

PROSPECTUS SUPPLEMENT
(To Prospectus Dated February 2, 2022)

16,666,667 Common Shares

Pre-Funded Warrants to Purchase 3,333,333 Common Shares

We are offering 16,666,667 common shares pursuant to this prospectus supplement.

We are also offering to certain investors the opportunity to purchase, in lieu of common shares, warrants, which we refer to as pre-funded warrants, to purchase 3,333,333 common shares. The purchase price of each pre-funded warrant will equal the price per share that our common shares are being sold to the public in this offering, minus \$0.001, and the exercise price of each pre-funded warrant will equal \$0.001 per share. This prospectus supplement also relates to the offering of the common shares issuable upon exercise of such pre-funded warrants. The pre-funded warrants will be immediately exercisable, subject to the limitations described in the section "Description of Pre-Funded Warrants—Exercisability," and may be exercised at any time after their original issuance.

Our common shares trade on the Nasdaq Global Select Market under the symbol "MIST." On February 28, 2024, the last reported sale price of our common shares was \$2.13 per share. There is no established public trading market for the pre-funded warrants, and we do not expect a market to develop. We do not intend to list the pre-funded warrants on the Nasdaq Global Select Market or on any other national securities exchange or nationally recognized trading system. Without an active trading market, the liquidity of the pre-funded warrants will be limited.

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

Investing in our securities involves a high degree of risk. See "Risk Factors" beginning on page S-9 of this prospectus supplement, page 7 of the prospectus and any related free writing prospectus we have authorized for use in connection with this offering and under similar headings in the other documents that are incorporated by reference into this prospectus supplement concerning factors you should consider before investing in our securities.

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.

	Per Share	Per Pre-Funded Warrant	Total
Offering price	\$ 1.50	\$ 1.499	\$ 29,996,666.667
Underwriting discounts and commissions ⁽¹⁾	\$ 0.09	\$ 0.08994	\$ 1,799,800.000
Proceeds, before expenses to us	\$ 1.41	\$ 1.40906	\$ 28,196,866.667

⁽¹⁾ See "Underwriting" beginning on page S-31 of this prospectus supplement for a description of all compensation payable to the underwriters.

We have granted the underwriters an option for a period of 30 days from the date of this prospectus supplement to purchase an aggregate of up to an additional 3,000,000 shares of our common shares. If the underwriters exercise their option in full, the total underwriting discounts and commissions payable by us will be \$2,069,800.000020 and the total proceeds to us, before expenses, will be \$32,426,866.666980.

The underwriters expect to deliver the common shares and the pre-funded warrants against payment on or about March 4, 2024.

Sole Book-Running Manager

Piper Sandler

Lead Manager

H.C. Wainwright & Co.

The date of this prospectus supplement is February 28, 2024.

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Prospectus

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ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement is a part of a registration statement that we have filed on Form S-3 with the U.S. Securities and Exchange Commission, or the SEC, utilizing a “shelf” registration process. By using a shelf registration statement, we may offer our common shares and pre-funded warrants from time to time under the prospectus and this prospectus supplement and on terms to be determined by, among other factors, market conditions at the time of the offering. Before buying any of our common shares or pre-funded warrants that we are offering, we urge you to carefully read this prospectus supplement, together with the information incorporated by reference as described under the headings “Where You Can Find More Information” and “Incorporation of Certain Information by Reference” in this prospectus supplement. These documents contain important information that you should consider when making your investment decision.

We provide information to you about this offering of our common shares and pre-funded warrants in two separate documents that are bound together: (1) this prospectus supplement, which describes the specific details regarding this offering, and (2) the accompanying prospectus, which provides general information, some of which may not apply to this offering. Generally, when we refer to this “prospectus,” we are referring to both documents combined. If information in this prospectus supplement is inconsistent with the accompanying prospectus, you should rely on this prospectus supplement.

This prospectus supplement describes the terms of this offering of our common shares and pre-funded warrants and also adds to and updates information contained in the documents incorporated by reference into this prospectus supplement. To the extent there is a conflict between the information contained in this prospectus supplement, on the one hand, and the information contained in any document incorporated by reference that was filed with the SEC before the date of this prospectus supplement, on the other hand, you should rely on the information in this prospectus supplement. 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 into this prospectus supplement—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 the underwriters have authorized anyone to provide any information or make any representations other than those contained or incorporated by reference in this prospectus supplement, the accompanying prospectus or any free writing prospectus that we have authorized for use in connection with this offering. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. Neither we nor the underwriters are making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted or in which the person making that offer or solicitation is not qualified to do so or to anyone to whom it is unlawful to make an offer or solicitation. You should assume that the information appearing in 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, is accurate only as of the date of those respective documents. Our business, financial condition, results of operations and prospects may have changed since those dates. You should read 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, in their entirety before making an investment decision.

We are offering to sell, and seeking offers to buy, our common shares and pre-funded warrants only in jurisdictions where offers and sales are permitted. The distribution of this prospectus supplement and accompanying prospectus and the offering of our common shares and pre-funded warrants in certain jurisdictions may be restricted by law. Persons outside the United States who come into possession of this prospectus supplement and accompanying prospectus must inform themselves about, and observe any

restrictions relating to, the offering of our common shares and pre-funded warrants and the distribution of this prospectus supplement and accompanying prospectus outside the United States. This prospectus supplement and 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 accompanying prospectus by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation.

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.

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 or pre-funded warrants. 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” beginning on page S-9 of this prospectus supplement and in the section entitled “Risk Factors” of our Annual Report on Form 10-K for the year ended December 31, 2022, our quarterly report on Form 10-Q for the quarter ended September 30, 2023 and in any subsequent reports we file with the SEC after the date of this prospectus supplement, 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.

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 heart 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 condition that causes a patient’s heart to suddenly start beating faster than normal. It can be life-altering as PSVT is highly symptomatic, characterized by unpredictable attacks of a racing heart, often exceeding 150 beats per minute. Symptoms of PSVT arise suddenly and may 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 often 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 more than 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 \geq 110 beats per minute. The occurrence of a rapid ventricular rate in patients with atrial fibrillation increases the likelihood of marked 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 a sudden episode of AFib-RVR, acute rate control is needed, and most treatments are 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 or adequate ventricular rate control due to a 30- to 90-minute delayed onset of action, and, as a result, many

patients need faster and more certain rate-reduction and symptom-resolution and so seek acute-medical care by going to the emergency department for 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 and the unpredictable nature of RVR episodes; 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, portable nasal spray treatment to be prescribed by a physician or appropriate health-care professional such that the patient with the indicated arrhythmia can carry etripamil with them for use wherever and whenever an attack of the arrhythmia occurs. If approved, we believe that etripamil will provide the patient with a portable treatment to stop an attack 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 SVT attack will occur. For health care providers, etripamil could represent a new tool they can offer to their patients to better self-manage their SVT attacks resulting in fewer calls to their office, a more efficient use of healthcare resources, and more empowered, satisfied patients.

Milestone recently completed and reported data from a Phase 2 clinical trial for assessing etripamil's 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. On November 11, 2023, we announced and publicly presented positive Phase 2 data that show etripamil nasal spray resulted in rapid and statistically superior ventricular rate reduction and improved symptom-relief in patients with AFib-RVR compared to placebo. Safety and tolerability reported in the 56-patient safety population who received etripamil was generally consistent with that observed in our PSVT program discussed above. We believe these data support the further development of self-administered etripamil with a Phase 3 study for the treatment of AFib-RVR.

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 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.

An estimated five million Americans suffer from AFib, a common arrhythmia marked by an irregular, disruptive and often rapid heartbeat. The incidence of AFib is expected to grow to approximately 10 million by 2025 and up to about 12 million by 2030. A subset of patients with AFib experience episodes of abnormally high heart rate most often accompanied by palpitations, shortness of breath, dizziness, and weakness. While these episodes, known as AFib-RVR, may be treated by oral calcium channel blockers and/or beta blockers, patients frequently seek acute care in the emergency department to address symptoms. In 2016, there were nearly 800,000 emergency department visits and hospital admissions due to AFib symptoms where treatment includes medically supervised intravenous administration of calcium channel blockers or beta blockers, or electrical cardioversion. With little available data for AFib-RVR, Milestone's initial market research indicates that 30% to 40% of patients with AFib experience one or more symptomatic episodes of RVR per year that require treatment, suggesting a target addressable market of approximately three to four million patients in 2030 for etripamil in patients with AFib-RVR. The American Heart Association (AHA) estimates a prevalence for AFib of more than 12 million by 2030, while the Centers for Disease Control (CDC) reports this prevalence as increasing to 12.1 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.

Recent Developments

Preliminary Balance of Cash and Cash Equivalents

We estimate that we had cash, cash equivalents and short-term investments of approximately \$66.0 million as of December 31, 2023.

Our actual financial results as of the year ended December 31, 2023 are not yet available. Our financial closing procedures for the year ended December 31, 2023 are not yet complete and, as a result, our final results upon completion of those procedures may differ materially from this preliminary estimate. The preliminary financial data presented above as of December 31, 2023 is not a comprehensive statement of our financial position or operating results, reflects our preliminary estimate based on information available as of the date of this prospectus supplement; and is subject to change, and those changes may be material. Accordingly, you should not place undue reliance upon this preliminary estimate.

The preliminary consolidated financial data presented above has been prepared by, and is the responsibility of, our management. Our independent registered public accounting firm, PricewaterhouseCoopers LLP, has not audited, reviewed, compiled or performed any procedures, and does not express an opinion or any other form of assurance with respect to any of such data.

New Drug Application Status

In October 2023 we submitted a New Drug Application, or NDA, for marketing approval in the United States for etripamil for the treatment of PSVT. On December 26, 2023 we announced that we received a refuse-to-file, or RTF, letter from the FDA. Upon preliminary review, the FDA determined that the NDA was not sufficiently complete to permit substantive review. The FDA requested clarification about the time of data recorded for adverse events in our Phase 3 clinical trials; FDA did not express concerns about the nature or severity of adverse events, or AEs.

In February 2024, we held a Type A Meeting with the FDA to determine next steps for the filing for marketing approval. The FDA indicated that the timing of AEs in question had minimal impact on the overall characterization of the etripamil safety profile, based on the FDA's review of the affected data which was mainly related to AEs associated with local drug administration site tolerability and, importantly, did not appear to affect the assessment of serious adverse events and/or AEs of special interest for a calcium channel blocker. To align with the FDA's guidance in preliminary response to our questions presented to the FDA in our Type A Meeting request, we plan to restructure the data sets that capture timing of reported AEs, reformat certain data files to facilitate FDA's analyses, and resubmit the NDA. Based on the guidance received during the Type A Meeting, we expect that this approach will address the RTF from the FDA. The FDA has not requested that we complete additional clinical efficacy or safety trials prior to resubmitting the NDA. We expect a standard NDA review period following resubmission of the NDA for etripamil for PSVT, which is planned for the second quarter of 2024.

