognized as the holder of that security. Global securities will be registered in the name of the depository or its participants. Consequently, for global securities, we will recognize only the depository as the holder of the securities, and we will make all payments on the securities to the depository. The depository passes along the payments it receives to its participants, which in turn pass the payments along to their customers who are the beneficial owners. The depository and its participants do so under agreements they have made with one another or with their customers; they are not obligated to do so under the terms of the securities.

As a result, investors in a global security will not own securities directly. Instead, they will own beneficial interests in a global security, through a bank, broker or other financial institution that participates in the depository’s book-entry system or holds an interest through a participant. As long as the securities are issued in global form, investors will be indirect holders, and not legal holders, of the securities.

Street Name Holders

We may terminate a global security or issue securities that are not issued in global form. In these cases, investors may choose to hold their securities in their own names or in “street name.” Securities held by an investor in street name would be registered in the name of a bank, broker or other financial institution that the investor chooses, and the investor would hold only a beneficial interest in those securities through an account he or she maintains at that institution.

For securities held in street name, we or any applicable trustee or depository will recognize only the intermediary banks, brokers and other financial institutions in whose names the securities are registered as the holders of those securities, and we or any such trustee or depository will make all payments on those securities to them. These institutions pass along the payments they receive to their customers who are the beneficial owners, but only because they agree to do so in their customer agreements or because they are legally required to do so. Investors who hold securities in street name will be indirect holders, not legal holders, of those securities.

Legal Holders

Our obligations, as well as the obligations of any applicable trustee or third party employed by us or a trustee, run only to the legal holders of the securities. We do not have obligations to investors who hold beneficial interests in global securities, in street name or by any other indirect means. This will be the case whether an investor chooses to be an indirect holder of a security or has no choice because we are issuing the securities only in global form.

For example, once we make a payment or give a notice to the holder, we have no further responsibility for the payment or notice even if that holder is required, under agreements with its participants or customers or by law, to pass it along to the indirect holders but does not do so. Similarly, we may want to obtain the approval of the holders to amend an indenture, to relieve us of the consequences of a default or of our

obligation to comply with a particular provision of an indenture, or for other purposes. In such an event, we would seek approval only from the holders, and not the indirect holders, of the securities. Whether and how the legal holders contact the indirect holders is up to the legal holders.

Special Considerations for Indirect Holders

If you hold securities through a bank, broker or other financial institution, either in book-entry form because the securities are represented by one or more global securities or in street name, you should check with your own institution to find out:

- how it handles securities payments and notices;
- whether it imposes fees or charges;
- how it would handle a request for the holders' consent, if ever required;
- whether and how you can instruct it to send you securities registered in your own name so you can be a holder, if that is permitted in the future;
- how it would exercise rights under the securities if there were a default or other event triggering the need for holders to act to protect their interests; and
- if the securities are in book-entry form, how the depository's rules and procedures will affect these matters.

Global Securities

A global security is a security that represents one or any other number of individual securities held by a depository. Generally, all securities represented by the same global securities will have the same terms.

Each security issued in book-entry form will be represented by a global security that we issue to, deposit with and register in the name of a financial institution or its nominee that we select. The financial institution that we select for this purpose is called the depository. Unless we specify otherwise in the applicable prospectus supplement, The Depository Trust Company, New York, New York, known as DTC, will be the depository for all securities issued in book-entry form.

A global security may not be transferred to or registered in the name of anyone other than the depository, its nominee or a successor depository, unless special termination situations arise. We describe those situations below under "— Special Situations When a Global Security Will Be Terminated." As a result of these arrangements, the depository, or its nominee, will be the sole registered owner and legal holder of all securities represented by a global security, and investors will be permitted to own only beneficial interests in a global security. Beneficial interests must be held by means of an account with a broker, bank or other financial institution that in turn has an account with the depository or with another institution that does. Thus, an investor whose security is represented by a global security will not be a legal holder of the security, but only an indirect holder of a beneficial interest in the global security.