Considering the revised timeline for NDA submission, we have undertaken certain cash conservation measures to reduce spend through program deferrals and team restructuring and expect that our existing cash resources will fund operations into mid-2025, including through the expected Prescription Drug User Fee Act date for the NDA resubmission. We expect the implementation of these cash conservation measures to be substantially completed in the first quarter of 2024. If FDA approval is granted, we expect to receive a \$75 million payment under an existing royalty agreement, which is intended to fund the potential commercial launch of etripamil for PSVT.

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 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, but are not limited to:

- 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 \$1.235 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 OFFERING

Common Shares Offered by Us	16,666,667 common shares (or 19,666,667 shares if the underwriters exercise their option to purchase additional shares in full).
Pre-Funded Warrants Offered by Us	We are also offering, in lieu of our common shares to certain investors that so choose, pre-funded warrants to purchase 3,333,333 of our common shares. The purchase price of each pre-funded warrant is equal to the price per share of our common shares at which our common shares are being sold in this offering, minus \$0.001, the exercise price of each pre-funded warrant. Each pre-funded warrant will be exercisable from the date of issuance until fully exercised, subject to an ownership limitation. See “Description of Pre-Funded Warrants.” This prospectus supplement also relates to the offering of our common shares issuable upon the exercise of such pre-funded warrants.
Option to Purchase Additional Shares	We have granted to the underwriters an option for a period of 30 days to purchase an aggregate of up to 3,000,000 additional shares of our common shares.
Common Shares to be Outstanding After this Offering	50,149,778 common shares (or 53,149,778 shares if the underwriters exercise their option to purchase additional shares in full), assuming no exercise of any pre-funded warrants offered and sold by us.
Use of Proceeds	We estimate that our net proceeds from this offering will be approximately \$28.2 million (or \$32.4 million if the underwriters exercise their option to purchase additional shares in full), after deducting underwriting discounts and commissions and estimated offering expenses payable by us. We intend to use the net proceeds we receive from this offering, together with our existing cash and cash equivalents, to continue the development of etripamil in our lead indication of PSVT and our subsequent indication of AFib-RVR, as well as for working capital and other general corporate purposes. See “Use of Proceeds” for additional information.
Risk Factors	Investing in our common shares and pre-funded warrants involves significant risks. Please read the information contained in and incorporated by reference under the heading “Risk Factors” in this prospectus supplement beginning on page S-9, the prospectus beginning on page 7, in our Annual Report on Form 10-K for the year ended December 31, 2022 and in our Quarterly Report on Form 10-Q for the quarter ended September 30, 2023 as well as under similar headings in the other documents that are incorporated by reference into this prospectus supplement, together with the other information included in or incorporated by reference into this prospectus supplement, before deciding whether to invest in our common shares and pre-funded warrants.
Nasdaq Global Market Symbol	Our common shares trade on the Nasdaq Global Select Market under the symbol “MIST.” We do not intend to list the pre-funded warrants on the Nasdaq Global Market or any other national securities exchange or nationally recognized trading system. Without an active market, the liquidity of the pre-funded warrants will be limited.

The above discussion and table are based on 33,481,787 common shares outstanding as of September 30, 2023, and exclude:

- 4,859,560 common shares issuable upon the exercise of outstanding options as of September 30, 2023, at a weighted-average exercise price of \$5.25 per share;
- 1,644,623 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;
- 1,463,936 common shares reserved for future issuance under our 2019 Employee Share Purchase Plan, or the ESPP, as of September 30, 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 September 30, 2023, at an exercise price of \$0.01 per share;
- \$47.3 million of our common shares remaining available for sale by us as of the date of this prospectus supplement pursuant to our Open Market Sale AgreementSM with Jefferies LLC, or Jefferies; and
- up to 14,315,689 common shares, of which (a) 9,846,319 common shares are issuable upon the conversion of Milestone's senior secured convertible promissory notes, or the Notes, and (b) 4,469,370 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 September 30, 2023.

RISK FACTORS

Investing in our securities involves a high degree of risk. You should carefully review the risks and uncertainties described below and under the heading “Risk Factors” contained in any related free writing prospectus, and under similar headings in our Annual Report on Form 10-K for the year ended December 31, 2022, in our quarterly report on Form 10-Q for the quarter ended September 30, 2023 and in any subsequent reports we file with the SEC after the date of this prospectus supplement that are incorporated by reference into this prospectus supplement and the related prospectus, before deciding whether to purchase our common shares or pre-funded warrants. 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.

Risks Related to Our Financial Position and Capital Needs

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

Since inception in 2003, we have incurred significant operating losses. Our net loss was \$46.1 million and \$58.4 million for nine months ended September 30, 2023 and the year ended December 31, 2022, respectively. As of September 30, 2023, we had an accumulated deficit of \$312.4 million. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. Since inception, we have devoted substantially all of our efforts to research and preclinical and clinical development of etripamil, as well as to expanding our management team and infrastructure. It could be several years, if ever, before we have a commercialized drug.

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

- continue our ongoing and planned development of etripamil, including our Phase 3 and potentially future Phase 4 clinical trials of etripamil for the treatment of PSVT and future Phase 3 clinical trials of etripamil for the treatment of AFib-RVR;
- seek marketing approvals for etripamil for the treatment of PSVT, AFib-RVR and other cardiovascular indications;
- establish a sales, marketing, manufacturing and distribution capability, either directly or indirectly with third parties, to commercialize etripamil or any future product candidate for which we may obtain marketing approval;
- build a portfolio of product candidates through development, or the acquisition or in-license of drugs, product candidates or technologies;
- initiate preclinical studies and clinical trials for etripamil for any additional indications we may pursue, and for any additional product candidates that we may pursue in the future;
- maintain, protect and expand our intellectual property portfolio;
- hire additional clinical, regulatory and scientific personnel;
- add operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts; and
- incur additional legal, insurance related, accounting and other expenses associated with operating as a public company.

To become and remain profitable, we must succeed in developing and eventually commercializing drugs that generate significant revenue. This will require us to be successful in a range of challenging activities, including completing clinical trials of etripamil and any future product candidates that way may pursue, obtaining regulatory approval, procuring commercial-scale manufacturing, marketing and selling etripamil

and any future products for which we may obtain regulatory approval, as well as discovering or acquiring and then developing additional product candidates. We are only in the preliminary stages of some of these activities. We may never succeed in these activities and, even if we do, may never generate revenues that are significant enough to achieve profitability.

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

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

For example, we received a refusal to file letter from the FDA for the NDA for self-administered etripamil nasal spray for the treatment of PSVT in December 2023. Upon preliminary review, the FDA determined that the NDA, submitted in October 2023, was not sufficiently complete to permit substantive review. The FDA requested clarification in the refusal to file letter about the time of data recorded for adverse events in our Phase 3 clinical trials. We held a Type A Meeting with FDA in February 2024. To align with FDA's guidance in preliminary response to our questions presented to the FDA in our Type A Meeting request, we will need to restructure the data sets that capture timing of reported AEs, reformat certain data files to facilitate FDA's analyses, and resubmit the NDA. We plan to resubmit the NDA for self-administered etripamil nasal spray for the treatment of PSVT in the second quarter of 2024. There is no guarantee that we will be able to resubmit the NDA on the expected timeline or that the FDA will accept the NDA for review following resubmission and, even if it does, there is no guarantee that the FDA will approve our NDA or, if approved, that we will ever generate sufficient revenue to achieve profitability.

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

Risks Related to the Development of Our Product Candidates

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

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

Prior to obtaining approval to commercialize etripamil and any other drug product candidate in the United States or elsewhere, we must demonstrate with substantial evidence from well controlled clinical trials, and to the satisfaction of the FDA or comparable foreign regulatory authorities, that such product candidates are safe and effective for their intended uses. Results from nonclinical studies and clinical trials can be interpreted in different ways. Even if we believe the nonclinical or clinical data for our product candidates are promising, such data may not be sufficient to support approval by the FDA and other regulatory authorities. The FDA may also require us to conduct additional nonclinical studies, including human factor studies, or clinical trials for our product candidates either prior to or post-approval, or it may

object to elements of our clinical development program. For example, the FDA has requested additional nonclinical study data and reformatted and restructured clinical data in connection with our NDA for self-administered etripamil nasal spray for the treatment of PSVT and may request that we complete additional nonclinical studies, including human factor studies, or clinical trials upon review of our resubmitted NDA for self-administered etripamil nasal spray for the treatment of PSVT. In addition, the FDA typically refers applications for novel drugs, like etripamil and potentially any future product candidates, to an advisory committee composed of outside experts. The FDA is not bound by the recommendation of the advisory committee, but it considers such recommendation when making its decision.

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

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

Additionally, we received a refusal to file letter from the FDA for the NDA for self-administered etripamil nasal spray for the treatment of PSVT in December 2023. Upon preliminary review, the FDA determined that the NDA, submitted in October 2023, was not sufficiently complete to permit substantive review. The FDA requested clarification in the refusal to file letter about the time of data recorded for adverse events in our Phase 3 clinical trials. We held a Type A Meeting with FDA in February 2024. To align with FDA's guidance in preliminary response to our questions presented to the FDA in our Type A Meeting request, we will need to restructure the data sets that capture timing of reported AEs, reformat certain data files to facilitate FDA's analyses, and resubmit the NDA. We plan to resubmit the NDA for self-administered etripamil nasal spray for the treatment of PSVT in the second quarter of 2024. There is no guarantee that we will be able to resubmit the NDA on the expected timeline or that the FDA will accept the NDA for review following resubmission.

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

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

As an organization, we have completed pivotal clinical trials, but we have never successfully submitted an NDA. We may be unable to do so for any product candidates we may develop.

After completing pivotal clinical trials, we will need to obtain the approval of the FDA and other regulatory agencies to market etripamil or any of our other product candidates. Carrying out later-stage clinical trials and the submission of a successful NDA is a complicated process. As an organization, we have completed two Phase 3 clinical trials, we have other trials ongoing, and we have limited experience in

preparing, submitting and prosecuting regulatory filings. Due to our limited experience with completing later stage trials, we may be unable to successfully and efficiently execute and complete necessary clinical trials in a way that leads to NDA submission and approval of etripamil for the treatment of PSVT. For example, we received a refusal-to-file letter from the FDA for the NDA for self-administered etripamil nasal spray for the treatment of PSVT in December 2023. Upon preliminary review, the FDA determined that the NDA, submitted in October 2023, was not sufficiently complete to permit substantive review. The FDA requested clarification about the time of data recorded for adverse events in our Phase 3 clinical trials. We held a Type A Meeting with FDA in February 2024. To align with FDA's guidance in preliminary response to our questions presented to the FDA in our Type A Meeting request, we will need to restructure the data sets that capture timing of reported AEs, reformat certain data files to facilitate FDA's analyses, and resubmit the NDA.