If the prospectus supplement for a particular security indicates that the security will be issued as a global security, then the security will be represented by a global security at all times unless and until the global security is terminated. If termination occurs, we may issue the securities through another book-entry clearing system or decide that the securities may no longer be held through any book-entry clearing system.

Special Considerations for Global Securities

As an indirect holder, an investor's rights relating to a global security will be governed by the account rules of the investor's financial institution and of the depository, as well as general laws relating to securities transfers.

We do not recognize an indirect holder as a holder of securities and instead deal only with the depository that holds the global security.

If securities are issued only as global securities, an investor should be aware of the following:

- an investor cannot cause the securities to be registered in his or her name, and cannot obtain non-global certificates for his or her interest in the securities, except in the special situations we describe below;
- an investor will be an indirect holder and must look to his or her own bank or broker for payments on the securities and protection of his or her legal rights relating to the securities, as we describe above;
- an investor may not be able to sell interests in the securities to some insurance companies and to other institutions that are required by law to own their securities in non-book-entry form;
- an investor may not be able to pledge his or her interest in the global security in circumstances where certificates representing the securities must be delivered to the lender or other beneficiary of the pledge in order for the pledge to be effective;
- the depositary's policies, which may change from time to time, will govern payments, transfers, exchanges and other matters relating to an investor's interest in the global security;
- we and any applicable trustee have no responsibility for any aspect of the depositary's actions or for its records of ownership interests in the global security, nor will we or any applicable trustee supervise the depositary in any way;
- the depositary may, and we understand that DTC will, require that those who purchase and sell interests in the global security within its book-entry system use immediately available funds, and your broker or bank may require you to do so as well; and
- financial institutions that participate in the depositary's book-entry system, and through which an investor holds its interest in the global security, may also have their own policies affecting payments, notices and other matters relating to the securities.

There may be more than one financial intermediary in the chain of ownership for an investor. We do not monitor and are not responsible for the actions of any of those intermediaries.

Special Situations When a Global Security Will Be Terminated

In a few special situations described below, a global security will terminate and interests in it will be exchanged for physical certificates representing those interests. After that exchange, the choice of whether to hold securities directly or in street name will be up to the investor. Investors must consult their own banks or brokers to find out how to have their interests in securities transferred to their own names, so that they will be direct holders. We have described the rights of holders and street name investors above.

Unless we provide otherwise in the applicable prospectus supplement, a global security will terminate when the following special situations occur:

- if the depositary notifies us that it is unwilling, unable or no longer qualified to continue as depositary for that global security and we do not appoint another institution to act as depositary within 90 days;
- if we notify any applicable trustee that we wish to terminate that global security; or
- if an event of default has occurred with regard to securities represented by that global security and has not been cured or waived.

The applicable prospectus supplement may also list additional situations for terminating a global security that would apply only to the particular series of securities covered by the prospectus supplement. When a global security terminates, the depositary, and neither we nor any applicable trustee, is responsible for deciding the names of the institutions that will be the initial direct holders.

PLAN OF DISTRIBUTION

We may sell the securities from time to time pursuant to underwritten public offerings, negotiated transactions, block trades or a combination of these methods. We may sell the securities to or through underwriters or dealers, through agents, or directly to one or more purchasers. We may distribute securities from time to time in one or more transactions:

- at a fixed price or prices, which may be changed;
- at market prices prevailing at the time of sale;
- at prices related to such prevailing market prices; or
- at negotiated prices.

We may also sell equity securities covered by this registration statement in an “at the market offering” as defined in Rule 415 under the Securities Act. Such offering may be made into an existing trading market for such securities in transactions at other than a fixed price on or through the facilities of Nasdaq or any other securities exchange or quotation or trading service on which such securities may be listed, quoted or traded at the time of sale.

Such at the market offerings, if any, may be conducted by underwriters acting as principal or agent.