Even if we resubmit the NDA for etripamil for PSVT, the FDA may refuse to accept it for review or issue a complete response letter rather than approval for commercial marketing. We may require more time and incur greater costs than our competitors and may not succeed in obtaining regulatory approvals of product candidates that we develop. Failure to commence or complete, or delays in, our planned clinical trials could prevent us from or delay us in commercializing etripamil for the treatment of PSVT or AFIB-RVR.

Additional Risks Related to this Offering

Management will have broad discretion as to the use of the proceeds from this offering and may not use the proceeds effectively.

Our management will have broad discretion in the application of the net proceeds from this offering, including for any of the purposes described in the section titled "Use of Proceeds," and you will not have the opportunity as part of your investment decision to assess whether the net proceeds are being used appropriately. Because of the number and variability of factors that will determine our use of the net proceeds from this offering, their ultimate use may vary substantially from their currently intended use. The failure by our management to apply these funds effectively could harm our business. Pending their use, we may invest the net proceeds from this offering in short-term or intermediate-term, investment-grade, interest-bearing securities. These investments may not yield a favorable return to our shareholders. If we do not invest or apply the net proceeds from this offering in ways that enhance shareholder value, we may fail to achieve expected financial results, which could cause our share price to decline.

If you purchase our common shares or pre-funded warrants in this offering, you will experience immediate and substantial dilution.

The offering price per share in this offering exceeds the net tangible book value per common share outstanding prior to this offering. Therefore, if you purchase common shares or pre-funded warrants in this offering, based on an offering price of \$1.50 per share and \$1.499 per pre-funded warrant, respectively, you will experience immediate dilution of \$0.52 per share, representing the difference between our as adjusted net tangible book value per share as of September 30, 2023 after giving effect to this offering and the offering price and assuming no exercise of the pre-funded warrants issued in this offering and no exercise of the underwriters' option to purchase additional shares. The conversion of the Notes, exercise of outstanding options or vesting of restricted stock units may result in further dilution of your investment. See the section titled "Dilution" below for a more detailed illustration of the dilution you will incur if you participate in this offering.

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

In order to raise additional capital, we expect to in the future offer additional common shares or other securities convertible into or exchangeable for our common shares. We cannot assure you that we will be able to sell shares or other securities in any other offering at a price per share that is equal to or greater 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 other securities convertible into or exchangeable for our common shares in future transactions may be higher or lower than the price per share in this offering.

The trading price of our common shares is highly volatile, which could result in substantial losses for our stockholders.

The trading price of our common shares has been, and is likely to continue to be, highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control. During the period from February 27, 2023 to February 27, 2024, the closing price of our common shares ranged from a high of \$4.40 per share to a low of \$1.40 per share. The stock market in general and the market for smaller pharmaceutical and biopharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, you may not be able to sell your common shares at or above the price you paid for your common shares in this offering.

There is no public market for the pre-funded warrants being offered in this offering.

There is no established public trading market for the pre-funded warrants being offered in this offering, and we do not expect a market to develop. In addition, we do not intend to apply to list the pre-funded warrants on any securities exchange or nationally recognized trading system, including the Nasdaq Global Select Market. Without an active trading market, the liquidity of the pre-funded warrants will be limited.

We will not receive any meaningful amount of additional funds upon the exercise of the pre-funded warrants.

Each pre-funded warrant will be exercisable until it is fully exercised and by means of payment of the nominal cash purchase price upon exercise or through a “cashless exercise” procedure. Accordingly, we will not receive any meaningful additional funds upon the exercise of the pre-funded warrants.

Except for the right to participate in certain dividends and distributions, holders of the pre-funded warrants will have no rights as common shareholders until such holders exercise their pre-funded warrants and acquire common shares.

Until holders of the pre-funded warrants exercise their pre-funded warrants and acquire common shares, such holders will have no rights with respect to the common shares underlying such pre-funded warrants. Upon exercise of the pre-funded warrants, the holders will be entitled to exercise the rights of a common shareholder only as to matters for which the record date occurs after the exercise date. See “Description of Pre-Funded Warrants — No Rights as a Shareholder.”

Significant holders or beneficial holders of common shares may not be permitted to exercise the pre-funded warrants that they hold.

A holder of the pre-funded warrants will not be entitled to exercise any portion of any pre-funded warrant that, upon giving effect to such exercise, would cause: (i) the aggregate number of common shares beneficially owned by such holder (together with its affiliates) to exceed 9.99% of the number of our common shares outstanding immediately after giving effect to the exercise; or (ii) the combined voting power of our securities beneficially owned by such holder (together with its affiliates) to exceed 9.99% of the combined voting power of all of our securities outstanding immediately after giving effect to the exercise, as such percentage ownership is determined in accordance with the terms of the pre-funded warrants. As a result, you may not be able to exercise your pre-funded warrants for common shares at a time when it would be financially beneficial for you to do so. In such a circumstance, you could seek to sell your pre-funded warrants to realize value, but you may be unable to do so in the absence of an established trading market and due to applicable transfer restrictions.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement 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 supplement, 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 of 1933, as amended, or the Securities Act, and Section 21E of the Exchange Act.

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 prospectus and the documents incorporated by reference herein and therein including, among other things:

- the initiation, timing, progress and results of our current and future clinical trials of etripamil, including our Phase 3 clinical trials of etripamil for the treatment of PSVT, our Phase 2 clinical trial of etripamil for the treatment of AFib-RVR, and of our research and development programs;
- the timing of and our ability to successfully resubmit our NDA for self-administered etripamil nasal spray for the treatment of PSVT;
- 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 expect to 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 Annual Report on Form 10-K for the year ended December 31, 2022, our Quarterly Report on Form 10-Q for the quarter ended September 30, 2023 and our other filings we make with the SEC.

The foregoing list of risks is not exhaustive. Other sections of this prospectus supplement and the related prospectus and the documents incorporated by reference herein and therein 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 and the related 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 this prospectus supplement and any related free writing prospectus, and under similar headings in the other documents that are incorporated by reference into this prospectus supplement and the related 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 supplement, the related prospectus and the documents that we incorporate by reference in this prospectus supplement and have filed as exhibits to the registration statement, of which the 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 supplement by these cautionary statements.

We may from time-to-time provide estimates, projections and other information concerning our industry, our business and the markets for our programs and product candidates. 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 that are assumed in this information. Unless otherwise expressly stated, we obtained this industry, business, market, and other data from our own internal estimates and research as well as from reports, research surveys, studies, and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data and similar sources. While we are not aware of any misstatements regarding any third-party information presented in this prospectus supplement or the accompanying prospectus, their estimates, in particular, as they relate to projections, involve numerous assumptions, are subject to risks and uncertainties and are subject to change based on various factors. You should read this prospectus supplement, the accompanying prospectus and the documents that we reference herein and therein and have filed with the SEC as exhibits thereto completely and with the understanding that our actual future results may be materially different from any future results expressed or implied by these forward-looking statements. These estimates involve numerous assumptions, are subject to risks and uncertainties and are subject to change based on various factors that could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, collaborations, joint ventures, or investments that we may make or into which we may enter.

USE OF PROCEEDS

We estimate that we will receive net proceeds from this offering of approximately \$28.2 million (or \$32.4 million if the underwriters exercise their option to purchase additional shares in full), after deducting underwriting discounts and commissions and estimated offering expenses payable by us. We will receive nominal proceeds, if any, from any exercise of pre-funded warrants.

As of December 31, 2023, we had cash, cash equivalents and short-term investments of approximately \$66.0 million. We anticipate that we will use the net proceeds from this offering, together with our existing cash and cash equivalents, to continue the development of etripamil in our lead indication of PSVT and our subsequent indication of AFib-RVR, as well as for working capital and other general corporate purposes.

This expected use of the net proceeds from this offering represents our intentions based upon our current plans and prevailing business conditions, which could change in the future as such plans and conditions evolve. Predicting the cost necessary to pursue our preclinical and clinical activities, regulatory approval and the commercialization of our current or future drug candidates can be difficult, and the amounts and timing of our actual expenditures may vary significantly depending on numerous factors, including the progress of our development, the status of and results from preclinical studies and clinical studies, any collaborations that we may enter into with third parties and any unforeseen cash needs. As a result, our management will retain broad discretion over the allocation of the net proceeds from this offering.

After the completion of this offering, assuming net proceeds to us, after deducting estimated offering expenses payable by us, of approximately \$28.2 million (assuming the underwriters do not exercise their option to purchase additional shares), we expect that our cash, cash equivalents and short term investments, will be sufficient to fund our current operating and capital expenditure plans into 2026. Our future capital requirements will depend on many factors, including those discussed in “Liquidity and Capital Resources” of our Quarterly Report on Form 10-Q for the quarter ended September 30, 2023.

As of the date of this prospectus supplement, we cannot specify with certainty all of the particular uses of the net proceeds from this offering. Accordingly, we will retain broad discretion over the use of such proceeds. Pending the use of the net proceeds from the sale of securities under this prospectus supplement as described above, we intend to invest the net proceeds in short and intermediate-term interest-bearing obligations, investment-grade instruments, certificates of deposit or direct or guaranteed obligations of the U.S. government.

DIVIDEND POLICY

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

DILUTION

Investors purchasing our common shares or pre-funded warrants 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 September 30, 2023 was approximately \$21.5 million, or \$0.64 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 September 30, 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 or pre-funded warrants 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 (i) 16,666,667 common shares in this offering at a public offering price of \$1.50 per share and (ii) pre-funded warrants to purchase 3,333,333 common shares at the offering price of \$1.49 per pre-funded warrant (which equals the price per share at which the common shares are being sold in this offering, minus the \$0.001 per share exercise price of each such pre-funded warrant), and after deducting estimated commissions and offering expenses payable by us and excluding common shares issuable upon and proceeds, if any, from the exercise of the pre-funded warrants issued pursuant to this offering, our as adjusted net tangible book value as of September 30, 2023 would have been \$49.3 million, or \$0.98 per share. This represents an immediate increase in net tangible book value of \$0.34 per share to existing shareholders and immediate dilution of \$0.52 per share to investors purchasing our common shares or pre-funded warrants in this offering at the public offering price. The following table illustrates this dilution on a per share basis:

Public offering price per share	\$ 1.50
Net tangible book value per share as of September 30, 2023	\$ 0.64
Increase in adjusted net tangible book value per share attributable investors purchasing common shares and pre-funded warrants in this offering	\$ 0.34
As adjusted net tangible book value per share as of September 30, 2023, after giving effect to this offering	\$ 0.98
Dilution per share to investors purchasing our common shares in this offering	\$ 0.52

If underwriters exercise their option to purchase shares of common shares in full, the as adjusted net tangible book value after this offering would be approximately \$1.01 per share, representing an increase in net tangible book value of approximately \$0.37 per share to existing shareholders and immediate dilution in net tangible book value of approximately \$0.49 per share to investors purchasing our common shares in this offering at the public offering price, in each case assuming no exercise of pre-funded warrants by holders who purchase pre-funded warrants in this offering.

If holders of pre-funded warrants purchased in this offering exercise such pre-funded warrants in full, our as adjusted net tangible book value as of September 30, 2023 per share after giving effect to this offering would have been \$49.3 million, or \$0.92 per share, which represents an immediate increase to existing shareholders of \$0.28 per share and immediate dilution to investors in this offering of \$0.58 per share.

The above discussion and table are based on 33,481,787 common shares outstanding as of September 30, 2023, and exclude:

- 4,859,560 common shares issuable upon the exercise of outstanding options as of September 30, 2023, at a weighted-average exercise price of \$5.25 per share;
- 1,644,623 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;
- 1,463,936 common shares reserved for future issuance under our 2019 Employee Share Purchase Plan, or the ESPP, as of September 30, 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 September 30, 2023, at an exercise price of \$0.01 per share;
- \$47.3 million of our common shares remaining available for sale by us as of the date of this prospectus supplement pursuant to our Open Market Sale AgreementSM with Jefferies LLC, or Jefferies; and
- up to 14,315,688 common shares, of which (a) 9,846,319 common shares are issuable upon the conversion of Milestone's senior secured convertible promissory notes, or the Notes, and (b) 4,469,370 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 September 30, 2023.

To the extent that outstanding options or warrants outstanding as of September 30, 2023 have been or may be exercised, the Notes are converted into common shares or other shares are issued, investors purchasing our common shares or pre-funded warrants 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, including pursuant to the Open Market Sale AgreementSM with Jefferies with respect to an at-the-market offering program under which we may issue and sell common shares having an aggregate offering price of up to \$47.3 million as of the date of this prospectus supplement, the issuance of these securities could result in further dilution to our shareholders.

DESCRIPTION OF PRE-FUNDED WARRANTS

The following is a brief summary of certain terms and conditions of the pre-funded warrants being offered pursuant to this prospectus supplement. The following description is subject in all respects to the provisions contained in the pre-funded warrants.

Form. The pre-funded warrants will be issued as individual warrant agreements to the investors. The form of pre-funded warrant will be filed as an exhibit to our Current Report on Form 8-K that we expect to file with the SEC.

Exercisability. The pre-funded warrants are exercisable at any time after their original issuance. The pre-funded warrants will be exercisable, at the option of each holder, in whole or in part by delivering to us a duly executed exercise notice and by payment in full in immediately available funds for the number of common shares purchased upon such exercise. As an alternative to payment in immediately available funds, the holder may, in its sole discretion, elect to exercise the pre-funded warrant through a cashless exercise, in which case the holder would receive upon such exercise the net number of common shares determined according to the formula set forth in the pre-funded warrant. No fractional common shares will be issued in connection with the exercise of a pre-funded warrant. In lieu of fractional shares, we will pay the holder an amount in cash equal to the fractional amount multiplied by the fair market value of any such fractional shares.

Term. The pre-funded warrants do not expire.

Exercise Limitations. Under the pre-funded warrants, neither we nor the holder may effect the exercise of any pre-funded warrant, and a holder will not be entitled to exercise any portion of any pre-funded warrant, which, upon giving effect to such exercise, would cause (i) the aggregate number of our common shares beneficially owned by the holder (together with its affiliates) to exceed 9.99% of the number of our common shares outstanding immediately after giving effect to the exercise, or (ii) the combined voting power of our securities beneficially owned by the holder (together with its affiliates) to exceed 9.99% of the combined voting power of all of our securities then outstanding immediately after giving effect to the exercise, as such percentage ownership is determined in accordance with the terms of the pre-funded warrants. However, any holder may increase or decrease such percentage, but not in excess of 9.99%, upon at least 61 days' prior notice from the holder to us.

Exercise Price. The exercise price per whole common share purchasable upon the exercise of the pre-funded warrants is \$0.001 per common share. The exercise price of the pre-funded warrants is subject to appropriate adjustment in the event of certain share dividends and distributions, share splits, share combinations, reclassifications or similar events affecting our common shares and also upon any distributions of assets, including cash, shares or other property to our shareholders.

Transferability. Subject to applicable laws, the pre-funded warrants may be offered for sale, sold, transferred or assigned without our consent.

Exchange Listing. We do not plan on applying to list the pre-funded warrants on The Nasdaq Global Select Market, any other national securities exchange, or any other nationally recognized trading system.

Fundamental Transactions. In the event of a fundamental transaction, as described in the pre-funded warrants and generally including any reorganization, recapitalization or reclassification of our common shares, the sale, transfer or other disposition of all or substantially all of our properties or assets, our consolidation or merger with or into another person, the acquisition of more than 50% of our outstanding common shares, or any person or group becoming the beneficial owner of 50% of the voting power represented by our outstanding common shares, the holders of the pre-funded warrants will be entitled to receive upon exercise of the pre-funded warrants the kind and amount of securities, cash or other property that the holders would have received had they exercised the pre-funded warrants immediately prior to such fundamental transaction without regard to any limitations on exercise contained in the pre-funded warrants.

No Rights as a Shareholder. Except by virtue of such holder's ownership of common shares, the holder of a pre-funded warrant does not have the rights or privileges of a holder of our common shares, including any voting rights, until the holder exercises the pre-funded warrant. In the event of certain distributions, including cash dividends, if any, to all holders of our common shares for no consideration, the holder of a

pre-funded warrant shall be entitled to participate in such distributions to the same extent as if such holder held the number of our common shares acquirable upon complete exercise of its pre-funded warrant (without regard to any limitations on exercise). If such distribution would result in such holder and its affiliates to exceed the exercise limitations described above, a portion of such distribution shall be held in abeyance for the benefit of such holder until such time as the ownership limitations would not be exceeded.

MATERIAL INCOME TAX CONSIDERATIONS

U.S. Federal Income Tax Information for U.S. Holders

The following is a description of the material U.S. federal income tax consequences to the U.S. Holders described below of owning and disposing of our common shares or pre-funded warrants. Our common shares and pre-funded warrants are collectively referred to herein as our “securities.” It is not a comprehensive description of all tax considerations that may be relevant to a particular U.S. Holder. This discussion applies only to a U.S. Holder that holds our securities as capital assets for U.S. federal tax purposes (generally, property held for investment). In addition, it does not describe all of the tax consequences that may be relevant in light of a U.S. Holder’s particular circumstances, including state and local tax consequences, estate tax consequences, alternative minimum tax consequences, the special tax accounting rules under Section 451(b) of the Internal Revenue Code of 1986, as amended, or the Code, and tax consequences applicable to U.S. Holders subject to special rules, such as:

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

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

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

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

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

- (ii) a corporation, or another entity taxable as a corporation, created or organized in or under the laws of the United States, any state therein or the District of Columbia;
- (iii) an estate the income of which is subject to U.S. federal income taxation regardless of its source; or
- (iv) a trust if (1) a U.S. court is able to exercise primary supervision over the administration of the trust and one or more U.S. persons have authority to control all substantial decisions of the trust or (2) the trust has a valid election to be treated as a U.S. person under applicable U.S. Treasury Regulations.

U.S. Holders are encouraged to consult their tax advisors concerning the U.S. federal, state, local and non-U.S. tax consequences of owning and disposing of our securities in their particular circumstances.

THIS DISCUSSION IS ONLY A SUMMARY OF CERTAIN U.S. FEDERAL INCOME TAX CONSIDERATIONS OF AN INVESTMENT IN OUR SECURITIES BY U.S. HOLDERS AND IS INTENDED AS A GENERAL GUIDE ONLY. WE STRONGLY ENCOURAGE ALL POTENTIAL U.S. HOLDERS WHO MAY PURCHASE OUR SECURITIES TO OBTAIN ADVICE IN ADVANCE OF DOING SO FROM THEIR OWN TAX ADVISORS AS TO THE U.S. FEDERAL, STATE AND LOCAL AND NON-U.S. TAX CONSEQUENCES OF THEIR ACQUISITION, OWNERSHIP AND DISPOSITION OF OUR SECURITIES IN THEIR OWN SPECIFIC CIRCUMSTANCES.

Treatment of Pre-Funded Warrants

Although it is not entirely free from doubt, we believe a pre-funded warrant should be treated as a common share for U.S. federal income tax purposes and a holder of a pre-funded warrant should generally be taxed in the same manner as a holder of a common share, as described below (except as otherwise noted below). However, our characterization is not binding on the IRS, and the IRS may treat the pre-funded warrants as warrants to acquire our common shares. If so, the tax consequences, including the amount and character of the holder's gain, with respect to an investment in our pre-funded warrants could change. Accordingly, each holder should consult his, her or its own tax advisor regarding the risks associated with the acquisition of pre-funded warrants pursuant to this offering (including potential alternative characterizations). The balance of this discussion generally assumes that the characterization described above is respected for U.S. federal income tax purposes unless otherwise noted.

Passive Foreign Investment Company Rules

In general, a non-U.S. corporation will be a "passive foreign investment company," or PFIC, for any taxable year in which (1) 75% or more of its gross income consists of passive income or (2) 50% or more of the quarterly value (determined on the basis of a weighted average) of its gross assets consists of assets that produce, or are held for the production of, passive income. For purposes of the above calculations, a non-U.S. corporation that directly or indirectly owns at least 25% (by value) of the shares of another corporation or entity treated as a partnership for income tax purposes is treated as if it held its proportionate share of the assets and received directly its proportionate share of the income of such other entity. Passive income generally includes dividends, interest, certain rents and royalties, and capital gains. Assets that produce, or are held for the production of, passive income generally include cash, cash equivalents and marketable securities.