A prospectus supplement or supplements (and any related free writing prospectus that we may authorize to be provided to you) will describe the terms of the offering of the securities, including, to the extent applicable:

- the name or names of any underwriters, dealers or agents, if any;
- the purchase price of the securities and the proceeds we will receive from the sale;
- any over-allotment options under which underwriters may purchase additional securities from us;
- any agency fees or underwriting discounts and other items constituting agents’ or underwriters’ compensation;
- any public offering price;
- any discounts or concessions allowed or reallocated or paid to dealers; and
- any securities exchange or market on which the securities may be listed.

Only underwriters named in the prospectus supplement are underwriters of the securities offered by the prospectus supplement.

If underwriters are used in the sale, they will acquire the securities for their own account and may resell the securities from time to time in one or more transactions at a fixed public offering price or at varying prices determined at the time of sale. The obligations of the underwriters to purchase the securities will be subject to the conditions set forth in the applicable underwriting agreement. We may offer the securities to the public through underwriting syndicates represented by managing underwriters or by underwriters without a syndicate. Subject to certain conditions, the underwriters will be obligated to purchase all of the securities offered by the prospectus supplement, other than securities covered by an over-allotment or other option. Any public offering price and any discounts or concessions allowed or reallocated or paid to dealers may change from time to time. We may use underwriters with whom we have a material relationship. We will describe in the prospectus supplement, naming the underwriter, the nature of any such relationship.

We may sell securities directly or through agents we designate from time to time. We will name any agent involved in the offering and sale of securities, and we will describe any commissions we will pay the agent in the prospectus supplement. Unless the prospectus supplement states otherwise, our agent will act on a best-efforts basis for the period of its appointment.

We may authorize agents or underwriters to solicit offers by certain types of institutional investors to purchase securities from us at the public offering price set forth in the prospectus supplement pursuant to

delayed delivery contracts providing for payment and delivery on a specified date in the future. We will describe the conditions to these contracts and the commissions we must pay for solicitation of these contracts in the prospectus supplement.

We may provide agents and underwriters with indemnification against civil liabilities related to any offering, including liabilities under the Securities Act, or contribution with respect to payments that the agents or underwriters may make with respect to these liabilities. Agents and underwriters may engage in transactions with, or perform services for, us in the ordinary course of business.

All securities we may offer, other than common shares will be new issues of securities with no established trading market. Any underwriters may make a market in these securities, but will not be obligated to do so and may discontinue any market making at any time without notice. We cannot guarantee the liquidity of the trading markets for any securities.

Any underwriter may engage in overallotment, stabilizing transactions, short covering transactions and penalty bids. Overallotment involves sales in excess of the offering size, which create a short position. Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum. Short covering transactions involve purchases of the securities in the open market after the distribution is completed to cover short positions. Penalty bids permit the underwriters to reclaim a selling concession from a dealer when the securities originally sold by the dealer are purchased in a stabilizing or covering transaction to cover short positions. Those activities may cause the price of the securities to be higher than it would otherwise be. If commenced, the underwriters may discontinue any of the activities at any time. These transactions may be effected on any exchange or over-the-counter market or otherwise.

Any underwriters or agents who are qualified market makers on Nasdaq may engage in passive market making transactions in the securities on Nasdaq in accordance with Rule 103 of Regulation M, during the business day prior to the pricing of the offering, before the commencement of offers or sales of the securities. Passive market makers must comply with applicable volume and price limitations and must be identified as passive market makers. In general, a passive market maker must display its bid at a price not in excess of the highest independent bid for such security; if all independent bids are lowered below the passive market maker's bid, however, the passive market maker's bid must then be lowered when certain purchase limits are exceeded. Passive market making may stabilize the market price of the securities at a level above that which might otherwise prevail in the open market and, if commenced, may be discontinued at any time.

In compliance with guidelines of the Financial Industry Regulatory Authority, or FINRA, the maximum consideration or discount to be received by any FINRA member or independent broker dealer may not exceed 8% of the aggregate amount of the securities offered pursuant to this prospectus and any applicable prospectus supplement.