We have not analyzed our PFIC status for our taxable year ending December 31, 2023. However, based on the nature and composition of our income, assets, activities and market capitalization for our taxable year ending December 31, 2023, it is possible that we were classified as a PFIC for our taxable year ending December 31, 2023. Based on the expected nature and composition of our income and assets for our taxable year ending December 31, 2024, it is also possible that we may be classified as a PFIC for our taxable year ending December 31, 2024. However, a separate determination must be made after the close of each taxable year as to whether we are a PFIC for that year. Our status as a PFIC will depend on the composition of our income (including, in part, whether we receive certain tax credits and whether such amounts will constitute gross income for purposes of the PFIC income test) and the composition and value of our assets, which may be determined in large part by reference to the market price of the common shares, which may fluctuate considerably. Fluctuations in the market price of the common shares may result in our being a PFIC for any taxable year including the current taxable year. The

application of the PFIC rules is subject to uncertainty in several respects, and therefore, no assurances can be provided with respect to our PFIC status in any past, the current, or any future taxable year. Because of the uncertainties involved in establishing our PFIC status, our United States tax counsel expresses no opinion regarding our PFIC status for any past, the current, or any future taxable year.

If we are classified as a PFIC in any year with respect to which a U.S. Holder owns our securities, we will continue to be treated as a PFIC with respect to such U.S. Holder in all succeeding years during which the U.S. Holder owns our securities, regardless of whether we continue to meet the tests described above unless (i) we cease to be a PFIC and the U.S. Holder has made a valid “deemed sale” election under the PFIC rules, (ii) we cease to be a PFIC and the U.S. Holder has a valid mark-to-market election in effect (as described below) or (iii) the U.S. Holder makes a valid “qualified electing fund” election, or QEF Election, with respect to all taxable years during such U.S. Holder’s holding period in which we are a PFIC. However, a U.S. Holder may make a QEF Election with respect to our securities only if we annually provide such U.S. Holder with certain tax information. If we are a PFIC for our taxable year ending December 31, 2024, or any subsequent taxable years, we expect to provide U.S. Holders, upon request, with a “PFIC Annual Information Statement,” with the information required to allow U.S. Holders to make a QEF Election for United States federal income tax purposes.

Under attribution rules, if we are a PFIC, U.S. Holders will be deemed to own their proportionate shares of the stock of non-U.S. corporations that we own and which are PFICs, or lower-tier PFICs, and will be subject to U.S. federal income tax according to the rules described in the following paragraphs on (1) certain distributions by a lower-tier PFIC and (2) a disposition of shares of a lower-tier PFIC, in each case as if the U.S. Holder held such shares directly, even though such holders have not received the proceeds of those distributions or dispositions directly.

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

If the “deemed sale” election is made, a U.S. Holder will be deemed to have sold the securities the U.S. Holder holds at their fair market value and any gain from such deemed sale would be subject to the rules described below. After the deemed sale election, so long as we do not become a PFIC in a subsequent taxable year, the U.S. Holder’s securities with respect to which such election was made will not be treated as shares in a PFIC and the U.S. Holder will not be subject to the rules described below with respect to any “excess distribution” the U.S. Holder receives from us or any gain from an actual sale or other

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

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

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

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

If we are a PFIC, U.S. Holders can avoid the interest charge on excess distributions or gain relating to the common shares by making a mark-to-market election with respect to the common shares, provided that the common shares are “marketable.” Common shares will be marketable if they are “regularly traded” on certain U.S. stock exchanges or on a foreign stock exchange that meets certain conditions. For these purposes, the common shares will be considered regularly traded during any calendar year during which they are traded, other than in de minimis quantities, on at least 15 days during each calendar quarter. Any trades that have as their principal purpose meeting this requirement will be disregarded. Our common shares are currently listed on Nasdaq, which is a qualified exchange for these purposes. Consequently, if our common shares remain listed on Nasdaq and are regularly traded, and you are a U.S. Holder that holds our common shares, we expect the mark-to-market election would be available to you if we are a PFIC. U.S. Holders should note that the pre-funded warrants are not likely to be treated as “regularly traded” and thus it is unlikely that a mark-to-market election can be made with respect to the pre-funded warrants. Each U.S. Holder should consult its tax advisor as to whether a mark-to-market election is available or advisable with respect to our securities.

A U.S. Holder that makes a mark-to-market election must include as ordinary income for each year an amount equal to the excess, if any, of the fair market value of the common shares at the close of the taxable year over the U.S. Holder’s adjusted tax basis in the common shares. Accordingly, such mark-to-market election may accelerate the recognition of income without a corresponding receipt of cash. An electing holder may also claim an ordinary loss deduction for the excess, if any, of the U.S. Holder’s adjusted basis in the common shares over the fair market value of the common shares at the close of the taxable year, but this deduction is allowable only to the extent of any net mark-to-market gains for prior years. Gains from an actual sale or other disposition of the common shares will be treated as ordinary income, and any losses incurred on a sale or other disposition of the common shares will be treated as an ordinary

loss to the extent of any net mark-to-market gains for prior years. Once made, the election cannot be revoked without the consent of the IRS, unless the common shares cease to be marketable. However, a mark-to-market election generally cannot be made for equity interests in any lower-tier PFICs that we own, unless shares of such lower-tier PFIC are themselves “marketable.” As a result, even if a U.S. Holder validly makes a mark-to-market election with respect to our common shares, the U.S. Holder may continue to be subject to the PFIC rules with respect to its indirect interest in any of our investments that are treated as an equity interest in a PFIC for U.S. federal income tax purposes. U.S. Holders should consult their tax advisors as to the availability and desirability of a mark-to-market election, as well as the impact of such election on interests in any lower-tier PFICs.

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

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

Taxation of Distributions

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

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

Sale or Other Taxable Disposition of Securities

Subject to the discussion above under “Passive Foreign Investment Company Rules,” gain or loss realized on the sale or other taxable disposition of securities will be capital gain or loss, and will be a long-term capital gain or loss if the U.S. Holder held the securities for more than one year. The amount of the gain or loss will equal the difference between the U.S. Holder’s adjusted tax basis in the securities disposed of and the amount realized on the disposition, in each case as determined in U.S. dollars. This gain or loss will generally be U.S. source gain or loss for foreign tax credit purposes. The deductibility of capital losses is subject to limitations.

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

Certain Adjustments to the Pre-Funded Warrants

The terms of each pre-funded warrant provide for an adjustment to the number of common shares for which the pre-funded warrant may be exercised in certain events, and a distribution upon exercise that corresponds to distributions, if any, made on our common shares after issuance of the pre-funded warrant and prior to exercise. Such adjustments may be treated as a constructive distribution to a U.S. Holder of the pre-funded warrant if, and to the extent that, such adjustment has the effect of increasing such U.S. Holder’s proportionate interest in our “earnings and profits” or assets, depending on the circumstances of such adjustment. Any such constructive distribution may be taxable whether or not there is an actual distribution of cash or other property. U.S. Holders should consult their tax advisors regarding the proper treatment of any adjustments to the pre-funded warrant and the interaction of any adjustments and the PFIC rules.

Exercise of a Pre-Funded Warrant

Subject to the PFIC rules described above and except as discussed below with respect to the cashless exercise of a pre-funded warrant, a U.S. Holder generally will not recognize gain or loss on the exercise of a pre-funded warrant and related receipt of common shares, unless cash is received in lieu of the issuance of a fractional common share. However, under a proposed Treasury Regulation (which is proposed to have retroactive effect), a U.S. Holder would recognize gain if the pre-funded warrant was treated as stock of a PFIC with respect to a U.S. Holder at the time of the exercise of the pre-funded warrant and the stock received upon the exercise was not treated as stock of a PFIC for the taxable year in which the exercise occurs.

A U.S. Holder’s initial tax basis in the common shares received on the exercise of a pre-funded warrant should be equal to the sum of (i) the U.S. Holder’s tax basis in the pre-funded warrant plus (ii) the exercise price paid by the U.S. Holder on the exercise of the pre-funded warrant. A U.S. Holder should consult its own tax advisor as to whether such U.S. Holder’s holding period for common shares received on exercise of a pre-funded warrant will or will not include the period during which the U.S. Holder held the pre-funded warrant.

The U.S. federal income tax treatment of a cashless exercise of pre-funded warrants into common shares is unclear, and the tax consequences of a cashless exercise could differ from the consequences of exercising a pre-funded warrant on a non-cashless basis described in the preceding paragraph. Due to the absence of authority on the U.S. federal income tax treatment of a cashless exercise, there can be no assurance as

to the tax treatment that would be adopted by the IRS or a court of law. Accordingly, U.S. Holders should consult their own tax advisors regarding the U.S. federal income tax consequences of a cashless exercise of pre-funded warrants.

Medicare Tax on Net Investment Income

Certain U.S. Holders that are individuals, estates or trusts are subject to a 3.8% tax on all or a portion of their “net investment income,” which may include all or a portion of their dividend income and net gains from the disposition of our securities. Each U.S. Holder that is an individual, estate or trust is urged to consult its tax advisors regarding the applicability of the Medicare tax to its income and gains in respect of its investment in our securities.

Information Reporting and Backup Withholding

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

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

Certain Reporting Requirements

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

U.S. Holders paying more than \$100,000 for our securities may be required to file IRS Form 926 reporting the payment of the offer price for our securities to us. Substantial penalties may be imposed upon a U.S. Holder that fails to comply. Additional U.S. tax filing obligations may apply depending on a U.S. Holder’s specific circumstances. Each U.S. Holder should consult its own tax advisor as to the possible obligation to file IRS Form 926 and all other U.S. tax filing obligations.

THE DISCUSSION ABOVE IS A SUMMARY OF THE U.S. FEDERAL INCOME TAX CONSEQUENCES OF AN INVESTMENT IN OUR SECURITIES AND IS BASED UPON LAWS AND RELEVANT INTERPRETATIONS THEREOF IN EFFECT AS OF THE DATE OF THIS PROSPECTUS SUPPLEMENT, ALL OF WHICH ARE SUBJECT TO CHANGE, POSSIBLY WITH RETROACTIVE EFFECT. EACH PROSPECTIVE INVESTOR IS URGED TO CONSULT ITS OWN TAX ADVISOR ABOUT THE TAX CONSEQUENCES TO IT OF AN INVESTMENT IN OUR SECURITIES IN LIGHT OF THE INVESTOR’S OWN CIRCUMSTANCES.

Canadian Federal Income Tax Considerations to Non-Resident of Canada

The following summary describes, as of the date hereof, the principal Canadian federal income tax consequences under the *Income Tax Act* (Canada), or the Canadian Tax Act, generally applicable to a holder, or a Holder, who acquires our common shares (including on exercise of a pre-funded warrant) or pre-funded warrants and who, for the purposes of the Canadian Tax Act, and at all relevant times, (1) is not (and is not deemed to be) resident in Canada, (2) will not use or hold (and will not be deemed to use or hold) the common shares or pre-funded warrants in, or in the course of, carrying on a business or part of a business in Canada, (3) beneficially owns the common shares or pre-funded warrants as capital property, and (4) deals at arm’s length with, and is not affiliated with, us or the underwriters, or a Non-Resident of Canada Holder. In addition, this discussion does not apply to a Non-Resident of Canada Holder that

carries on or is deemed to carry on, an insurance business in Canada and elsewhere or to an “authorized foreign bank,” as defined in the Canadian Tax Act. Any such Non-Resident Canada Holders should consult their own tax advisors.

This summary is not applicable to a Non-Resident of Canada Holder that, with respect to the common shares, has entered or that enters into a “synthetic disposition arrangement” or a “derivative forward agreement” as those terms are defined in the Canadian Tax Act. Any such Non-Resident of Canada Holders should consult their own tax advisors.

This summary is based upon the current provisions of the Canadian Tax Act, the regulations adopted thereunder, or the Canadian Tax Regulations, and counsel’s understanding of the administrative policies and assessing practices of the Canada Revenue Agency published in writing prior to the date hereof. The summary also takes into account all specific proposals to amend the Canadian Tax Act and the Canadian Tax Regulations that have been publicly announced by or on behalf of the Minister of Finance (Canada) prior to the date hereof, or the Canadian Tax Proposals, and assumes that all such Canadian Tax Proposals will be enacted in the form proposed. No assurance can be given that the Canadian Tax Proposals will be enacted in the form proposed or at all. This summary does not otherwise take into account or anticipate any changes in law, administrative policy or assessing practice, whether by way of legislative, regulatory, judicial or administrative action or interpretation, nor does it address any provincial, territorial or foreign tax considerations.

This summary is not exhaustive of all possible Canadian federal income tax considerations of acquiring common shares or pre-funded warrants. The summary is of a general nature only and is not intended to be, and should not be construed to be, legal, business, or tax advice to any prospective Holder. Prospective Holders should consult their own tax advisors as to the Canadian federal tax consequences, and the tax consequences of any other jurisdiction, applicable to them having regard to their own particular circumstances.

All amounts calculated in a currency other than the Canadian dollar relating to the acquisition, holding, disposition and, as applicable, exercise of the common shares or pre-funded warrants must be converted into Canadian dollars based on the exchange rates as quoted by the Bank of Canada for the applicable day or such other exchange rates determined in accordance with the Canadian Tax Act. The amount of dividends to be included in income, and capital gains and losses realized by a Non-Resident of Canada Holder, may be affected by fluctuations in the relevant exchange rates.

Exercise of Pre-funded Warrants

The exercise of a pre-funded warrant to acquire a common share will be deemed not to constitute a disposition of property for purposes of the Canadian Tax Act. As a result, no gain or loss will be realized by a Non-Resident of Canada Holder upon the exercise of a pre-funded warrant to acquire a common share. When a pre-funded warrant is exercised, the Non-Resident of Canada Holder’s cost of the common share acquired thereby will be equal to the aggregate of the Non-Resident of Canada Holder’s adjusted cost base of such pre-funded warrant and the exercise price paid for the common share. The Non-Resident of Canada Holder’s adjusted cost base of the common share so acquired will be determined by averaging the cost of the common share with the adjusted cost base to the Non-Resident of Canada Holder of all common shares owned by the Non-Resident of Canada Holder as capital property immediately prior to such acquisition.

The Canadian income tax consequences of a cashless exercise of a pre-funded warrant are different than those described above. Non-Resident of Canada Holders who acquire a common share by means of a cashless exercise of a pre-funded warrant should consult their own tax advisors in this regard.

Dividends on the Common Shares

Dividends paid or credited, or deemed to be paid or credited, to a Non-Resident of Canada Holder by the Company will be subject to Canadian withholding tax at the rate of 25% on the gross amount of the dividend unless such rate is reduced by the terms of an applicable income tax treaty or convention. For example, under the Canada-United States Income Tax Convention (1980), as amended, or the Treaty, the rate of withholding tax on dividends paid or credited to a Non-Resident of Canada Holder who is resident in the U.S. for purposes of the Treaty and entitled to the full benefits under the Treaty, or a U.S.

Holder, and who is the beneficial owner of the dividend is generally limited to 15% of the gross amount of the dividend (or 5% in the case of a U.S. Holder that is also a corporation that beneficially owns at least 10% of the company's voting shares). Non-Resident of Canada Holders should consult their own tax advisors to determine their entitlement to relief under an applicable income tax treaty or convention.

Dispositions of the Common Shares and Pre-funded Warrants

Upon a disposition or a deemed disposition of a common share (other than a disposition to the Company that is not a sale in the open market in the manner in which shares would normally be purchased by any member of the public in an open market) or pre-funded warrant (other than on the exercise thereof), a Non Resident of Canada Holder generally will realize a capital gain (or a capital loss) equal to the amount by which the proceeds of disposition of such security, as applicable, net of any reasonable costs of disposition, are greater (or are less) than the adjusted cost base of such security to the Non Resident of Canada Holder.

A Non-Resident of Canada Holder will not be subject to tax under the Canadian Tax Act in respect of any capital gain (and will not be entitled to claim a capital loss) realized by such Non-Resident of Canada Holder on a disposition, or deemed disposition, of the common shares or pre-funded warrants unless the common shares or pre-funded warrants constitute "taxable Canadian property," as defined in the Canadian Tax Act, of the Non-Resident of Canada Holder at the time of disposition and the Non-Resident of Canada Holder is not entitled to an exemption under the applicable income tax treaty or convention between Canada and the country in which the Non-Resident of Canada Holder is resident. In addition, capital losses arising on the disposition or deemed disposition of a common share or pre-funded warrant will not be recognized under the Canadian Tax Act, unless the common share or pre-funded warrant constitutes "taxable Canadian property" to the Non-Resident of Canada Holder thereof for purposes of the Canadian Tax Act. Generally, provided the common shares are listed on a "designated stock exchange" as defined in the Canadian Tax Act (which currently includes Nasdaq), at the time of disposition, the common shares and pre-funded warrants generally will not constitute taxable Canadian property of a Non-Resident of Canada Holder, unless at any time during the 60-month period preceding the disposition the following two conditions were satisfied concurrently: (i) one or any combination of (A) the Non-Resident of Canada Holder, (B) persons not dealing at arm's length with such Non-Resident of Canada Holder, and (C) partnerships in which the Non-Resident of Canada Holder or a person described in (B) holds a membership interest directly or indirectly through one or more partnerships, owned 25% or more of our issued shares of any class or series of the Company; and (ii) more than 50% of the fair market value of the common shares was derived, directly or indirectly, from one or any combination of: real or immovable property situated in Canada, "Canadian resource properties," as such term is defined in the Canadian Tax Act, "timber resource properties," as such term is defined in the Canadian Tax Act, or options in respect of, interests in, or for civil law rights in, any such properties whether or not the property exists. Notwithstanding the foregoing, a common share may otherwise be deemed to be taxable Canadian property to a Non-Resident of Canada Holder for purposes of the Tax Act in certain circumstances. If the common shares or pre-funded warrants are considered taxable Canadian property to a Non-Resident of Canada Holder, an applicable income tax treaty or convention may in certain circumstances exempt that Non-Resident of Canada Holder from tax under the Canadian Tax Act in respect of the disposition or deemed disposition of the common shares or pre-funded warrants. Non-Resident of Canada Holders whose common shares or pre-funded warrants are, or may be, taxable Canadian property should consult their own tax advisors for advice having regard to their particular circumstances.

UNDERWRITING

We and the underwriters for the offering named below have entered into an underwriting agreement with respect to the common shares and pre-funded warrants being offered. Subject to the terms and conditions of the underwriting agreement, each underwriter has severally agreed to purchase from us the number of common shares and pre-funded warrants set forth opposite its name below. Piper Sandler & Co. is the representative of the underwriter.

Underwriters	Number of Shares	Number of Pre-Funded Warrants
Piper Sandler & Co.	15,000,000	3,000,000
H.C. Wainwright & Co., LLC	1,666,667	333,333
Total	<u>16,666,667</u>	<u>3,333,333</u>

The underwriting agreement provides that the obligations of the underwriters are subject to certain conditions precedent and that the underwriters have agreed, severally and not jointly, to purchase all of the common shares and pre-funded warrants sold under the underwriting agreement if any of these shares or pre-funded warrants, other than those shares covered by the option to purchase additional shares described below, are purchased. If an underwriter defaults, the underwriting agreement provides that the purchase commitment of the non-defaulting underwriters may be increased or the underwriting agreement may be terminated.

We have agreed to indemnify the underwriters against specified liabilities, including liabilities under the Securities Act and the Exchange Act and to contribute to payments the underwriters may be required to make in respect thereof.

The underwriters are offering the shares and pre-funded warrants, subject to prior sale, when, as and if issued to and accepted by them, subject to approval of legal matters by their counsel and other conditions specified in the underwriting agreement. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

Option to Purchase Additional Shares. We have granted to the underwriters an option to purchase an aggregate of up to 3,000,000 additional common shares at the public offering price, less the underwriting discounts and commissions. This option is exercisable for a period of 30 days. To the extent that the underwriters exercise this option, the underwriters will purchase additional shares from us in approximately the same proportion as shown in the table above.

Discounts and Commissions. The following table shows the public offering price, underwriting discounts and commissions and proceeds, before expenses to us. These amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase additional shares.

We estimate that the total expenses of this offering, excluding underwriting commissions, will be approximately \$400,000 and are payable by us. We have agreed to reimburse the underwriters for an aggregate of up to \$150,000 for their counsel fees. In accordance with FINRA Rule 5110, this reimbursed fee is deemed underwriting compensation for this offering.

	Per Share	Per Pre-Funded Warrant	Total	
			Without Option	With Option
Public offering price	\$ 1.50	\$ 1.499	\$ 29,996,666.667	\$ 34,499,666.6
Underwriting discounts and commissions	\$ 0.09	\$ 0.08994	\$ 1,799,800.000	\$ 2,069,800.00020
Proceeds, before expenses, to Milestone	\$ 1.41	\$ 1.40906	\$ 28,196,866.667	\$ 32,426,866.666980

We are offering to those purchasers whose purchase of shares of common stock in this offering would result in the purchaser, together with its affiliates and certain related parties, beneficially owning more than 9.99% of our outstanding common shares following the consummation of this offering, the opportunity to purchase, in lieu of our common shares that would result in ownership in excess of 9.99%, pre-funded

warrants to purchase such excess common shares. Each pre-funded warrant will have an exercise price of \$0.001. The purchase price for each such pre-funded warrant equals the per share public offering price for the common shares in this offering less the \$0.001 per share exercise price of each such pre-funded warrant.