LEGAL MATTERS

Unless the applicable prospectus supplement indicates otherwise, the validity of the securities in respect of which this prospectus, and any supplement thereto, is being delivered and certain legal matters with respect to Canadian law will be passed upon by Osler, Hoskin & Harcourt LLP, Montréal, Canada. Certain matters in respect of U.S. securities laws may be opined upon by Cooley LLP. Additional legal matters may be passed upon for us or any underwriters, dealers or agents, by counsel that we will name in the applicable prospectus supplement.

EXPERTS

The consolidated financial statements incorporated in this prospectus by reference to the [Annual Report on Form 10-K for the year ended December 31, 2020](#) have been so incorporated in reliance on the report of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

This prospectus is part of a registration statement we filed with the SEC. This prospectus does not contain all of the information set forth in the registration statement and the exhibits to the registration statement. For further information with respect to us and the securities we are offering under this prospectus, we refer you to the registration statement and the exhibits and schedules filed as a part of the registration statement. You should rely only on the information contained in this prospectus or incorporated by reference. We have not authorized anyone else to provide you with different information. We are not making an offer of these securities in any state where the offer is not permitted. You should not assume that the information in this prospectus is accurate as of any date other than the date on the front page of this prospectus, regardless of the time of delivery of this prospectus or any sale of the securities offered by this prospectus.

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

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to "incorporate by reference" information into this prospectus, which means that we can disclose important information to you by referring you to another document filed separately with the SEC. The SEC file number for the documents incorporated by reference in this prospectus is 001-38899. The documents incorporated by reference into this prospectus contain important information that you should read about us.

The following documents are incorporated by reference into this document:

- [our Annual Report on Form 10-K for the year ended December 31, 2020, filed with the SEC on March 29, 2021;](#)
- our [Quarterly Report on Form 10-Q for the quarter ended March 31, 2021, filed with the SEC on May 17, 2021](#), our [Quarterly Report on Form 10-Q for the quarter ended June 30, 2021, filed with the SEC on August 11, 2021](#), and our [Quarterly Report on Form 10-Q for the quarter ended September 30, 2021, filed with the SEC on November 12, 2021;](#)
- our Current Reports on Form 8-K filed with the SEC on [May 17, 2021](#), [June 2, 2021](#), [June 21, 2021](#), and [November 12, 2021](#), to the extent the information in such reports is filed and not furnished;
- [our Proxy Statement filed with the SEC on April 30, 2021 to the extent the information therein is filed and not furnished; and](#)

- [the description of our common shares contained in our Registration Statement on Form 8-A, filed with the SEC on May 6, 2019, including any amendments or reports filed for the purposes of updating this description.](#)

Notwithstanding the statements in the preceding paragraphs, no document, report or exhibit (or portion of any of the foregoing) or any other information that we have “furnished” to the SEC pursuant to the Exchange Act shall be incorporated by reference into this prospectus.

We also incorporate by reference into this prospectus all documents (other than current reports furnished under Item 2.02 or Item 7.01 of Form 8-K and exhibits filed on such form that are related to such items) that are filed by us with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act (i) after the date of the initial filing of the registration statement of which this prospectus forms a part and prior to effectiveness of the registration statement, or (ii) after the date of this prospectus but prior to the termination of the offering. These documents include periodic reports, such as Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q and Current Reports on Form 8-K, as well as proxy statements.

We will provide to each person, including any beneficial owner, to whom a prospectus is delivered, without charge upon written or oral request, a copy of any or all of the documents that are incorporated by reference into this prospectus but not delivered with the prospectus, including exhibits that are specifically incorporated by reference into such documents. You should direct any requests for documents to Milestone Pharmaceuticals Inc., Attn: Company Secretary; 1111 Dr. Frederik-Philips Boulevard, Suite 420, Montréal, Québec, Canada H4M 2X6.

Any statement contained herein or in a document incorporated or deemed to be incorporated by reference into this prospectus will be deemed to be modified or superseded for purposes of the document to the extent that a statement contained in this document or any other subsequently filed document that is deemed to be incorporated by reference into this prospectus modifies or supersedes the statement.



**Up to \$47,249,368
Common Shares**

PROSPECTUS SUPPLEMENT

Jefferies

May 31, 2023