The underwriters propose to offer the common shares and pre-funded warrants to the public at the public offering price set forth on the cover of this prospectus supplement. The underwriters may offer the common shares and pre-funded warrants to securities dealers at the public offering price less a concession not in excess of \$0.054000 per common share and \$0.0539640 per pre-funded warrant. If all of the shares are not sold at the public offering price, the underwriters may change the offering price and other selling terms.

Our common shares are listed on the Nasdaq Global Select Market under the symbol "MIST". There is no established public trading market for the pre-funded warrants, and we do not expect a market to develop. We do not intend to list the pre-funded warrants on the Nasdaq Global Select Market, any other national securities exchange or any nationally recognized trading system.

Stabilization. In connection with this offering, the underwriters may engage in stabilizing transactions, overallotment transactions, syndicate covering transactions, penalty bids and purchases to cover positions created by short sales.

- Stabilizing transactions permit bids to purchase common shares so long as the stabilizing bids do not exceed a specified maximum, and are engaged in for the purpose of preventing or retarding a decline in the market price of the common shares while the offering is in progress.
- Overallotment transactions involve sales by the underwriters of common shares in excess of the number of shares the underwriters are obligated to purchase. This creates a syndicate short position which may be either a covered short position or a naked short position. In a covered short position, the number of shares over-allotted by the underwriters is not greater than the number of shares that they may purchase in the option to purchase additional shares. In a naked short position, the number of shares involved is greater than the number of shares in the option to purchase additional shares. The underwriters may close out any short position by exercising their option to purchase additional shares and/or purchasing shares in the open market.
- Syndicate covering transactions involve purchases of common shares in the open market after the distribution has been completed in order to cover syndicate short positions. In determining the source of shares to close out the short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared with the price at which they may purchase shares through exercise of the option to purchase additional shares. If the underwriters sell more shares than could be covered by exercise of the option to purchase additional shares and, therefore, have a naked short position, the position can be closed out only by buying shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that after pricing there could be downward pressure on the price of the shares in the open market that could adversely affect investors who purchase in the offering.
- Penalty bids permit the representative to reclaim a selling concession from a syndicate member when the common shares originally sold by that syndicate member is purchased in stabilizing or syndicate covering transactions to cover syndicate short positions.

These stabilizing transactions, syndicate covering transactions and penalty bids may have the effect of raising or maintaining the market price of our common shares or preventing or retarding a decline in the market price of our common shares. As a result, the price of our common shares in the open market may be higher than it would otherwise be in the absence of these transactions. Neither we nor the underwriters make any representation or prediction as to the effect that the transactions described above may have on the price of our common shares. These transactions may be effected on the Nasdaq Stock Market, in the over-the-counter market or otherwise and, if commenced, may be discontinued at any time.

Passive Market Making. In connection with this offering, underwriters may engage in passive market making transactions in our common shares on the Nasdaq Stock Market in accordance with Rule 103 of Regulation M under the Exchange Act, as amended, during a period before the commencement of offers or sales of common shares and extending through the completion of the distribution. A passive

market maker must display its bid at a price not in excess of the highest independent bid of that security. However, if all independent bids are lowered below the passive market maker's bid, such bid must then be lowered when specified purchase limits are exceeded.

Lock-Up Agreements. Pursuant to certain "lock-up" agreements, we and our executive officers and directors, have agreed, subject to certain exceptions, not to and will not cause or direct any of its affiliates to offer, sell, assign, transfer, pledge, contract to sell, or otherwise dispose of or announce the intention to otherwise dispose of, or enter into, or announce the intention to enter into any swap, hedge or similar agreement or arrangement (including, without limitation, the purchase or sale of, or entry into, any put or call option, or combination thereof, forward, swap or any other derivative transaction or instrument, however described or defined) that transfers, is designed to transfer or reasonably could be expected to transfer (whether by the stockholder or someone other than the stockholder) that transfers, in whole or in part, directly or indirectly the economic consequence of ownership of, directly or indirectly, or make any demand or request or exercise any right with respect to the registration of, or file with the SEC a registration statement under the Securities Act relating to, any common shares or securities convertible into or exchangeable or exercisable for any common shares without the prior written consent of Piper Sandler & Co., for a period of 90 days after the date of the pricing of the offering.

This lock-up provision applies to common shares and to securities convertible into or exchangeable or exercisable for common shares. The exceptions permit us, among other things and subject to restrictions, to: (a) effect the transactions contemplated by the underwriting agreement, (b) issue common shares or options to purchase common shares, or issue common shares upon exercise of options, pursuant to any stock option, stock bonus or other stock plan or arrangement described in this prospectus, (c) file one or more registration statements on Form S-8 and (d) offer, issue and sell common shares or any securities convertible into, or exercisable, or exchangeable for, common shares in connection with any merger, acquisition or strategic investment (including any joint venture, strategic alliance or partnership) as long as (x) the aggregate number of common shares issued or issuable does not exceed 5.0% of the number of common shares outstanding immediately after the issuance and sale and (y) each recipient of any such common shares issued or issuable agrees to the restrictions on the resale of securities that are consistent with those set forth in the lock-up agreement executed by our directors and officers in connection with this offering. The exceptions permit parties to the "lock-up" agreements, among other things and subject to restrictions, to: (a) make certain gifts, (b) if the party is a corporation, partnership, limited liability company or other business entity, make transfers to any shareholders, partners, members of, or owners of similar equity interests in, the party, or to an affiliate of the party, if such transfer is not for value, and (d) participate in tenders involving the acquisition of a majority of our stock. In addition, the lock-up provision will not restrict broker-dealers from engaging in market making and similar activities conducted in the ordinary course of their business.

The representative, in its sole discretion, may release our common shares and other securities subject to the lock-up agreements described above in whole or in part at any time. When determining whether or not to release our common shares and other securities from lock-up agreements, the representative will consider, among other factors, the holder's reasons for requesting the release, the number of shares for which the release is being requested and market conditions at the time of the request.

Electronic Offer, Sale and Distribution of Shares or Pre-Funded Warrants. A prospectus in electronic format may be made available on the websites maintained by one or more of the underwriters and one or more of the underwriters participating in this offering may distribute prospectuses electronically. The representative may agree to allocate a number of shares or pre-funded warrants to underwriters for sale to their online brokerage account holders. Internet distributions will be allocated by the underwriters on the same basis as other allocations. Other than the prospectus in electronic format, the information on these websites is not part of this prospectus or the registration statement of which this prospectus forms a part, has not been approved or endorsed by us or any underwriter in its capacity as underwriter, and should not be relied upon by investors.

Other Relationships. Certain of the underwriters and their affiliates have provided, and may in the future provide, various investment banking, commercial banking and other financial services for us and our affiliates for which they have received, and may in the future receive, customary fees.

Selling Restrictions

Canada. The common shares and pre-funded warrants offered by this prospectus supplement have not been qualified by prospectus for distribution in Canada, and may not be, directly or indirectly, offered or sold in Canada or to any residents of Canada, except in compliance with an exemption from Canadian prospectus requirements. Any sales of common shares and pre-funded warrants in any province of Canada will only be made by a securities dealer appropriately registered in that province to make such sales. Any common shares and pre-funded warrants acquired may not be sold in Canada, except in compliance with Canadian prospectus requirements or an exemption therefrom.

Switzerland. The securities will not be offered, directly or indirectly, to the public in Switzerland and this prospectus does not constitute a public offering prospectus as that term is understood pursuant to article 652a or 1156 of the Swiss Federal Code of Obligations.

European Economic Area and the United Kingdom. In relation to each Member State of the European Economic Area and the United Kingdom (each, a “Member State”), no shares or pre-funded warrants have been offered or will be offered pursuant to the offering to the public in that Member State prior to the publication of a prospectus in relation to the shares or pre-funded warrants which has been approved by the competent authority in that Member State or, where appropriate, approved in another Member State and notified to the competent authority in that Member State, all in accordance with the Prospectus Regulation, except that offers of shares or pre-funded warrants may be made to the public in that Member State at any time under the following exemptions under the Prospectus Regulation:

- A. to any legal entity which is a qualified investor as defined under the Prospectus Regulation;
- B. to fewer than 150 natural or legal persons (other than qualified investors as defined under the Prospectus Regulation), subject to obtaining the prior consent of the underwriters; or
- C. in any other circumstances falling within Article 1(4) of the Prospectus Regulation,

provided that no such offer of shares or pre-funded warrants shall require us or any underwriter to publish a prospectus pursuant to Article 3 of the Prospectus Regulation or supplement a prospectus pursuant to Article 23 of the Prospectus Regulation and each person who initially acquires any shares or pre-funded warrants or to whom any offer is made will be deemed to have represented, acknowledged and agreed to and with each of the underwriters and us that it is a “qualified investor” within the meaning of Article 2(e) of the Prospectus Regulation.

In the case of any shares or pre-funded warrants being offered to a financial intermediary as that term is used in Prospectus Regulation, each such financial intermediary will be deemed to have represented, acknowledged and agreed that the shares or pre-funded warrants acquired by it in the offer have not been acquired on a non-discretionary basis on behalf of, nor have they been acquired with a view to their offer or resale to, persons in circumstances which may give rise to an offer of any shares or pre-funded warrants to the public other than their offer or resale in a Member State to qualified investors as so defined or in circumstances in which the prior consent of the underwriters have been obtained to each such proposed offer or resale.

For the purposes of this provision, the expression an “offer to the public” in relation to shares or pre-funded warrants in any Member State means the communication in any form and by any means of sufficient information on the terms of the offer and any shares or pre-funded warrants to be offered so as to enable an investor to decide to purchase or subscribe for any shares or pre-funded warrants, and the expression “Prospectus Regulation” means Regulation (EU) 2017/1129.

References to the Prospectus Regulation includes, in relation to the United Kingdom, the Prospectus Regulation as it forms part of the United Kingdom domestic law by virtue of the European Union (Withdrawal) Act of 2018.

United Kingdom. In addition, in the United Kingdom, this document is being distributed only to, and is directed only at, and any offer subsequently made may only be directed at persons who are “qualified investors” (as defined in the Prospectus Regulation) (i) who have professional experience in matters relating to investments falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended (the “Order”) and/or (ii) who are high net worth companies (or persons to whom it may otherwise be lawfully communicated) falling within Article 49(2)(a) to (d) of the

Order and/or (iii) to whom it may otherwise be lawfully communicated (all such persons together being referred to as “relevant persons”) in circumstances which have not resulted and will not result in an offer to the public of the shares or pre-funded warrants in the United Kingdom within the meaning of the Financial Services and Markets Act 2000.

Any person in the United Kingdom that is not a relevant person should not act or rely on the information included in this document or use it as basis for taking any action. In the United Kingdom, any investment or investment activity that this document relates to may be made or taken exclusively by relevant persons.

Hong Kong. The shares and pre-funded warrants have not been offered or sold and will not be offered or sold in Hong Kong, by means of any document, other than (a) to “professional investors” as defined in the Securities and Futures Ordinance (Cap. 571 of the Laws of Hong Kong (the “SFO”) of Hong Kong and any rules made thereunder; or (b) in other circumstances which do not result in the document being a “prospectus” as defined in the Companies (Winding Up and Miscellaneous Provisions) Ordinance (Cap. 32) of Hong Kong) (the “CO”), or which do not constitute an offer to the public within the meaning of the CO. No advertisement, invitation or document relating to the shares or pre-funded warrants has been or may be issued or has been or may be in the possession of any person for the purposes of issue, whether in Hong Kong or elsewhere, which is directed at, or the contents of which are likely to be accessed or read by, the public of Hong Kong (except if permitted to do so under the securities laws of Hong Kong) other than with respect to shares or pre-funded warrants which are or are intended to be disposed of only to persons outside Hong Kong or only to “professional investors” as defined in the SFO and any rules made thereunder.

Singapore. Each underwriter has acknowledged that this prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, each underwriter has represented and agreed that it has not offered or sold any shares or pre-funded warrants or caused the shares or pre-funded warrants to be made the subject of an invitation for subscription or purchase and will not offer or sell any shares or pre-funded warrants or cause the shares or pre-funded warrants to be made the subject of an invitation for subscription or purchase, and has not circulated or distributed, nor will it circulate or distribute, this prospectus or any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the shares or pre-funded warrants, whether directly or indirectly, to any person in Singapore other than:

- A. to an institutional investor (as defined in Section 4A of the Securities and Futures Act (Chapter 289) of Singapore, as modified or amended from time to time (the “SFA”)) pursuant to Section 274 of the SFA;
- B. to a relevant person (as defined in Section 275(2) of the SFA) pursuant to Section 275(1) of the SFA, or any person pursuant to Section 275(1A) of the SFA, and in accordance with the conditions specified in Section 275 of the SFA; or
- C. otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where the shares or pre-funded warrants are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

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

securities or securities-based derivatives contracts (each term as defined in Section 2(1) of the SFA) of that corporation or the beneficiaries’ rights and interest (however described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the shares or pre-funded warrants pursuant to an offer made under Section 275 of the SFA except:

- (i) to an institutional investor or to a relevant person, or to any person arising from an offer referred to in Section 275(1A) or Section 276(4)(i)(B) of the SFA;
- (ii) where no consideration is or will be given for the transfer;

- (iii) where the transfer is by operation of law;
- (iv) as specified in Section 276(7) of the SFA; or
- (v) as specified in Regulation 37A of the Securities and Futures (Offers of Investments) (Securities and Securities-based Derivatives Contracts) Regulations 2018.

Singapore SFA Product Classification—In connection with Section 309B of the SFA and the CMP Regulations 2018, unless otherwise specified before an offer of shares or pre-funded warrants, we have determined, and hereby notify all relevant persons (as defined in Section 309A(1) of the SFA), that the shares and pre-funded warrants are “prescribed capital markets products” (as defined in the CMP Regulations 2018) and Excluded Investment Products (as defined in MAS Notice SFA 04-N12: Notice on the Sale of Investment Products and MAS Notice FAA-N16: Notice on Recommendations on Investment Products).

Israel. In the State of Israel this prospectus supplement shall not be regarded as an offer to the public to purchase common shares or pre-funded warrants under the Israeli Securities Law, 5728-1968, which requires a prospectus to be published and authorized by the Israel Securities Authority, if it complies with certain provisions of Section 15 of the Israeli Securities Law, 5728-1968, including, inter alia, if: (i) the offer is made, distributed or directed to not more than 35 investors, subject to certain conditions (the “Addressed Investors”); or (ii) the offer is made, distributed or directed to certain qualified investors defined in the First Addendum of the Israeli Securities Law, 5728-1968, subject to certain conditions (the “Qualified Investors”). The Qualified Investors shall not be taken into account in the count of the Addressed Investors and may be offered to purchase securities in addition to the 35 Addressed Investors. We have not and will not take any action that would require it to publish a prospectus in accordance with and subject to the Israeli Securities Law, 5728-1968. We have not and will not distribute this prospectus or make, distribute or direct an offer to subscribe for our common shares or pre-funded warrants to any person within the State of Israel, other than to Qualified Investors and up to 35 Addressed Investors.

Qualified Investors may have to submit written evidence that they meet the definitions set out in of the First Addendum to the Israeli Securities Law, 5728-1968. In particular, we may request, as a condition to be offered common shares or pre-funded warrants, that Qualified Investors will each represent, warrant and certify to us and/or to anyone acting on our behalf: (i) that it is an investor falling within one of the categories listed in the First Addendum to the Israeli Securities Law, 5728-1968; (ii) which of the categories listed in the First Addendum to the Israeli Securities Law, 5728-1968 regarding Qualified Investors is applicable to it; (iii) that it will abide by all provisions set forth in the Israeli Securities Law, 5728-1968 and the regulations promulgated thereunder in connection with the offer to be issued common shares or pre-funded warrants; (iv) that the common shares or pre-funded warrants that it will be issued are, subject to exemptions available under the Israeli Securities Law, 5728-1968: (a) for its own account; (b) for investment purposes only; and (c) not issued with a view to resale within the State of Israel, other than in accordance with the provisions of the Israeli Securities Law, 5728-1968; and (v) that it is willing to provide further evidence of its Qualified Investor status. Addressed Investors may have to submit written evidence in respect of their identity and may have to sign and submit a declaration containing, inter alia, the Addressed Investor’s name, address and passport number or Israeli identification number.

We have not authorized and do not authorize the making of any offer of securities through any financial intermediary on our behalf, other than offers made by the underwriters and their respective affiliates, with a view to the final placement of the securities as contemplated in this document. Accordingly, no purchaser of the shares or pre-funded warrants, other than the underwriters, is authorized to make any further offer of shares or pre-funded warrants on our behalf or on behalf of the underwriters.

LEGAL MATTERS

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. Certain legal matters in connection with this offering will be passed upon for the underwriters by Wilmer Cutler Pickering Hale and Dorr LLP, New York, New York, with respect to U.S. securities law.

EXPERTS

The consolidated financial statements incorporated in this prospectus supplement by reference to the [Annual Report on Form 10-K for the year ended December 31, 2022](#) (and as amended by the [Form 10-K/A, which was filed with the SEC on May 31, 2023](#)) 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 supplement and the related prospectus are part of a registration statement we filed with the SEC. This prospectus supplement and the related prospectus do 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 supplement and the related 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 supplement and the related prospectus or incorporated by reference herein or therein. 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 supplement or the related prospectus is accurate as of any date other than the dates on the front pages of this prospectus supplement and the related prospectus, respectively, regardless of the time of delivery of this prospectus supplement or any sale of the securities offered by this prospectus supplement and the related 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 supplement, and the inclusion of our website address in this prospectus supplement is an inactive textual reference only.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to "incorporate by reference" information into this prospectus supplement, 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 supplement is 001-38899. The documents incorporated by reference into this prospectus supplement 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, 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 31, 2023](#);
- Our Quarterly Report on Form 10-Q for the fiscal quarters ended March 31, 2023, June 30, 2023 and September 30, 2023, which were filed with the SEC on [May 11, 2023](#), [August 10, 2023](#) and [November 13, 2023](#), respectively;
- The information specifically incorporated by reference in our [Annual Report on Form 10-K for the year ended December 31, 2022](#), which was filed with the SEC on March 29, 2023, from our [Definitive Proxy Statement on Schedule 14A relating to our 2023 Annual Meeting of Shareholders](#), which was filed with the SEC on April 28, 2023;
- Our Current Reports on Form 8-K filed with the SEC on [March 27, 2023](#), [March 28, 2023](#), [March 31, 2023](#), [June 9, 2023](#), [October 24, 2023](#), [November 13, 2023 \(with respect to item 8.01\)](#), [December 26, 2023](#) and [February 26, 2024](#); and
- [The description of our 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 prospectus supplement and the related prospectus.

We also incorporate by reference into this prospectus supplement 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 after the date of this prospectus supplement 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.

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 45 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.

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.”

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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. 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
	directors, at an election of the class of directors of which he is a part.	
<i>Vacancies on the Board of Directors</i>	Under the DGCL, vacancies and newly created directorships may be filled by a majority of the directors then in office (even though less than a quorum) or by a sole remaining director unless (i) otherwise provided in the certificate of incorporation or bylaws of the corporation or (ii) the certificate of incorporation directs that a particular class of stock is to elect such director, in which case a majority of the other directors elected by such class, or a sole remaining director elected by such class, will fill such vacancy.	Under the 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.
<i>Board of Director Quorum and Vote Requirements</i>	Under the DGCL, a majority of the total number of directors shall constitute a quorum for the transaction of business unless the certificate of incorporation or bylaws require a greater number. The bylaws may lower the number required for a quorum to one-third the number of directors, but no less. Under the DGCL, the board of directors may take action by the majority vote of the directors present at a meeting at which a quorum is present unless the certificate of incorporation or bylaws require a greater vote.	Under the 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. Under the QBCA, a quorum of directors may exercise all the powers of the directors despite any vacancy on the board.
<i>Transactions with Directors and Officers</i>	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	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

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>	<p>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>	<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>

	Delaware	QBCA
	<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. 	
<i>Indemnification of Directors and Officers</i>	<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>

	Delaware	QBCA
	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.	before the anniversary date of the notice of meeting for the last annual shareholders' meeting. 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. 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. 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.
<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

	Delaware	QBCA
<i>Amendment of Bylaws</i>	<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>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>vote, that class or series is entitled to vote on the amendment whether or not it otherwise carries the right to vote.</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.



16,666,667 Common Shares

Pre-Funded Warrants to Purchase 3,333,333 Common Shares

PROSPECTUS SUPPLEMENT

Sole Book-Running Manager

Piper Sandler

Lead Manager

H.C. Wainwright & Co.

February 28, 2024
